UNIVERSIDADE DE LISBOA
FACULDADE DE MOTRICIDADE HUMANA

DEVELOPMENT OF A GLOBAL GAIT SYMMETRY SCORE USING BIOMECHANICAL PARAMETERS

Tese elaborada com vista à obtenção do Grau de Doutor em Motricidade Humana na Especialidade de Biomecânica

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Sílvia Arsénio Rodrigues Cabral
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2016

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Número do Cartão de Cidadão: 12637955

Título:

Development of a global gait symmetry score using biomechanical parameters

Orientadores:

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Ano de conclusão: 2016

Designação do ramo de conhecimento do Doutoramento:

Motricidade Humana na Especialidade de Biomecânica

Faculdade de Motricidade Humana – Universidade de Lisboa, 25/08/2016

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“The important thing is not to stop questioning.”

Albert Einstein

Dedication

To my cherished Father, who I will always remember,
my beloved Mother and my dear Husband

Acknowledgements

First and foremost, I would like to thank my supervisor, Professor António Veloso, for welcoming me into his laboratory and research group, and for believing in me and making me feel as a valuable part of the team since 2009. Throughout this journey, he has continuously supported my decisions, provided me with endless learning opportunities and introduced me to great colleagues and to highly recognized scientists in the biomechanics community, and for that I am ever grateful. He also presented me with various challenges that were essential to the development of new skills and enhancement of existing ones, therefore making me a more independent and confident researcher. I am truly grateful for his continuous support and encouragement throughout this journey.

I am also especially grateful to my co-supervisor, Dr W. Scott Selbie, for all his contribution, tremendous support and time devoted to helping me with this work. Despite his busy schedule, and the different time zones, he always found the time and resources to answer all my questions promptly and to sit down with me in person. I am truly grateful for his genuine interest in my work and his inspiring ideas, which made this thesis possible, and for providing me with the opportunity to visit him in Canada on various occasions to enrich my learning process. In this sense, I would like to extend my thanks to his lovely family for welcoming me into their home. During these visits, Scott introduced me to other researchers who, in addition to listening to me and providing me with feedback, also kindly shared their knowledge and ideas which further inspired me. In this regard, I am particularly thankful to Dr Niko Troje and Dr Stephen Scott, as well as their students, Séamas Weech and Tyler Cluff, and more importantly, to Dr. Kevin Deluzio and everyone in the Human Mobility Research Laboratory, at Queen's University. Kevin welcomed me into his laboratory, allowing me to collect data for the present thesis, and was essentially a source of good advice, learning and collaboration. I would like to thank all his present and past team members and students, in particular Amy Mourton, Renan Resende and Adam Clansey, for their collaboration, fruitful discussions, and above all their friendship. During my visits to Canada, I had the pleasure to work from Scott's offices and to meet part of his wonderful team (C-Motion), who made me feel welcome and who complemented my learning experience. I am particularly thankful to Shawn Leclaire and Marcus Brown for all their help and teaching moments, and to Thierry Chevalier for always being available to listen and teach me and for being a friend. In addition to the Canadian team, I am also particularly thankful to Tom Kepple for his collaboration and for being an extremely patient teacher throughout this journey.

I would also like to express my gratitude to all the members from the Neuromechanics Research Group for all their support and encouragement, their friendship, and for being willing to help and exchange their knowledge. In particular, I am genuinely grateful to Vera Moniz-Pereira, Rita Fernandes and Filomena Carnide. In addition to being great friends beyond my academic life, they are role models and very good colleagues who contributed significantly to my current knowledge and to both my professional and personal growth. Finally, I am forever grateful to Carlos Andrade for his valuable mathematical insights during the initial stages of development of the global indices proposed in this thesis.

At last but not least, I am deeply grateful to my closest friends and family, who complete my life, for their love, support and encouragement throughout this long journey. Namely, I would like to thank my beloved mother, Ana Cabral, my sisters, Rita Lopes and Patricia Cabral, their better halves, and my longtime best friends, Ana Marques and Marta Marques, for always being there and for providing me with enjoyable moments. Also I am most deeply grateful to my husband, Pedro Prates, for his everlasting patience, understanding and support throughout another stage in our lives.

Finally, I gratefully acknowledge the funding sources that made this work possible, explicitly the PhD grant supported by the Portuguese Foundation for Science and Technology (PhD Grant reference: SFRH/BD/69424/2010), and the congress travel grants awarded by the rectory of the Technical University of Lisbon and the International Society of Biomechanics.

Resumo

As implicações clínicas de um padrão de marcha assimétrico levaram ao crescente interesse na recuperação da simetria da marcha em populações clínicas. Isto requer uma avaliação precisa e fiável da simetria da marcha na sua globalidade. Dadas as limitações dos índices de simetria pré-existentes, o objectivo desta Tese foi desenvolver e testar um novo índice global de simetria da marcha que abrangesse informação dos membros inferiores, do tronco e da pélvis, ao longo do ciclo completo da marcha. Para alcançar este objectivo, foram realizados quatro estudos. No primeiro, este índice, desenvolvido com base nas diferenças bilaterais de ângulos articulares em 3D, foi testado através da comparação dos resultados obtidos por indivíduos saudáveis em três condições de marcha, nas quais diferentes níveis de assimetria foram induzidos artificialmente. Os segundo e terceiro estudos analisaram a concordância e fiabilidade inter-sessão deste e de outros índices globais, também num grupo saudável. Com base nos resultados obtidos, o primeiro índice foi aperfeiçoado, substituindo os ângulos inter-segmentares pelas posições lineares das articulações. O estudo final testou a capacidade deste novo índice detectar a presença de níveis de assimetria superiores num grupo de indivíduos, cujo padrão de marcha é expectavelmente assimétrico. Estes estudos mostraram que, enquanto os índices baseados em ângulos articulares conseguem detectar alterações agudas na simetria dentro da mesma sessão, a sua baixa repetibilidade entre sessões desaconselha a sua aplicação para avaliar diferenças na simetria ao longo do tempo e entre indivíduos. Por outro lado, o índice proposto nesta Tese apresenta uma boa concordância e fiabilidade inter-sessão, e é sensível ao nível de assimetria tipicamente encontrado em sujeitos com um padrão de marcha assimétrico.

Estas conclusões sugerem que este índice poderá ser uma ferramenta útil para a avaliação da simetria da marcha em contexto clínico.

Palavras-chave

Marcha, simetria, índices globais, teste-reteste, concordância, fiabilidade

Abstract

The clinical implications of an asymmetric gait pattern led to a growing interest in restoring gait symmetry in clinical populations. This entails the accurate and reliable assessment of overall gait symmetry. Given the limitations of pre-existing symmetry indices, the aim of this thesis was to develop and test a new global index for gait symmetry that comprised information from the lower limbs, trunk and pelvis, throughout the entire gait cycle. To achieve this goal, four studies were conducted. In the first study, a global symmetry index, based on the bilateral differences in 3D joint angles, was developed and tested by comparing the scores obtained by healthy individuals in three walking conditions, in which different levels of asymmetry were induced artificially. The second and third studies analysed the inter-session agreement and reliability of this and other global indices, also in a healthy group. Based on the obtained results, the first index was refined by replacing the joint angles with the joint linear positions. The final study tested the ability of this new index to detect the presence of higher levels of asymmetry in a group of patients with an expected asymmetric gait pattern. These studies showed that while symmetry indices based on joint angles can detect acute changes in symmetry within the same session, their poor inter-session repeatability prevents their application to assess differences in symmetry over time and among individuals. On the other hand, the final index proposed in this thesis has good inter-session agreement and reliability, and is sensitive to the increased level of asymmetry typically found in patients with an asymmetric gait pattern. These findings suggest that this index may be a useful tool to assess gait symmetry in a clinical context.

Keywords

Gait, symmetry, global indices, test-retest, agreement, reliability

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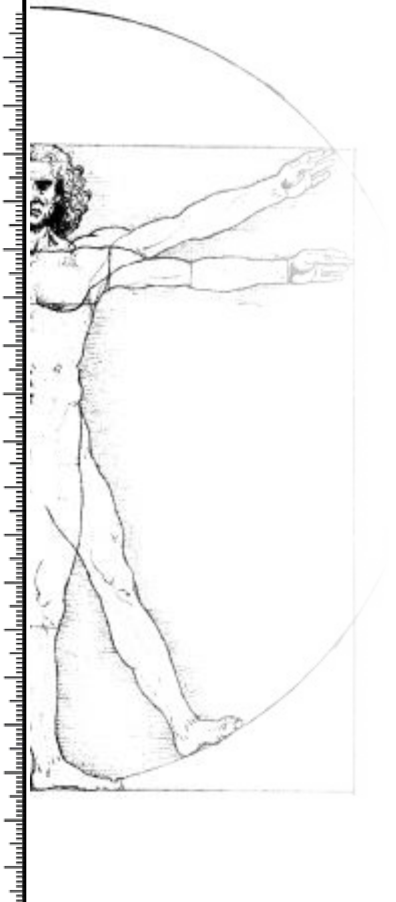
List of Abbreviations

95% LOA	95% limits of Agreement
ACL	Anterior cruciate ligament
AsymGPS	Symmetry index developed by Lundh et al (2014)
BMI	Body mass index
CAI	Comprehensive Asymmetry Index developed by Hoerzer et al (2015)
CAST	Calibrated anatomical system technique
CI	Confidence interval
GASI	Global Asymmetry Index developed by Hoerzer et al (2012)
GGA	Global gait asymmetry index developed in the first study of this thesis
GPS	Gait Profile Score developed by Baker et al (2009)
GRF	Ground reaction force
GVS	Gait variable score
ICC	Intraclass correlation coefficient
IQR	Interquartile range
KOA	Knee osteoarthritis
KOPS	Knee Osteoarthritis Pre-Screening questionnaire
LGGA	Linear global gait asymmetry index developed in the third study of this thesis
LLD	Leg length discrepancy
MDC	Minimal detectable change
OA	Osteoarthritis
PCA	Principal components analysis
RMSE	Root mean square error
SA	Symmetry Angle developed by Zifchock et al (2008)
SD	Standard deviation of the mean
SEM	Standard error of measurement
SI	Symmetry Index developed by Robinson et al (1987)

General Introduction



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Background

Gait symmetry, defined as the identical behaviour of both limbs (Sadeghi, Allard, Prince, & Labelle, 2000) during the gait cycle, has been increasingly reported in the literature because of its clinical importance (Patterson, Gage, Brooks, Black, & McIlroy, 2010). Deviations from symmetry are typically thought to be associated with pathology as augmented levels of gait asymmetry have been found in various clinical conditions, such as stroke (Allen, Kautz, & Neptune, 2011), lower limb amputations (Devan, Carman, Hendrick, Hale, & Ribeiro, 2015), osteoarthritis (C. Mills, Pain, & Yeadon, 2008) and arthroplasties (Tsai et al., 2015), as well as anterior cruciate ligament (ACL) injury (Winiarski & Czamara, 2012). Researchers have suggested that these patients develop an asymmetrical gait pattern to either protect and reduce pain on the affected side (i.e. the prosthetic limb (Nolan et al., 2003), the osteoarthritic joint (Christiansen & Stevens-Lapsley, 2010; Turcot, Sagawa, Hoffmeyer, Suvà, & Armand, 2015)) or compensate for an underlying impairment (i.e. impaired or loss of lower limb musculature (Allen et al., 2011; Devan et al., 2015)). Moreover, gait symmetry may be associated with efficiency and balance control (Patterson et al., 2008). Hence, it is one of the most widely used informal measures to assess the recovery of functional gait (Archer, Castillo, MacKenzie, & Bosse, 2006).

While it is often perceived as a consequence of pathology, gait asymmetry is also believed to have future repercussions. For example, the recovery of full symmetrical knee range of motion following ACL reconstructive surgery has been identified as the most important factor for the assurance of the best long-term successful surgery result and patient satisfaction (Shelbourne & Klotz, 2006). Furthermore, the increased reliance on the non-impaired limb has been suggested to predispose unilateral amputees and osteoarthritis patients to the development of musculoskeletal disorders such as low back pain and osteoarthritis on the contralateral limb (Briem & Snyder-Mackler, 2009; Devan et al., 2015; Nolan et al., 2003; White & Lifeso, 2005). Although longitudinal studies have yet to confirm these causal relationships, research has shown that unilateral amputees have greater amounts of joint degeneration and pain in their intact limb and lower back (in comparison to their residual limb and to healthy counterparts) (Nolan et al., 2003), and that osteoarthritis patients who underwent a second total joint replacement surgery (after a single unilateral joint replacement surgery) often replace the joints on the contralateral side (Shakoor, Block, Shott, & Case, 2002). Moreover, gait asymmetry may also be associated with the loss of bone mass density in the paretic lower limb of stroke survivors (Jorgensen, Crabtree, Reeve, & Jacobsen, 2000).

Considering the potential clinical implications of gait asymmetry, there has been a growing interest in restoring gait symmetry in clinical populations through gait retraining. For example, repeated split-treadmill training has been used to improve step length symmetry in stroke survivors (Reisman, McLean, Keller, Danks, & Bastian, 2013). In this study, seven out of twelve patients showed significant improvements in step length symmetry, not only after the four week training period, but also at one and three months follow up. This improvement exceeded the difference between the two baseline sessions (one week apart) prior to training, and was accompanied with an improvement in perceived exertion, but not in gait speed. Improvements in spatiotemporal symmetry in this population were also observed after a gait retraining program using real-time visual and proprioceptive feedback (Lewek, Feasel, Wentz, Brooks, & Whitton, 2012). In this case series, the improvements in symmetry were accompanied with small improvements in functionality and in comfortable gait speed. However, both participants were prescribed home based therapeutic exercises, which may be a confounding variable, despite the low compliance with these exercises. Furthermore, augmented feedback has also been used to improve spatiotemporal and/or loading symmetry in patients after transtibial amputation (Dingwell, Davis, & Frazier, 1996) and total hip arthroplasty (White & Lifeso, 2005). In the latter, patients who received visual feedback during an eight week program showed significant improvements in impulse symmetry in comparison to the control group and the group who walked without feedback, as well as an improvement in perceived exertion and in the Harris hip score. The previously mentioned studies show that the existing literature in interventions for the improvement of gait symmetry is scarce and presents several limitations. But considering these promising results and the vast use and success of augmented feedback in rehabilitation (Agresta & Brown, 2015; Shull, Jirattigalachote, Hunt, Cutkosky, & Delp, 2014; Stanton, Ada, Dean, & Preston, 2011), further research is needed to evaluate the efficacy and effectiveness of gait retraining with augmented feedback to restore gait symmetry in clinical populations. The predicament is that the current knowledge about gait symmetry and its measurement is still limited. To begin with, there is an ongoing debate as to whether unimpaired individuals walk symmetrically or not (Sadeghi et al., 2000). Historically, healthy gait was assumed to be symmetrical in order to simplify data collection and analysis (Sadeghi et al., 2000). But while some studies supported this assumption, others found bilateral differences in various gait parameters, suggesting that non-impaired individuals walk asymmetrically. For example, Herzog et al (1989) reported asymmetries in ground reaction force (GRF) during gait, contrasting with

Burnet et al (2011), who found GRF to be symmetrical. Similarly, Teichtahl et al (2009) found joint moments to be symmetric, while Lathrop-Lambach et al (2013) found asymmetries in joint moments. Additionally, Creaby et al (2012) reported symmetry in joint angles, whereas Forczek and Staszkiewiez (2012) found joint angles to be asymmetric (For more citations see Sadeghi et al (2000) and Seeley (2006)). To some extent, the presence of gait asymmetry in healthy individuals is conceivable when taking into account limb dominance (Sadeghi et al., 2000), differences in contralateral limb lengths (Ankaralı et al., 2015; Auerbach & Ruff, 2006) as well as intra-limb variability resulting from the coordination of a large number of degrees of freedom (Błażkiewicz, Wiszomirska, & Wit, 2014). Nonetheless, this asymmetry should not be considered pathological, as it may be related to compensations for subtle imbalances or to control and propulsion strategies (Sadeghi et al., 2000). Further, the level of asymmetry in healthy individuals is expected to be smaller than in clinical populations. However, due to their controversial results, the existing studies do not provide a solid understanding about the existence and role of asymmetry in healthy gait or about when it may become problematic. This knowledge is important and necessary to investigate the potential of gait retraining programs with augmented feedback to restore gait symmetry.

Seeley (2006) proposed that these contradictory results could be explained by three main factors. The first factor is related to variations in the definition used for gait symmetry. Some studies defined symmetry as the identical behaviour of both limbs, and as such most of these found asymmetries. Others defined symmetry as the lack of statistical differences between bilateral parameters, and therefore often found gait to be symmetrical. The second factor was related to the different statistical analyses that were used. Depending on whether correlations, t-tests or analyses of variance were performed, gait could either be considered symmetrical or asymmetrical. Additionally, by using statistical methods to compare bilateral parameters, the results highly depended on sample size and variability. Furthermore, the statistical methods required that mean data was pooled from several subjects, which could contribute to masking individual asymmetries. These two factors apply to studies that use statistical analyses to assess gait symmetry. However, we can speculate that the use of different symmetry indices in the aforementioned studies (Burnett et al., 2011; Creaby et al., 2012; Forczek & Staszkiewicz, 2012; Herzog et al., 1989; Lathrop-Lambach et al., 2013; Teichtahl et al., 2009), may also have contributed to the contradictory results found in the literature. The last factor that was proposed to explain the conflicting results was the variation in the biomechanical parameter used to assess symmetry, as some parameters may be more sensitive to asymmetries than others. This point was also highlighted by Patterson et al

(2010), who found no significant differences in double support time symmetry (in contrast to other spatiotemporal parameters) between stroke patients and healthy individuals. Overall, this shows that our knowledge about gait symmetry is being compromised by the different methodologies that have been used, which suggests that, in order to enhance our understanding of gait symmetry and the effect of interventions, there is a need to standardise the methods used to assess it. It is possible that more than one standardised method is needed depending on its application, as there is no one method that fits all purposes. Methods that provide detailed information on the direction and location of asymmetry as well as when it is present in the gait cycle may be more appropriate to enhance our understanding of the mechanisms and causes of gait asymmetry, and therefore to tailor the rehabilitation to the individual patient deficits (Patterson et al., 2010). Conversely, these methods may be too complex to judge the success of interventions, because a vast amount of data is produced, and it is difficult to draw an overall conclusion (Hoerzer et al., 2012) when some of the data suggests an improvement and some suggests the opposite.

One of the applications for symmetry measures is to provide real time feedback in gait retraining programs. Because the feedback on gait symmetry is being provided to the patients while he/she walks on a treadmill, the chosen symmetry measure must be calculated on an individual basis and presented in real time. The latter not only means that it must be computed using online processing, but also that all the contained information must be captured by the patient in a short period of time. More importantly, as any other outcome measure used for meaningful clinical decision-making and for the evaluation of clinical change over time, the symmetry measure must be valid and repeatable (de Vet, Terwee, Knol, & Bouter, 2006). Validity concerns the extent to which an instrument's score is able to measure what it is intended to measure (Portney & Watkins, 2009). Repeatability is concerned with the variation between measurements made on the same subject under identical conditions (Bartlett & Frost, 2008). The repeatability of an instrument's score is quantified in terms of agreement (i.e. how close the repeated scores are) and reliability (i.e. how well subjects can be distinguished) (Bartlett & Frost, 2008; de Vet et al., 2006), which depend highly on the measurement error. In the context of gait retraining with symmetry feedback, it is essential that symmetry measure provides a comprehensive representation of the patient's bilateral symmetry and that its measurement error is small and well known, so that important information is not concealed and small deviations between sessions are not over-interpreted (Schwartz, Trost, & Wervey, 2004). Assuming that the method used to assess symmetry accurately reflects the difference between bilateral biomechanical parameters, one can speculate that its measurement error is affected by that of the underlying biomechanical parameters. For example, the repeatability of a symmetry score that is calculated based on joint kinematics can be affect by marker placement inconsistencies, data processing or measurement equipment errors (McGinley, Baker, Wolfe, & Morris, 2009).

Symmetry measures can be categorized in a simplistic way into statistical analysis and indices, the latter consisting in difference or ratio equations (Sadeghi et al., 2000). Additionally, different biomechanical parameters can be use as inputs, either in isolation or in combination. The following sections will present most of the existing symmetry measures along with their limitations and suitability as augmented feedback, as well as their known psychometric properties.

Current symmetry measures

Some authors have analysed gait symmetry by looking for statistical differences between bilateral parameters. For example, Briem and Snyder-Mackler (2009) reported asymmetries in patients with medial knee osteoarthritis by comparing the knee kinematics and kinetics of both limbs using paired samples t-tests. Mills et al (2013), used a mixed-model analysis of variance to compare the symmetry in kinematic and spatiotemporal variables between healthy individuals and patients with unilateral or bilateral knee osteoarthritis. Sadeghi (2003) investigated the existence of local asymmetries in the face of global symmetry in healthy individuals using Principal Components Analysis (PCA). Rather than quantifying gait symmetry, these methods simply confirm or deny its existence on a group basis. These methods cannot measure symmetry on an individual basis, and are therefore not appropriate metrics for augmented feedback.

Contrastingly, there are several measures of symmetry that can be calculated individually, the most commonly used being the Symmetry Index (SI) (Robinson, Herzog, & Nigg, 1987) and the symmetry ratio. The symmetry ratio is simply the ratio between the variable obtained on the right side and the corresponding variable obtained on the left side. Alternatively, the ratio can be calculated between the dominant and non-dominant side or between the affected and non-affected side (Patterson et al., 2008), depending on the context. The strength of this index is that it is easy to compute and to interpret (Patterson et al., 2010). A ratio of 1 indicates perfect symmetry while ratios above or below 1 indicates, respectively, that the value on the numerator or denominator is higher. More specifically, a ratio of 0.5 or 2 indicates that the value on one side is twice as high as the corresponding value on the other side. The SI (Robinson et al., 1987) is the percent difference between the variables on each side, in relation to the mean value from both sides. Here 0% indicates perfect symmetry and greater absolute percentages indicate increasing asymmetry (with the sign indicating the direction of asymmetry). For example, a value of 50% indicates that the difference between the two sides is as high as half the mean value obtained from both sides. This mean value, used as reference, can also be replaced by the value on the uninjured side, or the maximum value on either side (Vagenas & Hoshizaki, 1992). However, this choice of a reference value has been identified as a limitation of this score, as it is not always an obvious choice, and using different reference values for the same data yields different results and makes the comparison of results from different studies and samples difficult (Zifchock, Davis, Higginson, & Royer, 2008). Additionally, in the presence of large asymmetries, the mean value of both sides does not reflect the performance of either limb and may mask the asymmetry, by lowering the score (Zifchock et al., 2008). Another limitation of the SI is its potential to artificially inflate the asymmetry level (Herzog et al., 1989). This inflation can occur when the reference value is small (i.e. maximum knee extension angle during stance that nears 0º) in comparison to the bilateral difference, which may not even be clinically relevant. Conversely, differences that are small in comparison to the reference value (i.e. peak vertical ground reaction force which nears 700N) tend to lower the final score, thus falsely reflecting symmetry (Herzog et al., 1989). The symmetry ratio can also artificially inflate the level of asymmetry when the values are small (Lauzière, Betschart, Aissaoui, & Nadeau, 2014). For example, considering the following hypothetical values for the left and right sides: 2º and 4º of maximum knee extension angle during stance, and 63º and 65º of maximum knee flexion during swing. Based on the symmetry ratios of these variables (0.50 and 0.97 respectively), this patient would be considered symmetric during swing but highly asymmetric during stance. To overcome these limitations, the Symmetry Angle (SA) was developed (Zifchock et al., 2008). This index quantifies symmetry by calculating the deviation (in degrees) from a line of perfect symmetry, which is obtained when the left and right side values are equal. However, once again variations in small values produce greater deviations from the line of perfect symmetry than variations in larger values, which means that this index is also limited by its potential for artificial inflation. In addition to these limitations, all the aforementioned indices calculate symmetry based on discrete values, or in other words, single values extracted from the gait curve at one specific point in time (i.e. peak GRF). These indices therefore neglect the information contained in the remainder of the gait cycle. Consequently, asymmetries that occur at a different phase of the gait cycle may be missed, as well as asymmetries due to temporal shifts of peak values with similar magnitudes (Nigg, Vienneau, Maurer, &

Nigg, 2013). Furthermore, these indices cannot assess symmetry at a global level. Often, spatiotemporal parameters are used, which fail to capture the complex angular displacements of the lower limbs. Additionally, when joint angles are used instead, each joint and each of its components is assessed in isolation (Hsiao-Wecksler, Polk, Rosengren, Sosnoff, & Hong, 2010). These indices are simple enough to be calculated and presented to a single patient in real time. However, the aforementioned limitations may deteriorate the validity of these symmetry indices, which means the patient could be provided with fallacious feedback. To assess gait symmetry accurately, the behaviour of the entire limb should be considered (Sadeghi et al., 2000). Further, this information should be gathered throughout the gait cycle, suggesting the need for more complex methods (Hsiao-Wecksler et al., 2010).

Crenshaw and Richards (2006) developed four distinct measures to capture gait symmetry using the entire gait waveforms: trend symmetry, phase shift, range offset and range amplitude ratio. Trend symmetry provides a general measure of symmetry between a bilateral joint angle by calculating the ratio between the variability about and along their eigenvector. Phase shift represents the temporal shift between the bilateral joint angles and is calculated by shifting one waveform in relation to the other and finding the temporal shift required to achieve the smallest trend symmetry. Finally, the range offset and range amplitude ratio provide information on symmetry based on the magnitude offset between sides. Another interesting method is the Symmetry Regions of Deviation analysis proposed by Shorter et al (2008). This method simply calculates the difference between an individual's bilateral joint angles, at each point of the gait cycle, and plots it in relation to the same difference obtained from a reference healthy database. Later on, DiBerardino et al (2010) proposed a method that allows the assessment of symmetry based on the phase-portraits of lower limb-segments (plot of each segment's angular position as a function of its angular velocity). This method yields three scores for each segment: one for complexity, based on the number of harmonics needed to describe the shape of the phase portrait, and two for variability, based on the area and the length of the path generated by the phase-portrait centroid during multiple cycles. The symmetry itself can be assessed by comparing the three scores obtained for a segment on one side to those obtained on the contralateral segment. Similarly, Haddad et al (2010) also assessed symmetry based on the position-velocity phase planes of the lower limb segments. However, in this case symmetry was calculated as the difference between the phase angles (derived from the plots) on one side and those on the contralateral side (Continuous relative phase analysis). Finally, Helwig et al (2010) proposed a method to assess symmetry by using Parallel Factor Analysis to compare the sagittal plane joint displacement (vertical displacement of a joint centre plotted against its anterior-posterior displacement) on both sides. Although all of these methods provide information about symmetry on various joints throughout the gait cycle (with those developed by Shorter et al (2008), Haddad et al (2010), and Helwig et al (2010) specifying where in the gait cycle it is more pronounced), several metrics (more than one per joint in some cases) are required to describe overall gait symmetry. This characteristic deems these methods inappropriate to use in gait retraining programs using real-time feedback on gait symmetry, because presenting several metrics could be overwhelming for the patient (Wulf & Shea, 2002), and (in the alternative of choosing only one) the improvement of a single metric may not necessarily reflect an improvement in overall gait symmetry.

Conversely, global symmetry indices have been developed recently. Similarly to gait indices, these measures have the ability to summarise information from continuous kinematic and/or kinetic gait waveforms from various joints into a single numerical score. Hoerzer et al (2012) developed a global symmetry index called GASI (Global Asymmetry Index), which quantifies symmetry using PCA. To compute GASI, the three components of the GRF, as well as the three components of the hip, knee and ankle joint angles, angular velocities and joint moments are obtained for each side and normalized in magnitude (to the corresponding peak values) and in time (to the stance phase). These waveforms are appended in series to create two row vectors, one for each side, which are then subtracted creating a single difference vector. The difference vectors from several subjects form the rows of the matrix used to calculate the principal components (PC's). Finally, the GASI of each subject is the root sum square of the first ten PC's of that subject. Later on, Hoerzer et al (2015) changed this index to CAI (Comprehensive asymmetry index), the difference being in the normalization and in the number of PC's used to calculate the index (in CAI the biomechanical variables are normalised to the corresponding average standard deviation, instead of the peak value, and eight PC's, not ten, are used for the final score). In both indices, a value close to zero would indicate that the level of symmetry of an individual is identical to the mean level of symmetry of that particular group of subjects (supposedly symmetric). Conversely, the GASI increases as the level of symmetry deviates from the mean (allegedly becoming more asymmetric). However, considering that healthy individuals are relatively but not perfectly symmetrical, one individual could be more symmetrical than the mean and still present an elevated GASI, thus falsely representing asymmetry. Furthermore, although the normalisation is needed to combine variables with different physical units, normalising the variables to either the peak values or the standard deviation could become problematic, as it could possibly mask asymmetry in variables with a large amplitude or with a high standard deviation, and inflate symmetry in the opposite variables. Besides these limitations, more information is needed as to how the GASI of a single individual could be calculated in a clinical context.

Nigg et al (2013) proposed a simpler method to quantify gait symmetry. This global index is the integral of the absolute differences (between sides) in various biomechanical variables (ankle joint angle and velocity in the sagittal and frontal planes, knee joint angle and velocity in the sagittal plane, hip joint angle and velocity in all three planes, and the vertical and anterior/posterior components of the ground reaction force), throughout the stance phase. Once more, because this index combines variables with different physical units, these differences are normalised to the corresponding average range, which again may mask or artificially inflate the level of symmetry. Furthermore, similarly to GASI, this index does not include the swing phase, therefore neglecting toe clearance and the preparation for heel strike.

Finally, Lundh et al (2014) also proposed a global symmetry index (more specifically, one for the lower limbs and one for the upper limbs). Based on the Gait Profile Score (a gait index developed by Baker et al (2009)), the proposed index computes the level of symmetry as the root mean square difference between the bilateral joint angles throughout the entire gait cycle. In particular, the index developed for the lower limb, which is called AsymGPS, includes all three components of the absolute pelvis angle and the hip joint angle, the sagittal component of the knee and ankle joint angles and the foot progression angle. As such, the AsymGPS, as well as the index developed by Nigg et al (2013), neglect certain kinematics in the frontal and transverse plane that can be valuable in the clinical context.

As summary measures, these global indices seem perfect to provide real-time feedback on gait symmetry. Although no studies have been conducted to test if participants can learn from a global symmetry measure, Michalak et al (2015) showed that subjects can change their gait pattern based on real-time feedback of a single global score, without being conscious of what it measured or which strategies they had to use to change it. This acquisition of skills without explicit knowledge about the performance is known as implicit learning (Maxwell, Masters, & Eves, 2000). Implicit learning processes have several advantages over explicit learning, as they are more resistant to the effects of psychological stress, disorders and dysfunctions, more durable and relatively independent of age and IQ (Maxwell et al., 2000). In addition, previous research has shown that the learning and retention of a complex motor skill is enhanced with external feedback related to the result of an individual’s actions rather than to the specific movements (Wulf & Shea, 2002). Based on these premises, global measures of symmetry seem to be perfect candidates for gait retraining with real-time feedback. However, given their potential to mask or artificially inflate gait asymmetry and to neglect important aspects of motion, the previously mentioned global symmetry indices may provide the wrong feedback to the patient and yield erroneous conclusions with regards to the patient's progress throughout the gait retraining program. Therefore, the need to develop a new global index that overcomes these limitations is justified.

Validity and repeatability of symmetry indices

Very little is known about these psychometric properties of symmetry indices. To the best of our knowledge only two studies have addressed some aspects of validity in symmetry indices. The first was the one published by Patterson et al (2010), who compared the scores and the discriminative ability of four symmetry indices (the SI, the symmetry ratio, one of its variations (Plotnik, Giladi, & Hausdorff, 2007) and the SA) in a group of healthy individuals and a group of stroke patients. These authors highlighted the importance of the mathematical equation as well as the biomechanical parameter used in the symmetry index, and therefore the various symmetry indices were compared using a variety of spatiotemporal parameters (step length, swing time, stance time, double support time, and the ratio between stance and swing time). This study showed that within each of the spatiotemporal parameters the different symmetry indices were highly correlated, but that within the same index (symmetry ratio) the correlations varied. Specifically, the double support time ratio was not correlated with any other spatiotemporal ratios, and the step length ratio was only poorly correlated. Furthermore, for most spatiotemporal parameters, the different indices had similar distributions and discriminative ability (identifying up to 60% of the patients as asymmetric), and were significantly different between groups. Conversely, when symmetry was calculated based on double support time (independently of the symmetry index used) the discriminative ability was much lower (~9%) and no differences were found between the groups. These results suggest that (excluding double support time) all these indices provide similar interpretations in terms of symmetry, showing that stroke patients are significantly more asymmetric than healthy individuals. Furthermore, this study shows that all indices have a similar, but only moderate discriminative ability for these patients. Finally, this study also supports the notion that the level of symmetry may differ, depending on the biomechanical parameter that is analysed. The second study was conducted by Błażkiewicz et al (2014), who also compared the scores and the discriminative ability of the same symmetry indices using a different selection of spatiotemporal parameters, but only in a group of healthy individuals. Although their methodology and results were not very clear, they also concluded that the scores obtained with the four indices were highly correlated and similarly distributed and that the four indices had a similar discriminative ability. Contrarily to the previous findings though, the discriminative ability was much higher (according to a Receiver Operating Characteristic Curve analysis, sensitivity, specificity and diagnostic precision were >0.90). However, these results should be interpreted with caution because, despite recognising that the symmetry ratio has several limitations (i.e. low sensitivity), the authors chose to use it as reference.

Despite their limitations, these studies only provide partial validation of these symmetry scores. Furthermore, as discussed in the previous session, these indices neglect the complex intersegmental motion throughout the gait cycle. Therefore, even if they are valid measures of spatiotemporal symmetry, they do not provide a comprehensive assessment of overall gait symmetry. This is demonstrated by Roerdink et al (2012), who found that the step length asymmetry of amputees (using a variation of the SI) varied inconsistently across participants and that in some of them the score suggested symmetry, even though their overall gait was asymmetric.

In terms of repeatability, only two studies have been done. Lewek and Randall (2011) analysed the repeatability of stance time, swing time and step length symmetry ratios in stroke patients, reporting inter-session intraclass correlation coefficient (ICC) values between 0.925 and 0.976, and minimal detectable change (MDC) percentages between 8% and 18%. These results suggest that the symmetry ratio is a reliable tool to measure spatiotemporal symmetry in stroke survivors. However, caution is advised when considering this interpretation, as the methods used to calculate the standard error of measurement (SEM) and ICC values are questionable. Conversely, Senden et al (2009) found that one of the variations of the SI presented very poor inter-session reliability in healthy individuals, with ICC values between 0.010 and 0.351. In this study, the authors failed to mention the measurement error and the ICC model used, which are essential to interpret the obtained results.

Once again, besides these limitations, these studies focused on indices that fail to capture the global aspect of gait symmetry. Further, to our best knowledge, no studies have been done to assess the validity and repeatability of global symmetry measures.

Aims and outline of the thesis

As discussed throughout this chapter, there are several methods available to assess gait symmetry. The limitations of some of these methods and the lack of standardised methods is limiting our ability to better understand the presence of asymmetry in healthy and pathological gait and the potential of interventions in restoring gait symmetry. In order to assess the efficacy of gait retraining programs using gait symmetry as augmented feedback, the chosen symmetry index must be valid and repeatable, and must be calculated and presented in real time. Considering the limitations of the existing symmetry measures and the lack of knowledge regarding their psychometric properties, the general aims of this thesis were to develop and test a new global index of gait symmetry. The specific aims of this thesis were:

- To develop a global gait symmetry index, using kinematic data from the lower limbs and trunk throughout the entire gait cycle
- To test the ability of the new index to measure gait symmetry, either by (1) artificially manipulating the level of symmetry in healthy individuals or (2) by comparing the symmetry scores of healthy individuals to those of individuals with knee osteoarthritis (KOA), whose asymmetry is expectedly higher
- To assess the inter-session agreement and reliability of the new index in a group of healthy individuals

To achieve these goals four studies were conducted. The first study (Chapter 2) aimed (1) to develop the global index based on the bilateral differences in joint angles (Global gait asymmetry index - GGA) and (2) to test it by artificially inducing gait asymmetry and checking if the index changed accordingly. In this study, participants walked at their comfortable speed on an instrumented treadmill, in three walking conditions: one symmetric and two asymmetric. In all conditions, participants wore custom made sandals, which differed bilaterally in the asymmetric conditions. The 3D trajectories of passive markers placed on the participants' skin were collected using an opto-electronic motion capture system. The markers were placed based on the calibrated anatomical system technique (CAST) (Cappozzo, Catani, Croce, & Leardini, 1995), and used to build a model with eight segments (trunk, pelvis, thighs, shanks and feet), using segment optimisation pose estimation. The following joint angles were resolved in the joint coordinate system (Grood & Suntay, 1983): ankle, knee and hip joint angles with respect to the proximal segment, trunk with respect to the pelvis, and pelvis absolute angle with respect to the laboratory coordinate system. To calculate the GGA, each component of each of these angles was time normalized to the gait cycle (fifteen signals per side in total). The bilateral difference between each of these signals, through the gait cycle, was computed as the magnitude of a difference vector with 101 components (one for each percent of the time normalised gait cycle). Specifically, the squared differences between the bilateral angles computed at each point were summed and the square root was taken. The final GGA score was the sum of the fifteen difference vectors. The final scores obtained in each of the three walking conditions were compared using a One-Way repeated measures ANOVA.

The aim of the second study (Chapter 3) was to assess the repeatability of the GGA using a prospective test-retest design. Participants underwent two three-dimensional gait analyses, spaced approximately by a week. In each session, the participants walked overground at their comfortable speed. Although the marker trajectory data was extracted from a previously published study (Fernandes, Armada-da-Silva, Pool-Goudzwaard, Moniz-Pereira, & Veloso, 2016), the data collection system, marker placement, modelling and data processing were the same. With the GGA scores computed in both sessions, the inter-session repeatability was analysed using the 95% limits of agreement (95% LOA), the SEM, the MDC and the ICC.

Based on the results obtained in Chapter 3, the following study (Chapter 4) was performed to understand how different characteristics of the global index could affect its repeatability. Hence, the aim of the third study was to compare the repeatability of three global indices of gait symmetry: (2) the index developed in Chapter 2 (GGA), (2) a modification of the latter, in which joint angles were replaced by the linear positions of the segments' distal extremities (Linear global gait asymmetry index - LGGA), and (3) a previously published index (AsymGPS) (Lundh et al., 2014), also based in the difference between bilateral joint angles, but that does not include the least reliable components. The processed data from the previous study was used. Additionally, the same repeatability parameters were calculated for each of the three indices and compared.

Again, based on the previous study, the final study was conducted to test the ability of the LGGA (modification of the GGA) to capture differences in gait symmetry. According to the literature, patients with knee osteoarthritis walk asymmetrically. Thus, the aim of the last study (Chapter 5) was to analyse whether the LGGA was higher in patients with knee osteoarthritis in comparison to healthy individuals. Once more, the motion capture data was extracted from previously published studies (Fernandes et al., 2016; Yázigi et al., 2013). Participants walked overground at their comfortable speed. All data was collected and processed as in the repeatability studies. The symmetry scores obtained in the healthy and pathological groups were compared using a Mann-Whitney U test.

Finally, the main findings of each study are summarised and discussed in Chapter 6, along with their inherent methodological considerations. This thesis constitutes only the initial steps required for the application of the global gait asymmetry index in the clinical context. Therefore, recommendations for potential future research are provided.

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A Global Gait Asymmetry Index

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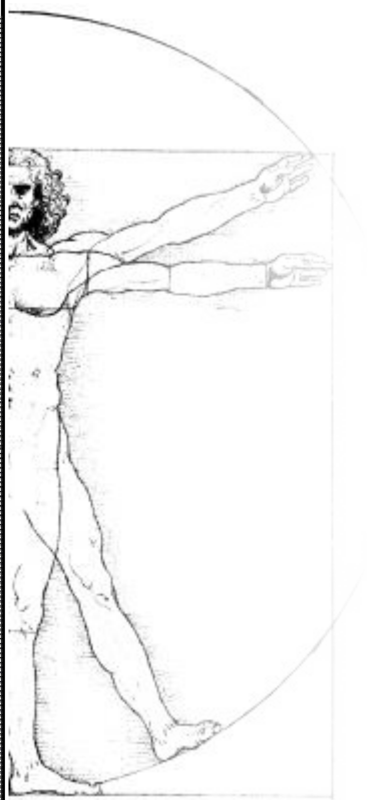
Based on:
J. Appl. Biomech. 32 (2016) 171–177



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Abstract

High levels of gait asymmetry are associated with many pathologies. Our long term goal is to improve gait symmetry through real-time biofeedback of a symmetry index. Symmetry is often reported as a single metric or a collective signature of multiple discrete measures. While this is useful for assessment, incorporating multiple feedback metrics presents too much information for most subjects to use as visual feedback for gait retraining. The aim of this article was to develop a global gait asymmetry (GGA) score that could be used as a biofeedback metric for gait retraining and to test the effectiveness of the GGA for classifying artificially induced asymmetry.

Eighteen participants (11 males; age 26.9 years (SD=7.7); height 1.8 m (SD=0.1) and body mass 72.7 Kg (SD=8.9)) walked on a treadmill in three symmetry conditions, induced by wearing custom made sandals: a symmetric condition (identical sandals) and two asymmetric conditions (different sandals). The GGA score was calculated, based on several joint angles, and compared between conditions. Significant differences were found among all conditions ($P<.001$), meaning that the GGA score is sensitive to different levels of asymmetry, and may be useful for rehabilitation and assessment.

Keywords

Symmetry, Gait, Joint Angles

1. Introduction

Cyclic activities such as walking and running are considered to be naturally symmetrical and gait asymmetry is often interpreted as pathological and considered an important clinical issue to be addressed (Sadeghi, Allard, Prince, & Labelle, 2000). While acknowledging that movement symmetry may not be the main goal for all pathological conditions, there are many circumstances in which symmetry is an important clinical target, particularly chronic orthopedic conditions, such as knee (Creaby, Bennell, & Hunt, 2012; Mills, Hettinga, Pohl, & Ferber, 2013) and hip osteoarthritis (Shakoor et al., 2011), ACL reconstructive surgery (Shelbourne & Klotz, 2006) and scoliosis (Kramers-de Quervain, Müller, Stacoff, Grob, & Stüssi, 2004). Inappropriate compensatory strategies caused by an impairment or as a result of interventions (such as joint bracing or surgery), may lead to the development of other pathologies (Mündermann, Dyrby, & Andriacchi, 2005; Toriyama et al., 2011). Asymmetric compensations by knee osteoarthritis patients are believed to have long-term consequences to the health of the contralateral-limb and may lead to the development of multiarticular osteoarthritis (Briem & Snyder-Mackler, 2009; Mills et al., 2013). The feasibility and efficacy of incorporating symmetry training into the rehabilitation of total joint replacement patients has been reported (White & Lifeso, 2005; Zeni, Abujaber, Flowers, Pozzi, & Snyder-Mackler, 2013). For many unilateral surgical procedures, such as reconstruction of lower limb ligaments or joint replacements, increasing symmetry during gait is desirable (Shelbourne & Klotz, 2006; White & Lifeso, 2005). The importance of achieving full symmetrical knee range of motion, both pre and post ACL reconstructive surgery, has been highlighted as it is considered to be the most important factor for ensuring the best long-term successful surgery result and patient satisfaction (Shelbourne & Klotz, 2006). Thus, while it may not be clear whether the presence of asymmetry is a risk factor or a consequence of pathology, or both, many patients frequently undergo training and rehabilitation programs to restore symmetry.

Our long term goal is to improve the clinician's ability to restore gait symmetry through gait retraining using real-time biofeedback. A prerequisite for restoring symmetry is the use of gait symmetry scores that are precisely defined and relevant to the context of the assessment and the therapy. Previous studies using biofeedback for gait symmetry use discrete local metrics, such as stance time asymmetry (Dingwell, Davis, & Frazier, 1996) or peak vertical ground reaction force asymmetry (White & Lifeso, 2005). A typical symmetry measure is the percent difference of a metric between two sides such as the Symmetry Index (SI) (Robinson, Herzog, & Nigg, 1987):

$$SI = \frac{X_R - X_L}{1/2(X_R + X_L)} \, . 100\%$$

, where X_R is a metric from the right side and X_L is an homologous metric from the left side.

Using the SI, McCrory and colleagues (McCrory, White, & Lifeso, 2001) found that a group of pain free individuals with a history of hip replacement were more asymmetrical with regards to a selection of discrete loading parameters than a group of healthy controls. Furthermore, the SI was also shown to be able to distinguish stroke patients from healthy individuals (Patterson, Gage, Brooks, Black, & McIlroy, 2010).

A limitation of the SI is the potential for artificial inflation (Herzog, Nigg, Read, & Olsson, 1989). This inflation can occur when clinically irrelevant differences between sides are divided by a much smaller reference value (Zifchock, Davis, Higginson, & Royer, 2008). For example, assuming that 0º is considered full knee extension and the knee joint angle increases with flexion, the same bilateral difference of 5º will result in higher SI values for knee extension, indicating greater asymmetry, than for knee flexion. Similarly, parameters that have large values but relatively small inter-limb differences tend to lower the index and reflect symmetry (Sadeghi et al., 2000).

Another limitation of the SI is the choice of a reference value (i.e. the denominator in equation 1), which is chosen differently based on the question being asked (Zifchock et al., 2008). In the presence of large asymmetries, using the average value of both limbs may not correctly reflect the performance of either limb (Sadeghi et al., 2000) and tends to mask the asymmetry by lowering the SI value (Zifchock et al., 2008), but choosing one side as the reference may not always be easy or the most appropriate. Lastly, the use of different reference values for the same data yields different results, and makes the comparison of results from different studies and samples difficult (Zifchock et al., 2008).

Simple symmetry measures such as the SI are useful at a local level, but it is difficult to make conclusive statements about the global aspect of gait symmetry and the influence of specific interventions when analyzing a multitude of asymmetry values per subject (Hoerzer et al., 2012). When treating knee osteoarthritis patients, it is important to consider not only the involved knee, but also other joints (Toriyama et al., 2011) because these patients adopt gait modifications that change the mechanics of adjacent as well as contralateral joints (Briem & Snyder-Mackler, 2009; Mündermann et al., 2005). For example, bracing the involved knee, has been shown to affect the ipsilateral hip as well as the contralateral hip and knee joints (Toriyama et al., 2011) and attempts to restore symmetry in a particular biomechanical parameter might lead to adaptations in other parameters, which should not be neglected or ignored (Sadeghi et al., 2000). Real-time feedback has been used successfully to restore symmetry (Dingwell et al., 1996; White & Lifeso, 2005; Zeni et al., 2013), but often a single discrete metric is targeted and monitored independently of any compensatory changes that cause other gait asymmetries. For example, Roerdink and colleagues (Roerdink, Roeles, van der Pas, Bosboom, & Beek, 2012) demonstrated that step length asymmetry in amputees was annulled by the existence of other local asymmetries, thus falsely implying gait symmetry in some of these patients. Walking is a complex movement skill that requires the control of several degrees of freedom and therefore the feedback given to the patient should describe the overall gait symmetry, without an overwhelming array of metrics. The isolated optimization of an individual metric may not necessarily mean that the overall gait symmetry is improved because there are a variety of control strategies that can be used to change discrete and local metrics like these and trying to consciously control these many degrees of freedom is nearly impossible (Gabriele Wulf & Shea, 2002). On the other hand, learning from a single, but more global, feedback measure requires the subject to rely more on sources of intrinsic feedback, and therefore on implicit learning processes. Michalak and colleagues (Michalak, Rohde, & Troje, 2015) demonstrated that subjects were able to acutely change their gait pattern using real-time feedback of a single global measure, even though they were not conscious of what it measured nor the strategy they used to change it. With this in mind, global symmetry measures, i.e. a single score that provides information about the symmetry of a collection of local parameters, could be a useful tool from a rehabilitation perspective.

Global symmetry measures comprising multiple discrete metrics, such as the composite score (Exell, Gittoes, Irwin, & Kerwin, 2012), have been developed. A limitation of using discrete metrics is that they neglect the temporal information in gait waveforms and their extraction is subjective and potentially difficult in atypical waveforms (Deluzio & Astephen, 2007). This means that important asymmetries could potentially be missed if for example the peak knee joint moment on both sides, despite being of similar magnitude, occurred at different times in the gait cycle (Nigg, Vienneau, Maurer, & Nigg, 2013). Or there may not even be a definite peak value (Deluzio, Harrison, Coffey, & Caldwell, 2014), making the extraction of this parameter near impossible. Another challenge is that the asymmetry is only significant if the difference observed between limbs is larger than the difference within limbs. The composite score attempts to overcome this limitation by assuring that asymmetry is only reported if the inter-limb differences are larger than the intra-limb differences (Exell et al., 2012). Unfortunately, because only variables with inter-limb differences that are larger than intra-limb differences are included in the score calculation, the result highly depends on the number of variables included, which may change from subject to subject or for the same subject over time.

Some global measures of symmetry include continuous kinematic and/or kinetic parameters. The strength of global symmetry measures composed of continuous variables is their ability to reduce all the information from various local parameters throughout the gait waveform in one score. Two symmetry scores (Hoerzer et al., 2012; Nigg et al., 2013) measured the difference between joint parameters on both sides of the body during the stance phase of gait. Based on the Gait Profile Score (Baker et al., 2009), Lundh and colleagues (Lundh, Coleman, & Riad, 2014) developed two symmetry measures, one for the lower limbs and one for the upper limbs, that include data from the entire gait cycle, thus characterizing the preparation phase for heel strike and accounting for tripping susceptibilities such as toe clearance. However, these scores neglect abnormal joint kinematic variables in the coronal and transverse planes that have been associated with several pathological gait conditions. For example, asymmetric foot pronation has been suggested to be one of the primary biomechanical factors leading to a static pelvic list and sciatic nerve irritation (Rothbart & Estabrook, 1988). Abnormal dynamic knee varus-valgus motion during gait may persist after knee arthroplasty surgery, which could have implications for abnormal knee joint loading and implant survival (Sosdian et al., 2014). Marked asymmetry in a torsional offset of the trunk in relation to the symmetrically rotating pelvis was found in scoliotic patients, which was correlated with the degree of scoliotic deformity (Kramers-de Quervain et al., 2004). Thus the aim of this study was to develop a global gait asymmetry (GGA) score that incorporates these planes of motion and can be calculated efficiently for biofeedback, and to test it under artificially induced asymmetric conditions.

Our hypothesis was that the GGA score would differ between conditions, being higher in the asymmetric conditions.

2. Methods

2.1 Participants

A convenience sample of 18 healthy and recreationally active subjects (11 males; age 26.9 years (SD=7.7); height 1.8 m (SD=0.1) and body mass 72.7 Kg (SD=8.9) volunteered for this study. All participants were free from any musculoskeletal impairment that could affect their gait pattern and were checked for leg length discrepancy (LLD). LLD was the bilateral difference of the distance from the anterior superior iliac spine and the ipsilateral medial malleolus measured while the subject was lying in a supine position. The mean of two readings was considered as it has been shown to have acceptable validity and reliability when used as a screening tool (Gurney, 2002).

Subjects with an LLD larger than 0.5 cm were not included in the study, to ensure that the asymmetric conditions would not be masked. Participants signed an informed consent form and the protocol was approved by the University Ethical Committee.

2.2 Symmetry conditions

Participants walked at their comfortable speed on an instrumented treadmill (AMTI, Watertown, MA, USA), under three different conditions: one symmetric and two asymmetric. The different symmetry conditions were induced by wearing 3 pairs of custom made sandals (Figure 1). Each pair came in two sizes (small [26.5 cm long] and large [29.5 cm long]). During the symmetric (Control) condition participants wore flat and identical sandals on both feet. In both asymmetric conditions the left sandal was kept the same as in the Control condition, however, the right sandal was changed to either a flat thinner sole (bilateral difference of 1.3 cm [small size] or 1.6 cm [large size]) (Thinsole condition) or a laterally wedged sole at the forefoot (WedgedSole condition).

Figure 1 - Sandals worn during the Control (left), ThinSole (middle) and WedgeSole (right) conditions.

Participants were allowed time to familiarize with the treadmill and the control sandals, and then changed to the other conditions in a randomized order. Kinematic data were collected for 20 s during each condition, and in the asymmetric conditions it started as soon as the participants achieved the same walking speed as during the Control condition.

2.3 Three-dimensional gait analysis

The three-dimensional trajectories of 47 reflective markers, placed on the participant's skin according to the Calibrated Anatomical System Technique (Cappozzo, Catani, Croce, & Leardini, 1995), were collected at 200 Hz using a Qualisys system with 6 Oqus cameras (Qualisys AB, Gothenburg, Sweden), and used to create a trunk and lower limb model. The 18 markers used to define the local coordinate systems of the segments were placed

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bilaterally on the acromia, anterior and posterior iliac spines, medial and lateral femoral condyles, medial and lateral malleoli and first and fifth metatarsal heads. Additionally, for segment tracking, 2 extra markers were placed on the iliac crests, 3 extra markers were placed on each foot (one on top of the midfoot, one laterally on the calcaneus and one at the most posterior aspect of the calcaneus), and a rigid cluster with four markers were placed laterally on each thigh and each shank. Each segment had 6 degrees of freedom. Joint angles were resolved into the joint coordinate system (Grood & Suntay, 1983) and filtered using a generalized, cross-validatory quintic spline (Woltring, 1986). All data processing and model building were done in Visual3D (Version 5.01.18, C-Motion, Inc, Rockville, USA).

2.4 Calculation of the asymmetry score

The three-dimensional joint angles of the hip, knee, ankle and trunk in relation to pelvis, and the pelvis angle relative to the laboratory were used to compute the GGA score. All variables were time normalized to the right and left gait cycle (from heel strike to ipsilateral heel strike), into 101 equally distributed points. For each cycle, the GGA score was calculated as shown in equation (2).

$$GGA = \sum_{v=v_1}^{v_{15}} \sqrt{\sum_{t=t_1}^{t_{101}} [x_l(t) - x_r(t)]^2} \quad (2)$$

, where *GGA* is the GGA score, *v* are the angular variables, *t* are the time normalized points and x_l and x_r are the values obtained for the left and right side, respectively.

The GGA is a sum of the magnitudes of 15 difference vectors (between consecutive left heel strikes for the left variables and between right heel strikes for the overlapping right signals), each with 101 components (the time normalized data points). The score is always positive in sign. The minimum obtainable value is zero, which represents perfect symmetry, and the score increases indefinitely with greater degrees of asymmetry.
The GGA score was calculated for 10 right and left consecutive cycles (hereafter called trials) for each condition, and averaged per condition. As an additional exploratory step, the GGA was also decomposed into its fifteen angular variables, by not adding them up.

2.5 Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics 21 (SPSS, Inc. Chicago, Illinois, USA) with an alpha level of 0.05. A One-Way repeated measures ANOVA (3 within-subject levels for symmetry condition) was performed to analyze the differences in GGA score among the three conditions. The normality and sphericity assumptions were checked using Shapiro-Wilk's and Mauchlys tests, respectively. All variables followed a normal distribution, and sphericity was assumed. One subject was identified as an outlier in the WedgeSole condition, as assessed by visual inspection of a boxplot for values greater than 1.5 box-lengths from the edge of the box. However, the authors believe this to be a legitimate case and decided to proceed with the analysis. The Bonferroni correction was used for multiple comparisons.

3. Results

Participants walked at an average speed of 1.1 m/s (SD=0.1). The GGA scores, and therefore the level of asymmetry, increased from the Control condition through to the ThinSole condition (Control mean=527 [SD=92], WedgedSole mean=581 [SD=93] and ThinSole mean=629 [SD=91]; (*P*<.001)) (Figure 2). The results from the multiple comparisons show that not only the scores obtained during the Control condition were significantly different from those obtained during the WedgeSole (*P*=.007) and the ThinSole (*P*<.001) conditions, but the scores obtained during the WedgeSole condition were also significantly different from those obtained during the ThinSole condition (*P*=.010).

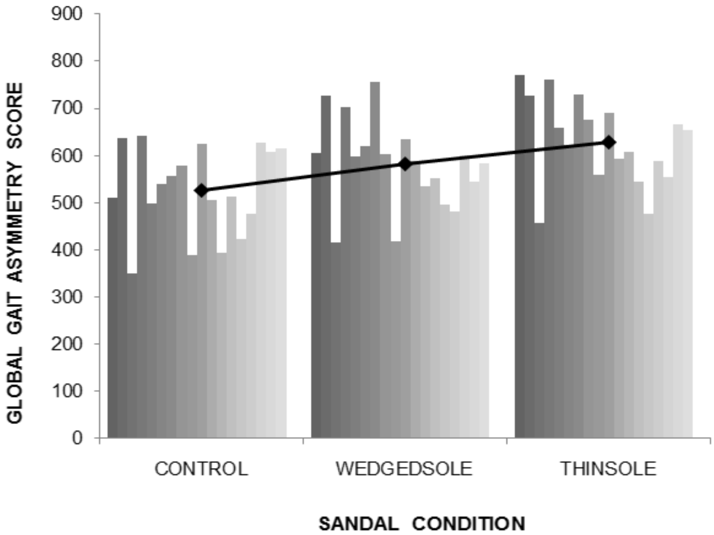

Figure 2 - Global gait asymmetry scores in the three conditions. Each column represents the score for a subject, averaged across 10 trials. Each condition is represented by each group of columns. The black line represents the average scores for all subjects.

The decomposition of the GGA score shows that the asymmetry in the hip transverse plane was the major contributor to the overall score (Figure 3).

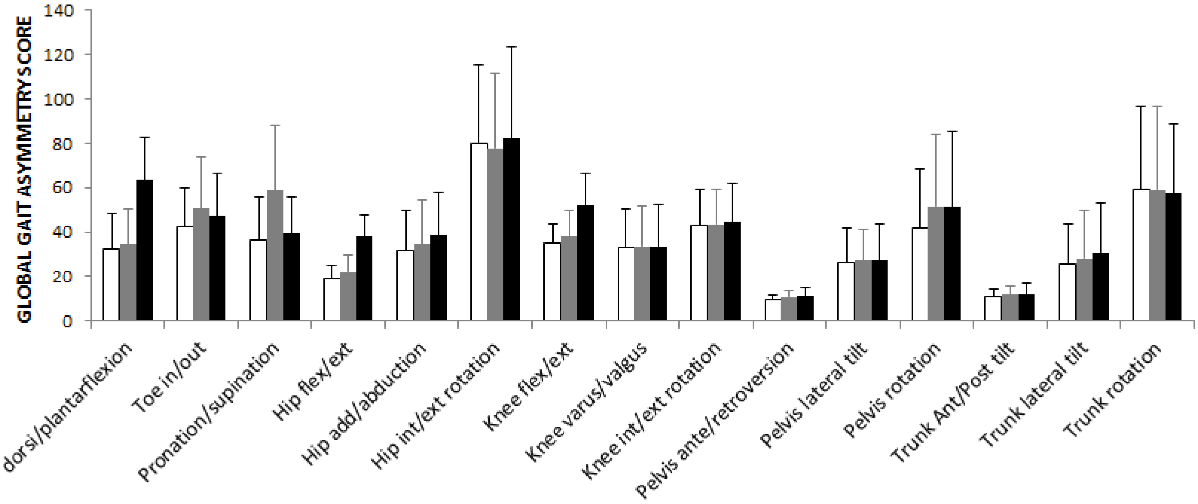

Figure 3 - Asymmetry values for the angular variables that compose the global gait asymmetry score. Each column represents an angular variable, averaged across the 10 trials and across the subjects, obtained during the Control (white), WedgeSole (grey) and ThinSole (black) conditions. The vertical lines represent the SD.

4. Discussion

To the authors' knowledge, this is the first study that tested a global symmetry measure under artificially manipulated conditions. The obtained results support our hypothesis as we found that, using the GGA score, not only the Control condition was significantly more symmetric than the other conditions, but also significant differences were found between the two asymmetric sandal conditions.

Overall, the largest differences were found between the Control and the ThinSole condition, which mimics a LLD of ~1.5 cm. These results are in conflict with Kaufman et al,(Kaufman, Miller, & Sutherland, 1996) who found that gait asymmetry was only significantly greater than that of a normal population when LLD was greater than 2 cm. Similarly, Liu and colleagues (Liu, Fabry, Molenaers, Lammens, & Moens, 1998) concluded that individuals with a LLD up to 2.33 cm presented acceptable gait symmetries. These conflicting results may be explained by the different symmetry measures used in the different studies. Among other differences, the symmetry indices used in the aforementioned studies were mainly composed of ground reaction force parameters, while our score is solely composed by joint angles. However, the results from White and colleagues (White, Gilchrist, & Wilk, 2004) suggest that a mild LLD (between 1 and 3 cm) results in unequal loading of limbs when walking, which could lead to musculoskeletal problems over the long term. Furthermore, Friberg (Friberg, 1983) found that the relative prevalence of LLD greater than 0.5 cm was 1.7 times greater in a group with low back pain when compared with a group of controls. Similarly, Friberg (Friberg, 1982) found that Finnish Army conscripts involved in extensive training, with a LLD as little as 1 cm, had a greater incidence of stress fractures than control.

The GGA score in the WedgeSole condition was significantly higher than in the Control. The former condition was expected to induce forefoot pronation on one side. Asymmetric foot pronation has been suggested to be one of the primary biomechanical factors leading to a static pelvic list and sciatic nerve irritation (Rothbart & Estabrook, 1988). Furthermore, it has been shown to dynamically shorten the ipsilateral lower limb and consequently increase the ipsilateral pelvic drop (Resende, Deluzio, Kirkwood, & Hassan, 2015). Pelvic drop may contribute to the development of low back pain (Menz, Dufour, Riskowski, Hillstrom, & Hannan, 2013), scoliosis and other pathological conditions of the lumbar spine (Gurney, 2002), and was shown to increase the contralateral external knee adduction moment (Resende et al., 2015), which is associated with knee osteoarthritis progression (Andriacchi & Mündermann, 2006). Thus, the GGA score differences found between conditions seem to be clinically relevant.

Finally, the GGA score was significantly higher in the ThinSole condition in comparison to the WedgeSole condition. This suggests that the GGA seems to be sensitive to different degrees of asymmetry, which may be useful in a clinical setting, as a supplementary measure, when assessing a patient's gradual progress throughout rehabilitation.

One of the limitations of the GGA score is that it neglects the direction of the asymmetries (i.e. is unable to indicate which side presents larger values). While the amount of asymmetry may be the same (for an equal bilateral difference) the information about the direction may be clinically relevant (Barton, Hawken, Holmes, & Schwartz, 2015). However, with the GGA score, introducing the direction of asymmetry could mask important asymmetries caused by compensations, as demonstrated by Roerdink and colleagues (Roerdink et al., 2012). Additionally, the lack of normalization does not allow for other physical quantities (i.e. kinetics) to be directly incorporated into the GGA score. However, it is possible that normalizing the score by dividing the bilateral differences by a reference number may contribute to the artificial inflation or lack of sensitivity that has been pointed as limitations in other scores.

Recently, Nigg and colleagues (Nigg et al., 2013) suggested that splitting the symmetry score into categories that represent the different planes of motion is preferred over a general measure of symmetry as it provides more information to tailor the clinical intervention to the patient's specific needs. This decomposition of a global score into its components may be advantageous as it provides useful insights as to which components contribute more to the overall score (Baker et al., 2009). This can easily be achieved with the GGA score by simply not adding up the 15 kinematic variables that compose the score, or by adding them separately according to the plane of motion. Thus, the GGA score could easily be adapted to the needs of the clinician, providing more information when needed. Looking at the asymmetry values for the 15 variables separately (Figure 3), it can be noted that the hip angle in the transverse plane presents the highest asymmetry scores in all conditions. In their study (Nigg et al., 2013), the authors reported higher asymmetry values in the transverse and frontal plane variables, and highlight that these variables are less reliable than those in the sagittal plane. It is possible that these higher scores could have been inflated by the normalization procedure used. The division of the bilateral differences in each variable by its corresponding range of motion means that the variables in these planes are divided by a smaller value (because the range of motion is smaller), which results in higher asymmetry scores. Another possible reason for the elevated scores is that these variables are not essential to the task and therefore are less controlled and consequently more variable (Scholz, Schoner, & Latash, 2000). A better solution might be to perform a weighted sum of the differences, assigning different weights to the variables according to their reliability or contribution to task success so that, for example, those variables known to be less reliable or less important to the task could contribute less to the overall score. In the present study, the asymmetry score was especially higher for the hip transverse plane angle, which low reliability has already been previously reported (McGinley, Baker, Wolfe, & Morris, 2009), suggesting that this variable will probably need to have the lowest weight.

The GGA score was developed with the long term goal of being used as real-time biofeedback in gait retraining programs, as a complement to traditional patient care. With walking being a complex motor skill that requires the control of many degrees of freedom, the premise of using this GGA score as a single biofeedback metric to restore gait symmetry may strengthen our approach in promoting learning of new long term gait patterns. In support of this claim, research has shown that when individuals focus on global movement aspects of the complex skill as opposed to the local level movements, the motor system can more naturally self-organize using unconscious control and therefore free up conscious aspects of attention, resulting in better motor learning and retention (Wulf & Shea, 2002). Furthermore, enhanced learning of a new complex skill has been associated with an external focus of attention, whereby, individuals focus on the effects of their actions, rather than focusing on the movements of the action itself (Vallacher & Wegner, 1987). Researchers believe that this enhancement in learning with an external focus approach could be related to the reduction in cognitive load of the working memory by taking advantage of the self-optimizing capabilities of the motor system (Wulf, McNevin, & Shea, 2001). The GGA provides the patient undergoing gait retraining with this external focus, thus being superior to local scores, such as the SI, in promoting the rehabilitation of gait symmetry.

Besides its potential use in gait retraining, the GGA score can be added to the traditional 3D gait analysis report, to quickly assess the impact of surgery or other interventions in a patient's overall symmetry. Additionally, it can be reported as it is and/or broken down into its components to provide the clinician with further information about the source of the asymmetry, and therefore help to guide the clinical assessment and rehabilitation goals.

In conclusion, this study tested the GGA by analyzing artificially induced asymmetrical gait, and showed that this score was able to distinguish different levels of asymmetry. We still need to analyze the score's repeatability over different testing sessions and its ability to distinguish groups of individuals with clinically identified differences. Improvements can also be made to address the lower reliability of variables outside of the sagittal plane, or to tailor the score to specific clinical conditions. More cost effective modalities need to be explored for those without 3D optical motion capture systems. The focus on a symmetry score based only on kinematics facilitates the translation to other common modalities (e.g. Inertial Measurement Units, or accelerometers) that are predominantly kinematic. Overall, this article suggests that the GGA score is a promising tool to analyze gait asymmetry.

Acknowledgements

We are grateful to Filomena Carnide and Júlia Teles for their kind assistance in the statistical treatment.

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Inter-session agreement and reliability of the Global Gait Asymmetry index in healthy adults

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Submitted to:
Gait & Posture

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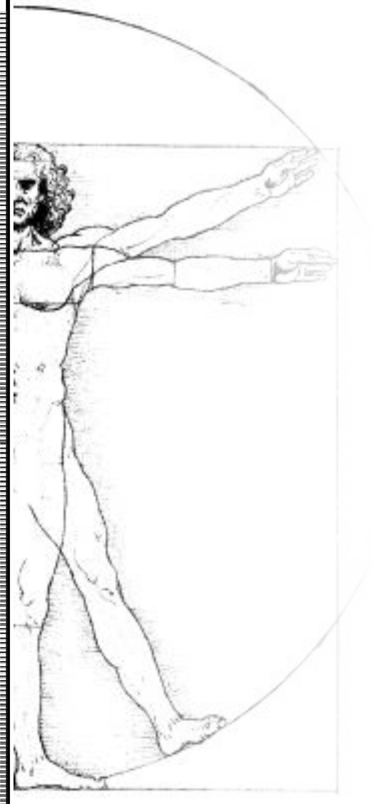

Abstract

There has been a growing effort in restoring gait symmetry in clinical conditions associated with pronounced gait asymmetry. A prerequisite to achieve this is that the chosen approach can accurately assess symmetry and detect/impose changes that exceed the natural day to day variability. Global symmetry indices are superior to local and discrete indices because they capture the patient's overall gait symmetry. However, their repeatability is unknown. This study assessed the inter-session agreement and reliability of the Global Gait Asymmetry index. Twenty-three healthy individuals participated in two 3D gait analyses, performed approximately one week apart. The 95% limits of agreement, standard error of measurement, smallest detectable change, and intraclass correlation coefficient were analysed. The obtained values showed this index has poor agreement and reliability between sessions. Therefore, it cannot be used to assess the patient's progress overtime nor to compare symmetry levels among groups.

Keywords

Gait, symmetry, test-retest, reliability, agreement

1. Introduction

Gait symmetry is generally defined as the identical behaviour of the left and right limbs during gait (Sadeghi, Allard, Prince, & Labelle, 2000). Pronounced asymmetry levels have been associated with pathological conditions such as stroke (Allen, Kautz, & Neptune, 2011), lower limb amputations (Devan, Carman, Hendrick, Hale, & Ribeiro, 2015), osteoarthritis (Mills, Hettinga, Pohl, & Ferber, 2013) and arthroplasties (Tsai et al., 2015), as well as anterior cruciate ligament injury (Winiarski & Czamara, 2012). Consequently, there has been a growing effort in restoring/increasing gait symmetry in several clinical conditions (White & Lifeso, 2005) back to those found in asymptomatic individuals.

Researchers have been studying the efficacy of gait retraining programs in improving gait symmetry (White & Lifeso, 2005). A prerequisite to restore gait symmetry is the ability of the chosen approach to impose changes that exceed the between-session variability (Lewek & Randall, 2011). Hence, knowledge of the measurement error and reliability of symmetry indices is required. However, to the best of the authors' knowledge only two studies (Lewek & Randall, 2011; Senden, Grimm, Heyligers, Savelberg, & Meijer, 2009) have analysed the repeatability (i.e. agreement and reliability under identical conditions (Bartlett & Frost, 2008)) of symmetry indices. Lewek and Randall (2011) analysed the repeatability of the Symmetry Ratio in stance time, swing time and step length for stroke patients. Accordingly, symmetry was calculated by dividing each of these parameters from the paretic limb by the corresponding parameter in the non-paretic limb (i.e. a step length ratio of 1 indicates perfect symmetry; whereas a ratio of 0.5 means that the step length from the paretic limb is half the step length from the non-paretic limb). These authors reported inter-session Intraclass Correlation Coefficient (ICC) (2,1) values between 0.925 and 0.976, and minimal detectable change (MDC) percentages between 8% and 18%. One of the limitations in this study is the wide range of days between the two visits (between 3 and 36 days). Secondly, although the ICC and MDC values were very good, the calculation of the standard error of measurement (SEM), and consequently the MDC are questionable. The SEM cannot be calculated using a model of ICC that includes systematic error as this is not reflected in the pooled standard deviation. Moreover, the calculation of SEM from the ICC is not recommended as it highly depends on the sample's heterogeneity (de Vet, Terwee, Knol, & Bouter, 2006). Senden et al. (Senden et al., 2009) examined the repeatability of step time asymmetry in healthy individuals, where step time asymmetry was the difference between the durations of successive left and right steps, divided by the mean duration between sides. These authors reported intra-session variation coefficients and ICC values from 29.25% to 47.88% and 0.509 to 0.787, respectively, and inter-session/observer ICC values between 0.010 and 0.351. These results suggest very poor inter-session reliability. Furthermore, the authors did not specify which ICC model was used, nor the measurement error, which are essential to interpret the ICC reported (Looney, 2000). The interpretation of ICC values is also incomplete without its confidence intervals, which are lacking in both studies.

Besides these limitations, these studies assessed the repeatability of local symmetry indices. This type of indices quantify symmetry based on a single discrete metric (i.e. vertical ground reaction force, step length or knee sagittal angle, among others) that only relates to a portion of the gait cycle (i.e. peak value), therefore neglecting the temporal information of gait waveforms (Deluzio & Astephen, 2007) as well as compensation strategies that affect other local parameters (Toriyama et al., 2011). Consequently, some patients may be considered symmetric based on their step length symmetry, for example, even though their overall gait is highly asymmetric (Roerdink, Roeles, van der Pas, Bosboom, & Beek, 2012). Alternatively, several local scores could be used, but it would be much harder for the clinician to assess the effectiveness of the intervention this way (Hoerzer et al., 2012). To overcome these limitations, global symmetry indices have been developed (Hoerzer et al., 2012; Lundh, Coleman, & Riad, 2014; Nigg, Vienneau, Maurer, & Nigg, 2013). Contrarily to local indices, global symmetry indices can reduce the information from various continuous gait waveforms (for example, the joint angles from the entire lower limbs, at each percentage of the gait cycle) into a single numeric score. Hoerzer et al. (2012) developed a global symmetry index which uses information from the three components of the ground reaction force, as well as the hip, knee and ankle joint angles, moments and velocities in all three planes of motion. Instead, the global symmetry index developed by Nigg et al. (2013) includes data from the vertical and anterior/posterior components of the ground reaction force as well as the angular positions and velocities at the hip (in all three planes of motion), the knee (sagittal plane only) and ankle (sagittal and frontal planes). However, these two indices only include information from stance phase, therefore neglecting toe clearance and the preparation for the heel strike. Additionally, the combination of quantities with different physical units requires normalization, which may mask or artificially inflate the level of symmetry (Cabral et al., 2016). The AsymGPS, a global symmetry index proposed by Lundh et al. (2014), overcomes these limitations by including data from the entire gait cycle and by limiting the analysis to the lower limb joint angles. However, this index does not include certain angles in the frontal and transverse planes which can be valuable to clinicians. Hence, the Global Gait Asymmetry (GGA) index was recently developed to include all three components of the joint angles at the lower limbs and trunk throughout the gait cycle.

Global symmetry indices may be more appropriate for gait retraining purposes as they provide information on overall gait symmetry in a single score, thus facilitating the assessment of a patient's progress and therefore of the effectiveness of a chosen intervention (Hoerzer et al., 2012). However, their repeatability has never been studied. The aim of the present study was to assess the inter-session agreement and reliability of the GGA (Cabral et al., 2016) in healthy adults.

2. Methods

2.1 Study design

This study followed a prospective test-retest (inter-session, within examiner) design.

2.2 Participants

The data used in this study was collected from the sample used in Fernandes et al. (2016). Sample size was calculated for a predefined 5% level of significance with 80% power, using the formula of Kraemer and Thiemann (1987). For a desired reliability coefficient of 0.90 with a minimum reliability of 0.70, a sample of 17 participants was required. Thus, to allow for non-attenders and increased precision, 23 participants (age: 34.8 ± 7.3 years, mass: 66.4 ± 9.2 Kg, height: 1.70 ± 0.07 m) were recruited. To be eligible, participants had to be between the ages of 18 and 65. Exclusion criteria were the existence of any clinical condition (musculoskeletal, neurological, cardiac or pulmonary) or symptom that could affect their gait. Written informed consent was obtained prior to participation, and the study's protocol was approved by the University Ethics Committee.

2.3 Protocol

Each participant underwent two three-dimensional gait analyses, spaced by 7 to 11 days (median of 7), and performed at the same time of the day to minimize the effects of diurnal variations in joint mechanics. This time period was believed to be enough to prevent recall from the examiner and at the same time to prevent changes in gait symmetry. Passive markers were placed on the participant's skin (Figure 4) based on the Calibrated Anatomical System Technique (CAST) (Cappozzo, Catani, Croce, & Leardini, 1995). Specifically, 18 markers were placed bilaterally on the acromia, anterior and posterior iliac spines, medial and lateral femoral condyles, medial and lateral malleoli and first and fifth metatarsal heads to define the segments' extremities (the medial femoral condyles and malleoli markers were removed for the walking trials). Additionally, for segment tracking, 3 markers were placed at T2, suprasternal notch, and xiphoid process, 2 extra markers were placed on the iliac crests, 1 extra marker was placed on each foot at the most posterior aspect of the calcaneus, and a rigid cluster with 4 markers were placed laterally on each thigh and each shank.

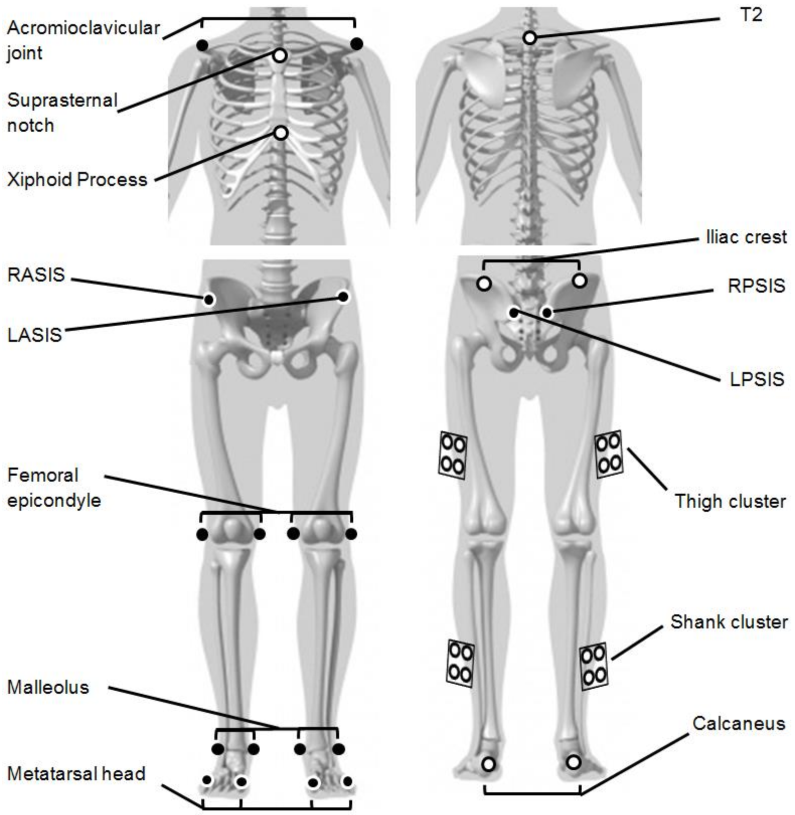

Figure 4 - Anterior (left) and posterior (right) views of the marker placement. The rigid clusters (squares with 4 markers) were placed on the lateral aspect of the thighs and shanks. Anatomical markers are in black, tracking markers are in white with a black outline, and anatomical markers also used for tracking are in black with a white outline.

Mass and height measurements and marker placement were performed by a single examiner for all subjects in both visits.

Participants walked barefoot at their self-selected speed along the laboratory's diagonal (14m long). They walked back and forward continuously during short periods of time (1-2min), for less than a total of 10min, to avoid fatigue. After a familiarization period, the markers' 3D trajectories were collected at 200Hz using a Qualisys system with 13 Oqus cameras (Qualisys AB, Gothenburg, Sweden).

2.4 Data Processing

The trajectories were low-pass filtered, using a 4^{th} order Butterworth filter with a cut off frequency of 10Hz. A model with 8 segments (thorax, pelvis, thighs, shanks and feet) was built, allowing 6 degrees of freedom per segment. All segments' frontal planes were aligned with their distal end markers. For the shanks, a second coordinate system, aligned with the femoral condyles (proximately biased), was created to account for tibial torsion. The GGA index was calculated for each consecutive left and right gait cycles. Accordingly, the angles of the hip, knee (using the proximately biased shank) and ankle joints, as well as the angles of the pelvis relative to the global coordinate system and of the trunk relative to the pelvis were computed into the joint coordinate system (Grood & Suntay, 1983). Explicitly, flexion/extension occurred around the medial axis of the proximal segment, adduction/abduction occurred around a floating axis, perpendicular to the other axes, and longitudinal rotation occurred around the longitudinal axis of the distal segment. All three components of these angles (15 waveforms) were used to calculate the GGA index, according to the equation below:

$$GGA = \sum_{v\,=\,v_1}^{v_{15}} \sqrt{\sum\nolimits_{t=t_1}^{t_{101}} [x_l(t) - \, x_r(t)]^2}$$

, where v are the angular variables, and $x_l(t)$ and $x_r(t)$ are the values obtained for the left and right sides of each angular variable, respectively, at *t* (each percentage of the time normalised gait cycle).

Gait speed was computed and normalised to standing height (Whittle, 2007).
All data processing and model building were done in Visual3D (Version 5.01.18, C-Motion, Inc, Germantown, USA).

2.5 Data analysis

The GGA scores of 5 bilateral gait cycles from each participant in each visit were averaged and used to assess the repeatability of the GGA index. Accordingly, the agreement (i.e. how close the repeated scores are) between the two averaged scores obtained per subject was assessed by calculating the Bland and Altman 95% limits of agreement (95% LOA), the SEM and the MDC. These were calculated using the following equations: 95% LOA = $\bar{X}_{diff} \pm 1.96 * SD_{diff}$ (Bland & Altman, 1999); SEM = $SD_{diff} / \sqrt{2}$ (de Vet, Terwee, Knol, et al., 2006), and MDC = $1.96 * \sqrt{2} * SEM$ (de Vet, Terwee, Ostelo, et al., 2006), where $\bar{X}_{diff}$ and SD_{diff} are the mean and standard deviation of the differences between visits. The reliability (i.e. how well subjects can be distinguished) was assessed via the ICC, using a two-way mixed-effects model ($ICC_{C,k}$) (McGraw & Wong, 1996) and associated 95% confidence intervals (CI). Because GGA scores are unfamiliar, the quality of the agreement results were interpreted in terms of percentages of the average score obtained between visits. For the reliability, the quality of the ICC values were interpreted in relation to the measurement error and the variation between subjects (Weir, 2005), considering a value equal or higher than 0.70 as acceptable (Nunnaly, 1978). Prior to these calculations, the presence of heteroscedasticity was assessed by visual inspection of the Bland and Altman plot, the normality of the differences was checked via a Shapiro-Wilk test, and the existence of a relationship between the differences and the mean of the measurements was analysed via a Spearman Correlation. In addition, the gait speeds in each visit were compared using a paired T-test. The agreement measures were calculated using Microsoft Excel 2010 (Microsoft Corporation, Redmond, WA). All other statistics were computed in IBM SPSS Statistics 21 (SPSS, Inc. Chicago, Illinois, USA), for an alpha level of 0.05.

3. Results

The participants' walking speed remained consistent between visits (0.71 ± 0.08 vs 0.71 ± 0.09 statures/s; $t(22) = 0.706$, $P = 0.488$). The GGA scores obtained in the first and second visits were 619 ± 177 (intra-individual SD: 6 to 79) and 605 ± 119 (intra-individual SD: 13 to 94), respectively. The mean difference in GGA (1st visit minus 2nd visit) was 14 ± 194 (95% CI: -70 to 98), with 95% LOA of -366 (-60%) and 394 (64%).

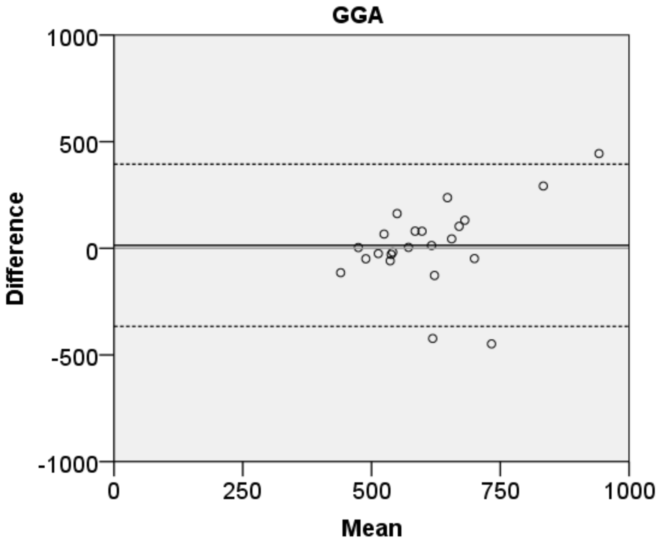

Figure 5 - Bland and Altman plot for GGA. The mean difference between visits (1st visit minus 2nd visit) is represented as a solid black line. The upper and lower 95% limits of agreement are represented by the dashed black lines.

As seen in the Bland and Altman Plot (Figure 5), the standard deviation of these differences remained constant throughout the GGA score magnitude (no heteroscedasticity). Additionally, the differences were normally distributed (P=0.077), even though 3 participants were identified as outliers. No correlation was found between these differences and the magnitude of the measurements ($r_s(21) = 0.359$, P=0.093).

The SEM was 137 and the MDC was 380, corresponding to 22.4% and 62.1% of the average score. The inter-session ICC was found to be 0.30 with 95% CI of -0.65 and 0.70.

4. Discussion

This is the first study to assess the repeatability of a global symmetry index in healthy individuals. The present results show that the GGA has very poor agreement and reliability between sessions.

The presence of outliers, in terms of the differences between visits, may have contributed to the poor repeatability of this index. However, the time between visits was very similar among participants. Moreover, the participants maintained their healthy condition and had both gait analyses performed at the same time of day. Thus, minimal changes in performance were expected between sessions. Therefore, these outliers are legitimate cases, and not a result of poor study design, and highlight the low repeatability of the index.

The SEM corresponds to 22% of the average score, which may be reasonable, however the other agreement measures are unacceptable. The calculated limits of agreement show that 95% of the differences in future measurements for the same subject would lay between -366 and 394. In other words, when assessing the progress of a patient over time, these results suggest that, even if there were no real changes in gait symmetry, the GGA index could increase or decrease by approximately 60% (Bland & Altman, 1999). Additionally, the smallest within-subject change that could be interpreted as real change (i.e. above measurement error) is as high as 62.1% of the average score (de Vet, Terwee, Knol, et al., 2006). This is extremely high, considering the 19% difference observed in GGA when a leg length discrepancy of approximately 1cm was artificially induced (Cabral et al., 2016). These results suggest that GGA has very poor agreement between sessions and is therefore not appropriate to assess gradual changes in symmetry overtime. This poor agreement stems from the high variability in the differences between visits (i.e. differences between visits were small for some participants but large for other participants).

The ICC of 0.30 means that only 30% of the variability observed in GGA was due to genuine differences in gait symmetry, with the remaining being due to error in the measurement process (Weir, 2005). This value is well below the recommended 0.70, and therefore unacceptable. Although the measurement error (SEM) is reasonable, the variance due to error is similar to the variance between subjects, thus making the distinction between subjects difficult (low reliability). Additionally, the 95% CI were extremely wide, with the lower CI reaching negative values, which means that the portion of variability that is due to error is very uncertain. Thus, the GGA index is not appropriate to compare gait symmetry between subjects.

These results are much worse than those reported for the Symmetry Ratio (Lewek & Randall, 2011), and similar to those reported by Senden et al. (Senden et al., 2009). However, this type of symmetry indices presents several limitations (Cabral et al., 2016) and may not be valid tools to assess overall gait symmetry, as demonstrated by Roerdink and et al. (Roerdink et al., 2012). In this sense, the GGA is superior, but in its current form, its low agreement and reliability prevents it from being applied in a clinical and research context.

In a previous study (Cabral et al., 2016), the GGA was sensitive to different symmetry levels when the markers were left in place. The low repeatability shown in this study may be related to differences in marker placement precision between visits and thus differences in the segment local coordinate systems. Although joint kinematics are sensitive to marker placement precision (Della Croce, Leardini, Chiari, & Cappozzo, 2005), the joint kinematics used to calculate the GGA in the present study were shown to be reliable and have a low measurement error (Fernandes et al., 2016). Thus, it is surprising that the GGA had such low repeatability. In test-retest studies, the left and right sides are usually analysed separately. Conversely, the GGA is the sum of bilateral differences in various joints within one gait cycle. This means that irrelevant bilateral differences are amplified, which may be the reason behind the low repeatability of this index. For example, there may be a 1º and a 3º bilateral difference (averaged within the gait cycle) in the first and second visit, respectively, that is simply due to error (i.e. a small marker placement imprecision). These bilateral differences are summed 101 times (in each of the 15 angle components) resulting in very different symmetry scores between visits. Additionally, the magnitude of this difference varied among participants, and this variability (within visits) seems to be as high as the variability between participants. The GGA might therefore be more sensitive to marker placement precision and soft tissue artefact than its comprising joint kinematics. Perhaps other global symmetry indices that either do not rely on precise segment anatomical coordinate systems between sessions, or compensate for the variability due to error, will be more repeatable and therefore useful in the context of gait rehabilitation.

A limitation of this study is that there was only one examiner. Therefore, these results should be taken carefully when interpreting assessments performed by several examiners. Additionally, these results were obtained from a group of healthy adults, which means that further studies are needed to assess the repeatability of the GGA in specific pathological populations.

Conclusion

The values obtained for reliability and measurement error prevent the application of the GGA as a measure of symmetry for monitoring progress, both in a research and clinical context. These results highlight the importance of testing the repeatability of other global symmetry indices before being used to assess the outcome of gait interventions. In addition, this study suggests that global indices composed of kinematics that are less sensitive to marker placement precision and soft tissue artifact might be more repeatable.

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Comparison of inter-session agreement and reliability among three global gait symmetry indices in healthy adults

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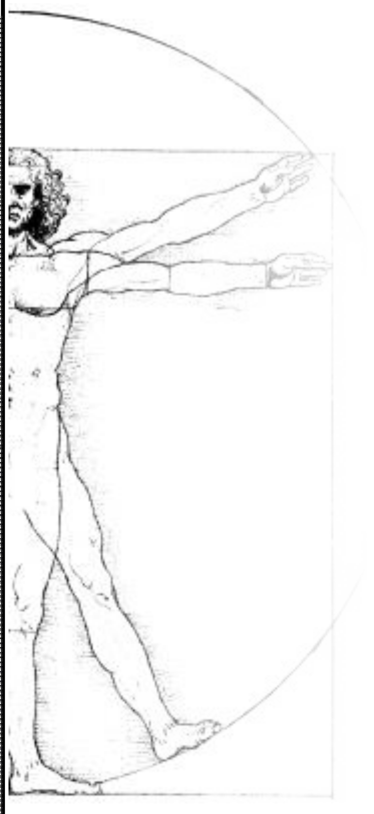
Submitted to:
Journal of Biomechanics



4

Abstract

With the growing development of gait retraining programs aiming to improve gait symmetry, comes the need to analyse the repeatability of symmetry indices. However, these studies are scarce and focused on discrete and local indices, which fail to assess overall gait symmetry. On the other hand, the repeatability of global symmetry indices based on joint angles may be hampered by the sensitivity of these variables to marker placement imprecision. The aim of this study is to compare the inter-session agreement and reliability of three global gait symmetry indices: two based on joint angles, where one of these excludes the least reliable angle components, and one based on linear distances. Two 3D gait analyses were performed on separate days (a week interval) on twenty-three healthy adults. The 95% limits of agreement, standard error of measurement, smallest detectable change, and intraclass correlation coefficient were assessed and compared among the three symmetry indices. The symmetry indices based on joint angles presented very poor agreement and reliability, particularly the index that excluded the least reliable angle components. On the other hand, the symmetry index based on linear distances was reliable and presented acceptable measurement error, thus being a more promising tool to assess overall gait symmetry.

Keywords

Gait, symmetry, test-retest, reliability, agreement

1. Introduction

An essential requirement of any outcome measure used for meaningful clinical decision-making and for the evaluation of clinical change over time is that they are consistent and reliable (de Vet, Terwee, Knol, & Bouter, 2006; Klejman, Andrysek, Dupuis, & Wright, 2010). Despite the extensive use of symmetry indices in the literature and the existing growing effort to restore gait symmetry in clinical populations (Lewek, Feasel, Wentz, Brooks, & Whitton, 2012; Lewek & Randall, 2011; Reisman, McLean, Keller, Danks, & Bastian, 2013; White & Lifeso, 2005), only three studies (see below) have analysed the repeatability of symmetry indices.

In the first two studies, using spatio-temporal parameters, Lewek and Randall (2011) and Senden et al. (2009) respectively reported high inter-session reliability for the Symmetry Ratio, and poor inter-session reliability for a score similar to the Symmetry Index (Robinson, Herzog, & Nigg, 1987). However, a limitation of this type of indices is that symmetry is calculated based on a single variable, such as step-length, a joint angle, or ground reaction force. Assessing gait symmetry from a spatio-temporal parameter alone is flawed, because step length may be symmetric even though overall gait is highly asymmetric (Roerdink, Roeles, van der Pas, Bosboom, & Beek, 2012). The same can probably be said for other types of variables if used alone to evaluate gait symmetry. Furthermore, symmetry indices such as the Symmetry Ratio and the Symmetry Index require the extraction of a single discrete value, which means that they neglect the temporal information of gait waveforms (Deluzio & Astephen, 2007), and may fail to capture important asymmetries that occur in other portions of the gait cycle (Nigg, Vienneau, Maurer, & Nigg, 2013). Additionally, discrete values are prone to generating false positives (Pataky, Vanrenterghem, & Robinson, 2016).

The third study (Chapter 3) analysed the repeatability of a global symmetry index called GGA (Cabral et al., 2016). This type of index overcomes the limitations above, by including continuous gait data from various local parameters (specifically for the GGA these are the three components of the trunk, pelvis, hip, knee and ankle joint angles). However, the GGA presented very poor reliability and agreement between sessions, possibly as a result of the cumulative sum (throughout the gait cycle and at various joints) of bilateral differences that are functionally irrelevant and/or caused by marker placement inconsistency.

Errors in anatomical landmark position determination are known to affect the position and orientation of a segment’s anatomical frame (Ugo Della Croce, Leardini, Chiari, & Cappozzo, 2005). These errors have been shown to be particularly detrimental to the precision of the longitudinal orientation component, especially on the femur and tibia.

Furthermore, joint angles have been shown to be highly sensitive to these variations in anatomical frame orientations and to be less reliable for those components undergoing small variations. More specifically, while standing, transverse plane angles were generally the least precise, particularly at the knee. During motion, coronal and transverse plane angles were generally less reliable, and for the knee joint only, precision in these components depended on the level of flexion/extension (Della Croce, Cappozzo, & Kerrigan, 1999). Thus, a global symmetry index that excludes these less precise and reliable angles might be more repeatable than the GGA. The AsymGPS (Lundh, Coleman, & Riad, 2014) is a global index that, like the GGA, calculates symmetry based on joint angles, but does not include the knee joint angles in the coronal and transverse planes nor the ankle joint angle in the coronal plane. However, to the best of our knowledge, its repeatability has never been studied.

Although the exclusion of the least reliable joint angles might improve the index's repeatability, the sensitivity of the remaining joint angles to errors in the anatomical frame orientation may still be detrimental to the repeatability of a symmetry index. An alternative would be to not include angles at all, but to use the relative 3D locations of the joints. Considering the relationship between a segment's angular and linear positions, joint angles could be replaced by the linear position of the segments' distal end. For example, based on the 3D linear displacement of several joints, Troje (2002) was able to identify and model walking patterns there are distinct between males and females. Similarly, gait symmetry could be reported from the bilateral differences in the linear positions of segments' extremities, instead of the bilateral differences in joint angles. An advantage of calculating symmetry this way is that the segments' end positions are not affected by the longitudinal orientation of the segment coordinate system, which is the most affected by marker placement inconsistency (Della Croce et al., 2005). Therefore, this alternative might be more repeatable than symmetry indices comprising joint angles.

With this in mind, the aim of this study was to assess and compare the agreement and reliability of the AsymGPS and the GGA, as well as a newly developed linear alternative of the GGA (LGGA). The authors hypothesised that the AsymGPS will be more repeatable than the GGA, but that LGGA will be more repeatable than both angular indices.

2. Methods

2.1. Study design

This study followed a prospective test-retest (inter-session, within examiner) design.

2.2. Participants

The data analysed in this study was extracted from the sample used in Fernandes et al. (2016). According to the equation of Kraemer and Thiemann (1987), seventeen was the minimum sample size required for a predefined 5% level of significance with 80% power, and for a desired reliability coefficient of 0.90 with a minimum reliability of 0.70. Twenty-three subjects were recruited to allow for non-attenders and increased precision. Participants were aged between 18 and 65 years and were free from any clinical condition (musculoskeletal, neurological, cardiac or pulmonary) or symptom that could affect their gait.

2.3. Protocol

After providing us with written informed consent, each participant underwent two three-dimensional gait analysis, spaced by 7 to 11 days (median of 7), and performed at the same time of the day to minimize the effects of diurnal variations in joint mechanics. This time period was believed to be enough to prevent recall from the examiner and at the same time to prevent changes in gait symmetry. Before marker placement, mass and height were measured. Passive markers were placed on the participant's skin based on the Calibrated Anatomical System Technique (Cappozzo, Catani, Croce, & Leardini, 1995), as shown in Figure 6. In each visit, participants walked barefoot along a 14m walkway, at their self-selected speed, during short periods of time (1-2min) to avoid fatigue. Once participants were familiarized, the markers' 3D trajectories were recorded at 200Hz using a Qualisys system with 13 Oqus cameras (Qualisys AB, Gothenburg, Sweden).

2.4. Data processing

The marker trajectories were low-pass filtered using a 4th order Butterworth filter with a cut off frequency of 10Hz. A model with 8 segments (thorax, pelvis, thighs, shanks and feet) was built, allowing 6 degrees of freedom per segment. All segments' frontal planes were aligned with their distal end markers. For the shanks, a second coordinate system, aligned with the femoral condyles (proximately biased), was created to account for tibial torsion. The angles of the hip, knee (using the proximately biased shank) and ankle joints were computed into the joint coordinate system (Grood & Suntay, 1983). Accordingly, flexion/extension occurred around the medial axis of the proximal segment, adduction/abduction occurred around a floating axis, perpendicular to the other axes, and longitudinal rotations occurred around the longitudinal axis of the distal segment. The same method was used to compute the angle of the pelvis with respect to the global coordinate system, the angle of the trunk with respect to the pelvis, and the foot progression angle. All angles were time normalised to 101 data points, one for each percentage of the gait cycle.

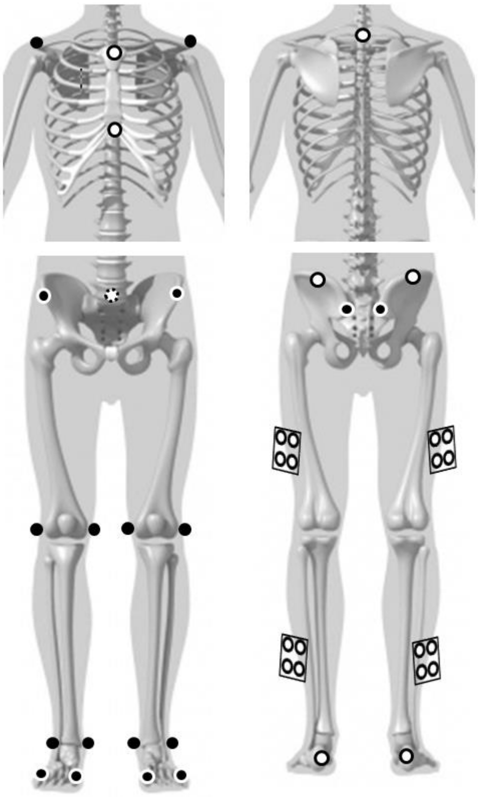


Figure 6 - Anterior (left) and posterior (right) views of the marker placement. The rigid clusters (squares with 4 markers) were placed on the lateral aspect of the thighs and shanks. Anatomical markers are in black, tracking markers are in white with a black outline, and anatomical markers also used for tracking are in black with a white outline. The white marker with dotted black outline is a virtual marker created at the origin of the pelvis (midpoint between the anterior and posterior superior iliac spines (ASIS and PSIS), which was used to define the trunk.

Three global gait symmetry indices were calculated for each left and right consecutive gait cycles: the GGA, the AsymGPS and the LGGA.

GGA

This index was calculated as described in (Cabral et al., 2016), using the equation below:

$$GGA = \sum_{v = v_1}^{v_{15}} \sqrt{\sum\nolimits_{t=t_1}^{t_{101}} [x_l(t) - x_r(t)]^2}$$

, where *v* are the angular variables (all three components of the hip, knee and ankle joint angles, of the absolute pelvis angle, and of the trunk angle in relation to the pelvis), and $x_l(t)$ and $x_r(t)$ are the values obtained for the left and right sides, respectively, at *t* (each percentage of the time normalised gait cycle).

LGGA

This index was calculated using the same equation as the GGA, but the angular variables were replaced by the 3D components of the Euclidean distances from the "joint centres" to the pelvis origin (Figure 7). The positions of the "joint centres" were given by the 3D coordinates of the distal extremities of the feet, shanks, thighs and thorax. For the pelvis, the 3D coordinates of the left and right midpoints between the ipsilateral ASIS and PSIS were used instead of the hip joint centres, for real-time technical reasons.

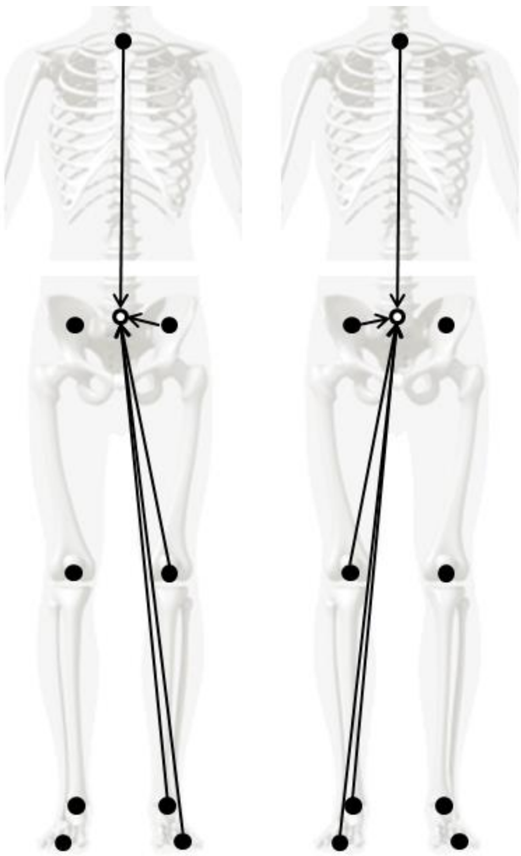


Figure 7 - Vectors for the Euclidean distances computed during the right gait cycle (right) and during the left gait cycle (left) for the LGGA calculation. The 3D components of each of these vectors are the input *v* in this index's equation.

AsymGPS

This index was calculated using the equation below (adapted from Lundh et al. (2014) to match the current notation):

$$AsymGPS = \sqrt{\frac{\sum_{k=1}^{N}[x_l(k) - x_r(k)]^2}{N}}$$

, where k is a vector with 909 components (N), representing the 101 time normalized data points for each of 9 angles (all three components of the pelvis absolute angle and the hip joint angle, the sagittal knee and ankle joint angles, and the foot progression angle), and $x_l(k)$ and $x_r(k)$ are the values obtained for the left and right sides, respectively, at k.

Gait speed was also computed and normalised to standing height. All data processing and model building were done in Visual3D (Version 5.01.18, C-Motion, Inc, Germantown, USA).

2.5. Data analysis

Each of the symmetry indices was calculated for 5 gait cycles from each participant in each visit. These were then averaged to assess the repeatability of each index between visits. The Bland and Altman 95% limits of agreement (95% LOA), the Standard Error of Measurement (SEM) and the Minimal Detectable Change (MDC) were calculated to assess the agreement of each index, using the following equations: 95% LOA = $\bar{X}_{diff} \pm 1.96 * SD_{diff}$ (Bartlett & Frost, 2008); SEM = $SD_{diff} / \sqrt{2}$ (de Vet, Terwee, Knol, et al., 2006), and MDC = $1.96 * \sqrt{2} * SEM$ (de Vet, Terwee, Ostelo, et al., 2006), where $\bar{X}_{diff}$ and SD_{diff} are the mean and standard deviation of the differences between visits. The Intraclass Correlation Coefficient (two-way mixed-effects model - $ICC_{C,k}$) (McGraw & Wong, 1996) and associated 95% confidence intervals (CI) were also calculated to assess the reliability of each index. In order to compare results among the different symmetry indices, the quality of the agreement results were interpreted in terms of percentages of the average of the respective index obtained between visits. For the reliability, the quality of the ICC values were interpreted in relation to the measurement error and the variation between subjects (Weir, 2005), considering a value equal or higher than 0.70 as acceptable (Nunnaly, 1978). Prior to these calculations, the presence of heteroscedasticity was assessed by visual inspection of the Bland and Altman plots, the normality of the differences was checked via a Shapiro-Wilk test, and the existence of a relationship between the differences and the mean of the measurements was analysed via a Spearman Correlation. In addition, the gait speeds in each visit were compared using a paired T-test, after checking for normality. The agreement measures were calculated using Microsoft Excel 2010 (Microsoft Corporation, Redmond, WA). All other statistics were computed in IBM SPSS Statistics 21 (SPSS, Inc. Chicago, Illinois, USA), for an alpha of 0.05.

3. Results

The participants' age, body mass and height were, respectively, 34.8 ± 7.3 years, 66.4 ± 9.2 Kg and 1.70 ± 0.07 m. Their walking speed remained consistent between visits (0.71 ± 0.08 vs 0.71 ± 0.09 statures/s; $t(22)=0.706$, $P=0.488$). The differences in symmetry between visits were normally distributed for the GGA ($P=0.077$), but not for the LGGA and AsymGPS ($P=0.014$ and $P=0.009$, respectively). Visual inspection of the difference between visits boxplots showed the existence of 1 outlier in LGGA and 3 outliers in both the GGA and AsymGPS, two being extreme in AsymGPS. The standard deviation of these differences remained constant throughout the scores' magnitude (no heteroscedasticity), as observed in the Bland and Altman Plots (Figure 8).

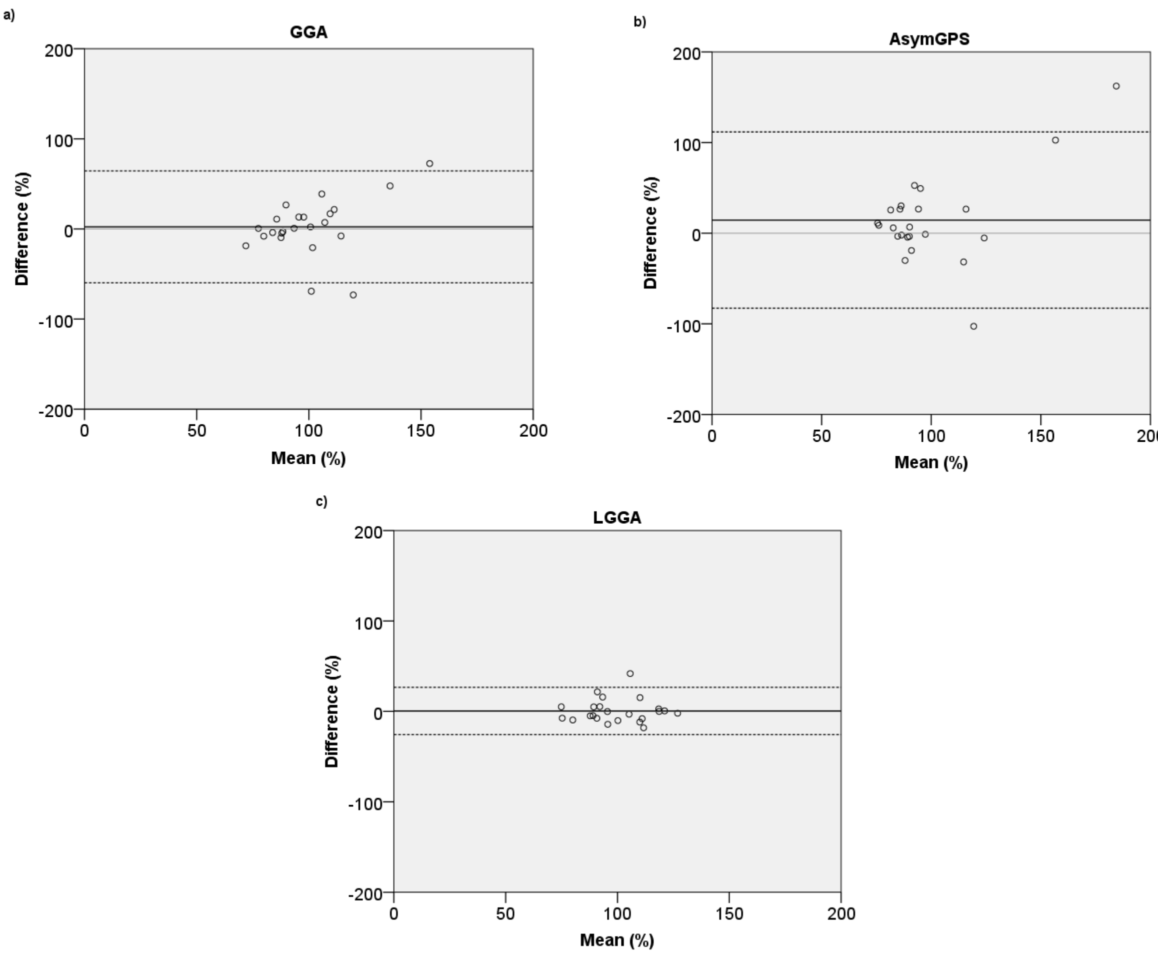


Figure 8 - Bland and Altman plots for GGA (a), AsymGPS (b) and LGGA (c). The mean difference between visits (1st visit minus 2nd visit) is represented as a solid black line. The 95% Limits of Agreement are represented by the dashed black lines. Both the vertical and horizontal axes are in percentage of the mean (of the respective) score between visits, and are equally scaled to accommodate the maximum value among all scores (200%).

Furthermore, these differences were not related to the magnitude of the scores (GGA: $r_s(21)=0.359$, $P=0.09$; AsymGPS: $r_s(21)=0.068$, $P=0.757$; LGGA: $r_s(21)=-0.016$, $P=0.943$). The values obtained for the different symmetry indices are presented in Table 1.

Table 1 - Asymmetry score values obtained during both visits. Mean values and differences between visits were also calculated, as well as the standard deviation and 95% CI of the differences. The differences and corresponding standard deviations are also presented as a percentage of the mean score between visits.

Symmetry Scores	1st Visit	2nd Visit	Mean	Diff (%)	SD_{diff} (%)	95% CI_{diff}
GGA	619 ± 177	605 ± 119	612	14 (2.3%)	194 (31.7%)	-70 to 98
AsymGPS	5.06 ±2.11	4.38 ± 1.16	4.72	0.68 (14.4%)	2.34 (49.6%)	-0.33 to 1.69
LGGA	1.71 ±0.28	1.70 ± 0.27	1.71	0.01 (0.6%)	0.23 (15.5%)	-0.09 to 0.11

The AsymGPS presented the largest differences between visits as well as the highest variability in these differences (SD_{diff}). The LGGA presented the smallest differences between visits with the least variability.

Table 2 shows the agreement and reliability results. The LGGA presented the narrowest 95% LOA and the lowest SEM and MDC values, with the widest and highest values being obtained by the AsymGPS. Both the GGA and AsymGPS presented very low ICC values and wide 95% CI, with the lower CI reaching negative values. Conversely, the LGGA presented the narrowest 95% CI and an ICC above 0.70.

Table 2 - Agreement and reliability values. Agreement is also presented as a percentage of the mean score.

Symmetry Scores	95% LOA (%)	SEM (%)	MDC (%)	ICC	95% CI_{ICC}
GGA	-366 to 394 (-59.8% to 64.4%)	137 (22.4%)	380 (62.1%)	0.30	-0.65 to 0.70
AsymGPS	-3.91 to 5.27 (-82.8% to 111.7%)	1.66 (35.2%)	4.59 (97.2%)	0.10	-1.12 to 0.62
LGGA	-0.44 to 0.45 (-25.6% to 26.6%)	0.16 (9.4%)	0.45 (26.1%)	0.79	0.51 to 0.91

4. Discussion

This study assessed and compared the repeatability of three global symmetry indices for gait: the GGA (Cabral et al., 2016), the AsymGPS (Lundh et al., 2014) and the newly developed LGGA. As hypothesised, the LGGA presented the highest reliability and agreement between sessions. However, contrary to the initial hypothesis, the AsymGPS was the least repeatable index.

A strength of this study is its careful design. The time between visits was approximately equal and close to 7 days for all participants, with the second visit being performed at the same time of day as the first. Furthermore, participants were allowed a familiarisation period before data collection, and did not know when data were being recorded. These characteristics assured identical testing conditions and trustworthy data. Additionally, the present data set has been shown to be highly repeatable (Fernandes et al., 2016). Therefore, the identification of outliers in each index, particularly those comprising joint angles, is independent of the study design and data quality. On the other hand, the current results are limited to a single examiner and therefore should not be extrapolated to studies performed by multiple examiners. Another limitation was the use of the same methods to calculate the 95% LOA in all three indices, even though the differences between visits were not normally distributed in two of the indices and extreme outliers were present in AsymGPS. However, the non-normal distribution of the differences does not have a great impact on the limits of agreement, as 5% of the observations are still likely within two standard deviations of the mean (Bland & Altman, 1999). Furthermore, although the extreme outliers may have an influence on the 95% LOA, an exploratory analysis showed that the use of nonparametric alternatives suggested by Bland and Altman (1999) widened the LOA but still led to the same conclusions. Because these alternatives are generally less reliable (Bland & Altman, 1999), and for the sake of uniformity of comparison methods, the authors chose to use the same method for all indices.

As expected, the GGA and AsymGPS were less reliable and presented higher measurement error than LGGA. Specifically, their reliability was extremely low (ICC's were 0.30 and 0.10) because the variability within subjects was very high in relation to the variability between subjects (as per the within and between mean squares of the ANOVA - not shown). Furthermore, the 95% CI for their ICC values were extremely wide and reached negative values, contributing to uncertainty in the findings. Consequently, these indices are not appropriate to compare symmetry values between individuals. In terms of agreement, the 95% LOA of these indices were quite wide, meaning that large differences are expected between repeated measurements, with the 95% LOA for the AsymGPS surpassing 100% (i.e. symmetry could more than double or halve between repeated measurements, in 95% of the cases). As seen in Fig. 1, the presence of extreme outliers may have widened these limits, as most of the differences are well below them. Nevertheless, given that all indices were calculated on the same data, the presence of extreme outliers alone highlights the large variability of AsymGPS, in comparison to LGGA. Moreover, the values obtained for SEM (GGA: 22.4% and AsymGPS: 35.2%) and for MDC (GGA: 62.1% and AsymGPS: 97.2%) suggest that these indices have moderate measurement error and only significant differences can be interpreted as real changes in symmetry (i.e. above measurement error). Due to the scarcity of literature and standards regarding the repeatability of symmetry indices, the interpretation of these results is limited. Lewek and Randall (2011) reported MDC values for the Symmetry Ratio of several spatiotemporal parameters that ranged between 8% and 18%. Additionally, the SEM and MDC values obtained for LGGA in the present study were 9.4% and 26.1%, respectively. The results obtained for the GGA and the AsymGPS are much worse, and therefore the use of these indices to monitor changes in symmetry over time is not recommended.

Surprisingly, the agreement and reliability of AsymGPS were lower than those of GGA. The AsymGPS was expected to be more repeatable because it did not include the knee angles in the coronal and transverse planes nor the ankle angles in the coronal plane, which are known to be less reliable (Della Croce et al., 1999). However, these are not the only differences between the two angular indices. While the GGA is the sum of 15 left-right difference vectors (each with 101 components), the AsymGPS is the root mean square error (RMSE) between sides. On one hand, by calculating the mean, one could expect the RMSE to smooth the bilateral differences across the gait cycle and the "error" differences among trials, therefore lowering the measurement error. On the other hand, the RMSE gives more weight to larger absolute differences than to smaller absolute differences (Chai & Draxler, 2014) (because the mean of the squared differences is calculated before the square root is taken), thus inflating asymmetry. Additionally, as the largest differences are found in the coronal and transverse planes, particularly at the hip and pelvis angles (Cabral et al., 2016), the AsymGPS gives more weight to less reliable angle components. Hypothetically, if in the first and second visit there was, respectively, a 1º and a 3º bilateral difference (in one of the angle components, averaged within a gait cycle) due to marker placement imprecision, both the GGA and the AsymGPS would exaggerate the increase in asymmetry in the second visit, in their own way. However, by comparing the Bland and Altman plots of these indices (Figures 8a and 8b), and the differences between visits (Table 1), the discrepancies between visits seem to be more exaggerated in AsymGPS, hence the lower agreement and reliability of this index. These findings are supported by Armstrong and Callopy (1992), who also found the RMSE to be an unreliable tool to measure the accuracy of forecasting models, but are partially in contrast with those of Rasmussen et al. (2015). In their study, the inter-session ICC of the gait variable scores (GVS) (root mean square differences between the gait curves of an individual and the mean gait curve of a reference sample) ranged from 0.22 to 0.78. Additionally, the SEM% and MDC% ranged from 7.21 to 28.91% and from 18.33 to 80.53%, respectively. However, the comparison of these results requires caution due to the different methodologies (namely the biomechanical models, and the calculation of ICC and SEM%), the different populations (their variability), and the different number of variables between the AsymGPS and each GVS. Nevertheless, they reported worse results for all GVS's then for the Gait Profile Score (GPS), again suggesting the lower repeatability of the RMSE.

As expected, the LGGA presented the highest agreement and reliability. The SEM and MDC were slightly higher than those reported for the Symmetry Ratio (Lewek & Randall, 2011). The reliability was lower in comparison to the same study, but reached the minimum recommended value. Despite this lower agreement and reliability, the LGGA overcomes the limitations of the Symmetry Ratio and other local and discrete symmetry indices (Cabral et al., 2016). Besides, these indices are often computed on mean curves from non-consecutive steps, thus failing to capture the response to the previous step, which may be relevant for gait retraining. This study also suggests that the LGGA is much better, in terms of agreement and reliability, than global symmetry indices based on joint angles. Furthermore, because the LGGA calculates symmetry based on the linear displacement of joints, instead of joint angles, it is comparable across different modelling conventions (Sigal, Balan, & Black, 2010), and therefore across different labs.

In conclusion, this study shows that the GGA and AsymGPS are unreliable and have high measurement error and therefore are not appropriate to assess individual/group differences or the effect of interventions on symmetry. Therefore, the repeatability of other symmetry indices based on joint angles should be analysed before their use. Additionally, the newly developed global symmetry index (LGGA) showed acceptable agreement and reliability, thus being a promising tool for researchers and clinicians.

Acknowledgements

The authors gratefully thank Niko Troje for his intellectual contribution.

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Global gait asymmetry of knee osteoarthritis patients in comparison to healthy adults

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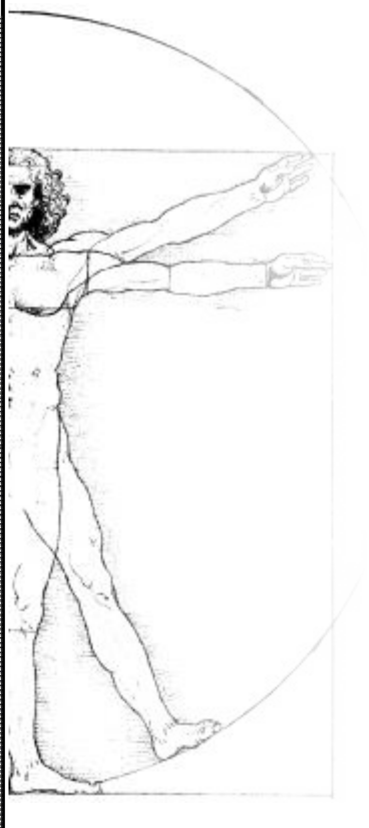
Submitted to:
Archives of physical medicine and rehabilitation



5

Abstract

Objective: To compare gait symmetry between knee osteoarthritis (KOA) patients and healthy adults, using the Linear Global Gait Asymmetry (LGGA) index.

Design: Cross-sectional

Setting: Laboratory based

Participants: Population-based sample of twelve individuals diagnosed with clinical and radiographic KOA and a convenience sample of twelve healthy controls.

Interventions: Not applicable.

Main Outcome Measure: The LGGA was calculated from a 3-dimensional gait analysis, based on the bilateral differences in the positions of segments' extremities throughout the gait cycle.

Results: The LGGA scores of the KOA group (median: 2.16; 25th quartile: 2.11; 75th quartile: 2.42) were significantly higher (P<0.001; Cohen's d = 1.90) than those of the Control group (median: 1.61; 25th quartile: 1.46; 75th quartile: 1.79), indicating that patients with KOA walked more asymmetrically than healthy individuals.

Conclusions: The LGGA seems to be an appropriate index to detect the increased asymmetry typically found in KOA patients. Studies analysing LGGA's agreement, reliability and minimally important difference in KOA patients are needed to support these results. Future research should also analyse the effect of simpler biomechanical models on LGGA before it is applied in usual clinical settings.

Keywords

Gait; symmetry; knee osteoarthritis

1. Introduction

Previous studies have reported an increased level of asymmetry in patients with knee osteoarthritis (KOA) (Asay, Mündermann, & Andriacchi, 2009; Bejek, Paróczai, Illyés, & Kiss, 2006; Christiansen & Stevens-Lapsley, 2010; Creaby, Bennell, & Hunt, 2012; Mills, Hettinga, Pohl, & Ferber, 2013; Turcot, Sagawa, Hoffmeyer, Suvà, & Armand, 2015; Viton et al., 2000). These studies analysed level gait (Bejek et al., 2006; Creaby et al., 2012; Mills et al., 2013), stair ascent (Asay et al., 2009), sit to stand transitions (Christiansen & Stevens-Lapsley, 2010), quiet standing (Turcot et al., 2015), and gait initiation (Viton et al., 2000), which suggests that KOA patients are generally asymmetric. This asymmetry seems to be a compensation mechanism to reduce loading of the affected joint (Asay et al., 2009; Christiansen & Stevens-Lapsley, 2010; Turcot et al., 2015; Viton et al., 2000). However, this inevitably increases the load on the contralateral limb, which has been suggested to contribute to degenerative changes at these joints and consequently to the development of multiarticular osteoarthritis (OA) (Briem & Snyder-Mackler, 2009; Mills et al., 2013; Turcot et al., 2015; White & Lifeso, 2005). Although no longitudinal studies have been conducted to support this speculation, it is in line with the non-random evolution of OA found in the lower limbs. In a very large cross-sectional study, Shakoor et al. (2002) found that, after a single unilateral total joint replacement (a validated surrogate marker of end-stage OA), patients who underwent a second total joint replacement most often replaced the joints on the contralateral side (particularly the paired joint). Furthermore, even though osteoarthritis may have an asymmetrical onset (Shakoor et al., 2002), a large prospective study found that KOA tends to develop into bilateral disease (Metcalfe, Andersson, Goodfellow, & Thorstensson, 2012). Therefore, although several factors contribute to the onset and progression of KOA (Zhang & Jordan, 2010), the preservation or recovery of symmetry may be beneficial for these patients (Mills et al., 2013).

When assessing gait symmetry in KOA patients, it is important that the chosen index captures overall symmetry. In other words, it must not focus on a single local variable or at a single point in time. As demonstrated by Roerdink et al. (2012), patients may be considered symmetric based on step length, even though their overall gait is highly asymmetric. And the same may be true for other variables, if used in isolation to assess gait symmetry. Furthermore, as pointed out by Nigg et al. (2013), asymmetries can be missed if the calculation is made at a different portion of the gait cycle (from that in which it occurred). Conversely, the advantage of using a global symmetry index is that symmetry is quantified based on various discrete parameters at multiple points in time, and is reduced to a single score, thus overcoming the aforementioned limitations. Another important requirement is that the chosen index has low measurement error and high reliability. Very few studies have analysed the repeatability of symmetry indices, particularly of global indices (Lewek & Randall, 2011; Senden, Grimm, Heyligers, Savelberg, & Meijer, 2009). Of these, only the LGGA (Chapter 4) has been found to have acceptable measurement error and high reliability, in healthy adults. However, its ability to distinguish the symmetry level of healthy individuals from that of patients with KOA has never been studied.

The aim of this study was to investigate if the LGGA index of KOA patients is different from that of healthy individuals. The authors hypothesise that the LGGA of a group of patients with KOA will be significantly higher than that of a group of healthy individuals.

2. Methods

2.1. Study design

This study followed a cross-sectional design.

2.2. Participants

3D Motion capture data was extracted from previously published studies (Fernandes, Armada-da-Silva, Pool-Goudzwaard, Moniz-Pereira, & Veloso, 2016; Yázigi et al., 2013) and used to measure symmetry. For the Control group, data from a convenience sample of twelve healthy adults (4 men, 8 women), recruited from university staff and their associates, were extracted from Fernandes et al. (2016). To be eligible, participants had to be aged between 18 and 65 years and free from any clinical condition (musculoskeletal, neurological, cardiac or pulmonary) or symptom that could affect their gait. Pregnant women were excluded. For the KOA group, data from a convenience sample of twelve patients (3 men, 9 women), recruited from the Lisbon area through advertising (social networks, television, newspapers), were extracted from Yázigi et al. (2013). Eligible participants were independently mobile and diagnosed with clinical and radiographic KOA (according to the American College of Rheumatology criteria) by a rheumatologist. Participants who had hip or knee replacement, or other knee surgery within the 6 months prior to the study, or knee injections within the 3 months prior to the study, as well as those with unstable medical conditions were excluded. Both original studies followed a standardized recruitment protocol, based on predefined inclusion/exclusion criteria, to minimise selection bias. Further details are provided elsewhere (Fernandes et al., 2016; Yázigi et al., 2013). All participants signed an informed consent, and the studies' protocols were approved by the University Ethical Committee.

2.3. Protocol

Participants underwent a three-dimensional gait analysis. Passive markers were placed on their skin based on the Calibrated Anatomical System Technique (Cappozzo, Catani, Croce, & Leardini, 1995), as shown in Figure 9.

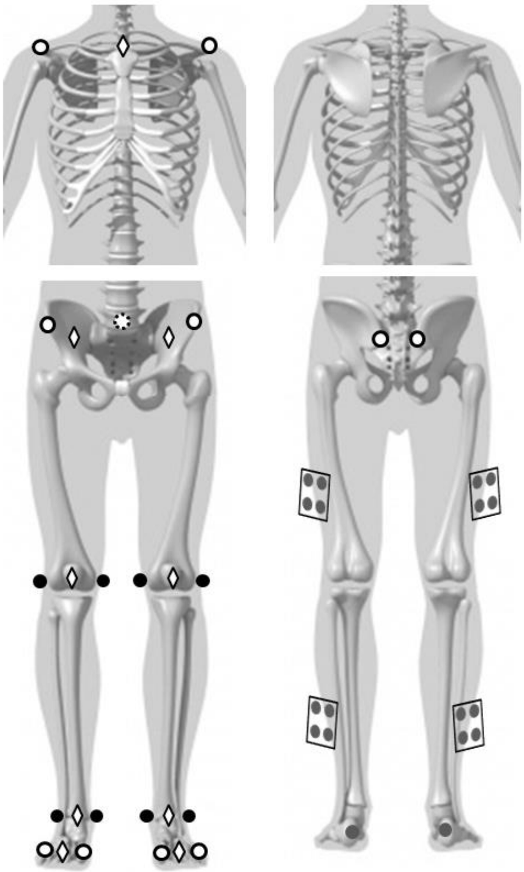


Figure 9 - Anterior (left) and posterior (right) views of the marker placement. The rigid clusters (squares with grey markers) were placed on the lateral aspect of the thighs and shanks. Anatomical markers are in black, tracking markers are in grey, and anatomical markers also used for tracking are in white with a black outline. The white marker with dotted outline is a virtual marker placed at the origin of the pelvis (midpoint between the anterior and posterior superior iliac spines), which was used to define and track the trunk. The white diamonds, with black outline, represent the segment extremities used in the calculation of the LGGA.

Participants walked along a 14m walkway, barefoot and at their self-selected speed, during short periods of time (1-2 min) to avoid fatigue. After a familiarisation period, the markers' three-dimensional trajectories were recorded at 200Hz using an optoelectronic system with Oqus 300 cameras (Qualisys AB, Gothenburg, Sweden).

2.4. Data processing

These trajectories were then low-pass filtered using a 4th order Butterworth filter with a cut off frequency of 10Hz, and used to build a model with 8 segments (trunk, pelvis, thighs, shanks and feet), each with 6 degrees of freedom. The positions of the segments' ends, during the walking trials, were calculated as the 3D coordinates of the distal extremities of the feet, shanks, thighs and trunk, and of the bilateral midpoints between the ASIS (anterior superior iliac spine) and the PSIS (posterior superior iliac spine) for the pelvis. These were then used to calculate the Linear Global Gait Asymmetry (LGGA) index for each left and right consecutive gait cycles, according to the equation below:

$$LGGA = \sum_{v\,=\,v_1}^{v_{15}} \sqrt{\sum\nolimits_{t=t_1}^{t_{101}} [x_l(t) - x_r(t)]^2}$$

, where v are all three components of the distances from each segment's end to the origin of the pelvis (midpoint between the four superior iliac spines), and $x_l(t)$ and $x_r(t)$ are the values obtained for the left and right sides, respectively, at t (each percentage of the time normalised gait cycle). For the trunk and pelvis, the same respective v was used for the left and right sides, but it was time normalized to the left and right gait cycles, respectively. Additionally, the medio-lateral component of all distances was negated for the left side. The final score increases with the level of asymmetry. The minimum score is zero, indicating perfect symmetry, which is unrealistic.

The LGGA accounts for bilateral differences in motion pattern as well as bilateral differences in segment's dimensions. Therefore, segment length and distal end radius were measured for the thighs, shanks and feet, using their respective proximal and distal anatomical markers during the standing trial, and the absolute bilateral difference between these metrics was calculated. Additionally, given the possible influence of walking speed on gait symmetry (Bejek et al., 2006), gait speed was calculated and normalised to standing height. All data processing and model building were done, using an automated command line, in Visual3D (Version 5.01.18, C-Motion, Inc, Germantown, USA).

2.5. Data analysis

The average from 3 LGGA scores was calculated per subject. According to the Shapiro-Wilk test, the scores for the KOA group did not follow a normal distribution. Nevertheless, the shapes of the distributions of the LGGA scores of both groups were similar. A Mann-Whitney U test was used to compare the differences in LGGA between the control and KOA groups. This was followed by a post hoc effect size and power analysis for the

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corresponding statistic. Additionally, the height, body mass, body mass index (BMI) and gait speed, as well as the bilateral differences in segments lengths and radii were also compared between groups using a Mann-Whitney U test. The post hoc power and effect size analysis was conducted in G*Power (Version 3.1.7, Germany), while all other statistics were computed in IBM SPSS Statistics 21 (SPSS, Inc. Chicago, Illinois, USA), for an alpha of 0.05.

Results

The LGGA scores (median; 25th to 75th quartiles; 95% confidence intervals of the median (CI)) of the KOA group (2.16; 2.11 to 2.42; 2.10 - 2.52) were higher than those of the Control group (1.61; 1.46 to 1.79; 1.38 - 1.86). These differences were statistically significant (P = 0.001; power = 0.99) and presented a large effect size (Cohen's d = 1.90), as seen by the lack of overlap in the groups' CI.

Most patients (83.2%) presented with mild KOA, i.e. with a Kellgren-Lawrence grade <3 (Table 3). Additionally, the majority of patients presented radiographic evidence of bilateral KOA (Table 3), with both knees presenting equal severity (Table 4).

Table 3 - Number of KOA patients - n (%) - per Kellgren-Lawrence grade of the most painful knee. The percentage is in relation to the total number of patients (12).

K-L Grade	Unilateral (n = 4)	Bilateral (n = 8)
I	3 (25.0)	2 (16.6)
II	1 (8.3)	4 (33.3)
III	0 (0.0)	2 (16.6)
IV	0 (0.0)	0 (0.0)

Table 4 - Number of bilateral KOA patients - n (%) - whose least painful knee has less, the same, or more radiographic severity than the most painful knee. The percentage is in relation to the number of bilateral patients (8).

Severity in least painful vs most painful*	Bilateral (n=8)
Less severe	2 (25.0)
Same	6 (75.0)
More severe	0 (0.0)

* according to Knee Osteoarthritis Pre-Screening questionnaire (KOPS) (Flavia Yázigi, Carnide, Espanha, & Sousa, 2014)

The Control and KOA groups were different in terms of age, height, body mass and BMI. Those in the healthy group were significantly younger and taller, had less body mass and consequently lower BMI. On the other hand, both groups walked at similar speeds (Table 5). The CI for age and BMI did not overlap, and both groups presented wide CI for body mass.

Table 5 - Gait and anthropometric parameters for the control and KOA groups.

		Control Median (IQR)	**95% CI**	**KOA** Median (IQR)	**95% CI**
Age (years)		34 (29-40)	28 to 44	61 (56-65)**	56 to 65
Height (m)		1.69 (1.63-1.74)	1.62 to 1.74	1.59 (1.52-1.68)*	1.51 to 1.68
Body mass (Kg)		64.5 (56.1-74.7)	53.8 to 77.0	82.1 (73.6-96.8)*	71.6 to 99.2
BMI (Kg/m^2)		22.8 (20.7-24.5)	20.5 to 24.7	32.2 (30.9-35.7)**	30.7 to 36.4
Speed (statures/s)		0.75 (0.70-0.79)	0.69 to 0.80	0.71 (0.63-0.75)	0.62 to 0.76
Absolute bilateral difference (cm)	**Thigh radius**	0.1 (0.1-0.2)	0.1 to 0.2	0.4 (0.1-0.6)	0.1 to 0.6
	Thigh length	0.6 (0.3-1.2)	0.2 to 1.3	1.4 (0.5-1.8)	0.2 to 1.9
	Shank radius	0.1 (0.1-0.2)	0.0 to 0.2	0.1 (0.1-0.3)	0.1 to 0.3
	Shank length	0.9 (0.5-1.4)	0.5 to 1.5	1.1 (0.5-1.8)	0.3 to 1.9
	Foot radius	0.3 (0.1-0.4)	0.0 to 0.4	0.3 (0.2-0.4)	0.2 to 0.4
	Foot length	0.5 (0.3-0.6)	0.2 to 0.6	0.7 (0.3-1.0)	0.2 to 1.1

* P-value < 0.05; ** P-value < 0.001; IQR is the interquartile range between the 25th and the 75th quartiles; 95% CI are the 95% confidence intervals of the median

The bilateral discrepancies in segment lengths and radii tended to be higher in the KOA group, however the difference in medians between groups was mostly below 2 mm, except for the thigh length, where the groups' medians differed by 8 mm. These differences were not statistically significant (Table 5). The CI were similar between groups, presenting large overlap. The CI for segment lengths were wider than those for radii, particularly for the KOA group.

Discussion

This study analysed whether there were differences in LGGA between KOA patients and healthy individuals. As hypothesised, KOA patients presented higher LGGA scores (were more asymmetric) than healthy individuals, and this difference was above the index measurement error. To the best of the authors' knowledge, this was the first study to use a global index to compare gait symmetry between KOA patients and healthy individuals, taking into account the measurement error. Although local symmetry indices are more popular in the clinical setting, due to their simplicity, they fail to capture asymmetries that occur in other parameters (Roerdink et al., 2012) and at other portions of the gait cycle (Nigg et al., 2013). Global symmetry indices, on the other hand, reduce all information from various parameters throughout the gait cycle into a single numeric score. Just like gait indices, such as the GPS (Gait Profile Score) (Baker et al., 2009), are routinely used in the assessment of children with cerebral palsy as a tool to quickly assess overall gait quality, global symmetry indices could complement the typical gait analysis of patients with KOA, by providing a quick assessment of overall gait symmetry. This study is one of the initial steps towards this goal.

The median LGGA scores of the KOA group were higher than the scores measured on healthy individuals. Although the width of the CI is difficult to interpret (considering how recent the index is), there was no overlap between the two groups and the effect size was large, suggesting that we can be confident to find a difference in symmetry between these populations. Furthermore, the difference between the groups (0.55) was above the SEM (0.16) and MDC (0.45), established in a previous study (Chapter 4), indicating that the group differences are beyond the measurement error. Most researchers reported greater asymmetries in KOA patients, when compared to controls, in various kinetic as well as in some (but not all) kinematic and spatiotemporal parameters (Asay et al., 2009; Bejek et al., 2006; Christiansen & Stevens-Lapsley, 2010; Creaby et al., 2012; Mills et al., 2013; Turcot et al., 2015; Viton et al., 2000). The results of the present study are supported by this body of literature, thus suggesting that the LGGA is a useful tool to assess gait symmetry in this clinical population. Conversely, Liikavainio et al. (2007) did not find asymmetries in the kinematics or kinetics of mild KOA patients during level walking, though asymmetries were reported in ground reaction force during stair ambulation, as well as in peak plantar pressures during level walking and stair ambulation. However, these results may be questionable as patients were only considered asymmetric when their absolute symmetry index was above 10%, a cut off value once arbitrarily defined by Robinson et al. (1987). Further, without a control group, there is no way to tell whether the patients' symmetry levels were equal or different from those of healthy individuals.

While most evidence of asymmetries in individuals with KOA is based on patients with more severe and mostly unilateral KOA, the current study was based on a sample with mostly mild and bilateral KOA patients. These findings are supported by Mills et al. (2013), who also found mild and bilateral patients to be more asymmetric. Assuming that KOA has an asymmetrical onset (Shakoor et al., 2002) and tends to progress into bilateral disease, the present study may suggest that the LGGA has potential for identifying early changes in the asymmetry of these patients, i.e. those patients supposedly at higher risk for the progression of OA at other joints of the lower limb. The advantage in doing this is that the clinician could be alerted at an earlier stage and, in parallel to the recommended interventions for the management of these patients, decide to implement strategies aiming to reduce the burden on the contralateral limb (i.e. quadriceps strengthening, use of insoles, etc.). Further research with longitudinal designs is needed to confirm this speculation.

Study Limitations

One of the limitations in the present study is that each group's data were extracted from different studies. However, the data were collected at the same laboratory, using the same the methodology. Differences in marker placement between assessors are believed to be the greatest source of variability in gait data (Gorton, Hebert, & Gannotti, 2009). Nonetheless, the reliability of gait kinematics and kinetics among assessors and even laboratories has been generally good to excellent (Benedetti, Merlo, & Leardini, 2013; K. Kaufman et al., 2015; McGinley, Baker, Wolfe, & Morris, 2009; Wilken, Rodriguez, Brawner, & Darter, 2012). Marker placement imprecision is greater within a segment's horizontal plane (Della Croce, Cappozzo, & Kerrigan, 1999). If these errors affected the segment's extremity position in the same plane, the segments' distal radii would differ between limbs (assuming a true equal radii in both limbs), and the LGGA score would be affected. However, the median bilateral difference in these metrics was very small (4 mm max) and similar between groups. Therefore, the influence of the assessors on the results is expected to be small. Nevertheless, the analysis of the inter-assessor repeatability of the LGGA is recommended and should be used to complement the present results.

The LGGA can also be influenced by leg length discrepancies. Ideally, this should have been measured using a full limb standing radiographs. However, this was not a variable of interest in the original studies. Alternatively, segment length was estimated using the motion capture system, which may present a limitation. The lack of statistically significant differences in bilateral segment length discrepancies between the two groups suggests the two groups were similar in terms of leg length discrepancies, and therefore the latter may not have influenced the final results. This lack of statistical significance may be a result of the wide CI for these metrics in both groups, particularly in the KOA group (indicating uncertainty), and their large overlap. Nevertheless, even though the median bilateral differences tended to be higher in the KOA group, the differences in group medians were fairly small and the magnitude of the bilateral discrepancies could not justify the overall difference in LGGA between the groups. In other words, although the bilateral discrepancies could potentially contribute to an increase in LGGA, the increased asymmetry found in the KOA group was most likely due to asymmetric movement patterns, rather than structural asymmetries.

Another potential limitation is that the groups were not matched by age, height, weight and BMI. Those in the control group were younger and taller, and those in the KOA group were heavier and had greater BMI. However, this study was not set to identify the cause of the asymmetry. Rather, the purpose of this study was to test the hypothesis that the LGGA scores of KOA patients were higher than those of healthy individuals, assuming (based on the previously mentioned body of evidence) that KOA patients were more asymmetric. Although the authors cannot guarantee that the aforementioned group differences did not increase the differences in symmetry between the two groups, no evidence was found to suggest an effect of age (Lythgo, Wilson, & Galea, 2011; Patterson, Nadkarni, Black, & McIlroy, 2012), height, body mass or BMI on gait symmetry. Therefore, the authors speculate that these group differences did not affect the study's results, but further studies with similar groups are required to confirm this speculation. The influence of gait speed, on the other hand, has been analysed and yielded controversial results (Bejek et al., 2006; Lythgo et al., 2011). However, both groups walked at similar speeds and at their self-selected speed, thus minimising the effect of this potential confounding variable. Given the low severity of KOA in this study, this lack of significant differences in self-selected walking speed is consistent with the literature. Most studies report no significant differences in self-selected walking speed between controls and patients with mild to moderate KOA (Kellgren and Lawrence grade ≤ 3) (Landry, McKean, Hubley-Kozey, Stanish, & Deluzio, 2007; Phinyomark, Osis, Hettinga, Kobsar, & Ferber, 2016; Zeni & Higginson, 2009). Only those with more severe KOA seem to walk slower than healthy controls (K. R. Kaufman, Hughes, Morrey, Morrey, & An, 2001; Mündermann, Dyrby, Hurwitz, Sharma, & Andriacchi, 2004).

Conclusions

In conclusion, this study shows that the LGGA of KOA patients is higher than that of healthy individuals, suggesting that this index is able to detect increases in gait asymmetry in these patients. Further studies are needed to confirm the validity of these results when groups are more similar and measured by the same examiner. Additionally, future research should analyse both the intra- and inter-examiner repeatability, as well as the minimally important difference, of the LGGA in this clinical population. The effect of simpler biomechanical models on LGGA scores should also be analysed before this index is applied to usual clinical settings.

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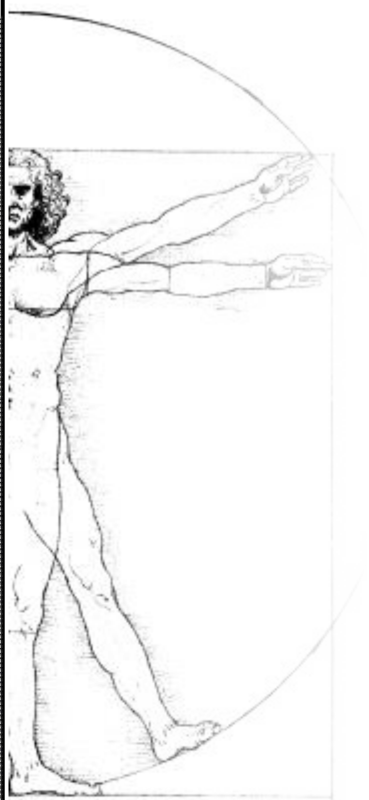
6

General Discussion



1. Discussion

The aim of this thesis was to develop a global index of gait symmetry from marker based optical 3D motion capture that could be used as real time feedback in gait rehabilitation programs. This thesis comprises the implementation and testing of a series of indices, with each index being a refinement of the previous one, based on its ability to consistently measure and distinguish different levels of gait symmetry. The first index was based on a review of the candidate indices in the literature and was tested by comparing the scores obtained in different walking conditions, in which two different levels of asymmetry were induced artificially. The index was refined iteratively based on experimental tests of its repeatability to consistently measure gait symmetry in the same individual and to reliably distinguish between individuals. The final index was tested for its ability to detect the presence of higher levels of asymmetry in a group of patients with an expected asymmetric gait pattern.

This chapter will summarise and discuss the main findings of each of four studies, and will address important methodological considerations leading to the iterative refinement of the index. A general conclusion and suggestions for future research will be provided.

1.1. Main findings

Study 1 - A Global Gait Asymmetry Index

The limitations of the pre-existing symmetry indices prompted the need for the creation of a new index that could comprehensively measure overall gait symmetry. Hence, the aim of the first study (Chapter 2) was to develop and test a global gait asymmetry index (GGA) that comprised the 3D joint angles of the thorax, pelvis, hip, knee, and ankle. Accordingly, the left side data (including thorax and pelvis) were extracted from a full left stride (left foot contact to left foot contact), and the right side data (including thorax and pelvis) were extracted from the consecutive full right stride (right foot contact to right foot contact). These bilateral signals were time normalized to 101 points and subtracted, forming a difference vector with 101 components for each of the 3D joint angles. Symmetry was defined as the sum of the magnitudes of these difference vectors.

The GGA was tested experimentally with healthy individuals in which asymmetry was induced artificially. To the best of our knowledge, this was the first time that a global index of gait symmetry was tested under artificially induced levels of asymmetry. Asymmetry was achieved by having each participant walking with three different pairs of sandals: one with identical sandals on both feet, to preserve the participants' natural symmetry level (Control), one with a laterally wedged sandal on one foot, to induce more forefoot pronation on one side (WedgeSole), and another with different sole thickness on each side, to mimic a discrepancy in leg length (ThinSole). As expected, the results showed that the GGA scores obtained in the WedgeSole and ThinSole conditions were significantly higher (indicating greater asymmetry) than those obtained in the Control condition. Additionally, the GGA scores were significantly different between the two asymmetric conditions. These results confirm that the GGA index is sensitive to the increased asymmetry induced by the asymmetric sandal conditions.

The novelty of this study limits the comparison of the obtained results with the literature. Nonetheless, we can speculate that, as intended, the GGA is superior to discrete indices such as the symmetry ratio and the SI in two aspects. First, it may be more sensitive to smaller differences in gait symmetry. In this study, the GGA was significantly different between the control condition and the ThinSole condition, which mimicked a leg length discrepancy of approximately 1.5 cm. Conversely, the symmetry ratio values were only significantly different from those reported in a healthy population when the leg length discrepancy was greater than 2 cm (Kaufman, Miller, & Sutherland, 1996), and the SI values were acceptable in participants with a leg length discrepancy up to 2.33 cm (Liu, Fabry, Molenaers, Lammens, & Moens, 1998). This is however a crude comparison, given the methodological differences between these studies. Secondly, the success of a given intervention is more easily assessed by analysing a single global score, such as the GGA, rather than a multitude of values (Hoerzer et al., 2012). This difficulty was shown by Liu et al (1998) who found that the effects of heel lifts on gait symmetry were difficult to predict because some SI values improved while others got worse, depending on the biomechanical signals used in the SI equation (i.e. pelvic tilt, knee flexion, vertical GRF, medial GRF) .

Although the GGA was designed to combine the symmetry information from all joints in one single numeric score, it can also be decomposed into its 15 difference vectors to provide greater insights on which components contribute more to the overall score (Baker et al., 2009) and therefore to tailor the clinical intervention to the patient’s specific needs (Nigg, Vienneau, Maurer, & Nigg, 2013). The analysis of these components also provided further confirmation that the GGA score reflected the gait changes induced by the sandals. Specifically, during the WedgeSole condition the increased overall score is mostly explained by an increase in asymmetry around the foot’s longitudinal axis and its vertical axis, which were the variables directly manipulated by the sandal. Similarly, during the ThinSole condition there was a great increase in asymmetry in the sagittal component of the ankle as well as of the knee and hip joint angles. These changes in the sagittal plane are in line with previously reported (Gurney, 2002) compensation mechanisms to lengthen the short limb and shorten the long limb in patients with leg length discrepancy.

Furthermore, this analysis also showed that (1) in comparison to the sagittal plane, the asymmetry was progressively greater in the frontal and the transverse planes, particularly at the hip, pelvis and trunk, (2) the level of asymmetry in these variables remained relatively unchanged between conditions, and (3) that the asymmetry in the transverse component of the hip joint angle was the greatest contributor to the overall GGA score. These results may suggest that the GGA is considerably affected by marker placement inconsistency, since the lowest precision and reliability have been generally reported for the kinematics outside of the sagittal plane (Collins, Ghoussayni, Ewins, & Kent, 2009; Della Croce, Cappozzo, & Kerrigan, 1999; McGinley, Baker, Wolfe, & Morris, 2009; Schwartz, Trost, & Wervey, 2004), particularly at the hip joint (McGinley et al., 2009). Although pelvis rotation has been suggested to be free from palpation error and to present high precision and reliability values (Della Croce et al., 1999), the same trend of increasing asymmetry from the sagittal to the transverse plane can also be observed at the pelvis. A potential explanation for these results is the higher inter-trial variability (intra-session) found in this plane, in comparison to the other pelvic planes (Schwartz et al., 2004). However, the individual curves show the existence of a small offset (~2º) between the bilateral curves, suggesting again either marker placement error or a true small asymmetric alignment.

By artificially manipulating asymmetry in repeated conditions, without removing the markers, this study allowed us to understand how well the GGA responded to known differences in symmetry, thus giving us confidence that this new index measures what it was intended to. Furthermore, the results from this study showed us that the sources of error in joint kinematics seem to have a great impact on the overall score. Knowledge of the measurement error is important to ensure that the GGA does not conceal important deviations from symmetry and that small changes in GGA between days are not falsely interpreted as meaningful. This is particularly important in the case of a global index, where the outcome score is difficult to relate to. Therefore, the analysis of the inter-session agreement and reliability of the GGA was essential.

Study 2 - Inter-session agreement and reliability of the Global Gait Asymmetry index in healthy adults

The second study (Chapter 3) was conducted to assess the inter-session agreement and reliability of the GGA index. This was the first study to analyse the repeatability of a global symmetry index. Even though the agreement and reliability of the angular kinematics used to compute the GGA were very good (Fernandes, Armada-da-Silva, Pool-Goudzwaard, Moniz-Pereira, & Veloso, 2016) and in line with the literature (McGinley et al., 2009), the GGA index presented very poor agreement and reliability between sessions. Specifically, the average difference in GGA between sessions was small (corresponding only to 2.3%), but the standard deviation was relatively large (31.7%), which means that the inter-session differences in GGA were small for some participants but large and in opposite directions in others. Consequently, even though the SEM was 22% of the average score, the 95% LOA were extremely wide and the MDC was very high (both being ~60%). These results indicate that, in repeated measurements, this index would present very large but meaningless fluctuations, and that only a very large change would be considered real. For example, an increase in leg length discrepancy of approximately 1.5 cm, shown to increase the GGA by approximately 19% (Cabral et al., 2016), would be considered below the minimal detectable change above measurement error and would therefore be overlooked. This poor agreement between sessions prevents the GGA from being used to monitor gradual changes in symmetry over time. The comparison with other symmetry scores is limited but demonstrates that the present MDC values were much worse than those reported for the symmetry ratio in spatiotemporal parameters in a group of stroke patients (between 8% and 18%) (Lewek & Randall, 2011). The GGA was also shown to have very poor reliability, with an ICC value (0.30) well below the recommended (0.70) (Nunnaly, 1978). This low reliability indicates that the variability within participants was very high in comparison to the variability between participants, making the distinction between individuals difficult. Furthermore, the 95% CI were extremely wide, with the lower CI reaching negative values, suggesting tremendous uncertainty in the proportion of variance that represents true score variability. These results preclude the application of the GGA to compare gait symmetry between subjects (i.e. between a patient and the normative database). In relation to other symmetry indices, the ICC value was comparable to the values obtained for another symmetry index (between 0.01 and 0.35) (Senden, Grimm, Heyligers, Savelberg, & Meijer, 2009) but worse than those obtained with the symmetry ratio (between 0.93 and 0.98) (Lewek & Randall, 2011). Thus, even though the GGA was designed to overcome the limitations of pre-existing indices, these findings show that its repeatability is worse and prevents its application in a clinical and research context, in its current form.

The variations between visits arise from both intrinsic and extrinsic sources. While intrinsic variability concerns the natural inter-trial and day to day variation of individuals, extrinsic variability results from experimental error (Schwartz et al., 2004). This study was carefully designed to minimise intrinsic variations. Specifically, the participants maintained their healthy status, the interval between sessions was small enough to prevent real changes in gait patterns, with both sessions occurring at the same time of day to minimise diurnal changes and, in each session participants were allowed sufficient time to familiarise with the experimental setting and to stabilise their gait pattern. Therefore, the large variation between sessions suggests high experimental error, as suspected in the first study. For angular kinematics, the most common experimental errors result from marker placement inconsistency and soft tissue artifact (Leardini, Chiari, Della Croce, & Cappozzo, 2005). Nevertheless, the joint kinematics used to compute the GGA were highly repeatable (Fernandes et al., 2016), similarly to previous studies (McGinley et al., 2009), which suggests that the experimental error was introduced by the mathematical calculation of symmetry itself. By summing the bilateral difference in each joint angle component at each percentage of the gait cycle, the GGA amplifies the error in the joint kinematics. In other words, a small deviation (i.e. 1º) in a segment coordinate system orientation between sessions will result in a large change in the symmetry score. Thus, for GGA to become more repeatable, it has to be less sensitive to this source of experimental error. In exploratory analyses, the use of different mathematical formulas yielded the same poor repeatability results, suggesting that the high sensitivity of joint angles to errors in the estimation of the local coordinate system orientation was a greater contributing factor.

Study 3 - Comparison of inter-session agreement and reliability among three global gait symmetry indices in healthy adults

Based on the previous findings, the following study (Chapter 4) was conducted to investigate if the experimental error could be reduced by removing some of the angular components that are known to be less reliable, or by replacing angles with a potential surrogate measure. To achieve this goal, two more global indices were used: the AsymGPS (Lundh, Coleman, & Riad, 2014), which also calculated symmetry from the bilateral differences in joint angles, but that did not include the knee frontal and transverse plane angles, nor the ankle frontal plane angle, and a modification of the GGA (LGGA) where all joint angles were replaced by the linear positions of the distal extremity of the segments. All three indices were calculated, using the same data that was used in the second study, along with their 95% LOA, SEM, MDC and ICC values. The comparison of these repeatability measures showed that the LGGA was by far the most repeatable index. Specifically, the ICC obtained for the LGGA (0.79) was much higher than those obtained for the other two indices (< 0.30), surpassing the minimum recommended for research purposes (0.70) (Nunnaly, 1978). Although for clinical measurements the general recommendation for ICC values is higher (>0.90), these recommendations are not absolute standards, leaving space for the judgement of the researcher or clinician within the context of the specific score (Portney & Watkins, 2009). Based on this premise, the present study shows that, in comparison to the LGGA, the GGA and the AsymGPS are not appropriate to compare symmetry levels among individuals, but further studies are necessary to verify the LGGA's ability to discriminate individuals with clinically relevant differences in gait symmetry. It is possible that the LGGA may still be highly reliable, despite having an ICC bellow the general recommendation for clinical measurements. According to a previous repeatability study (Lewek & Randall, 2011), the ICC values obtained for symmetry ratio (between 0.93 and 0.98) were higher than those obtained for the LGGA. [For the point we are trying to make, we will leave out the potential difference in samples heterogeneity (which affect the ICC values) and the methodological limitations of the aforementioned study]. Despite the high levels of ICC, the ability of the symmetry ratio to discriminate stroke survivors from healthy individuals was not very good (Patterson, Gage, Brooks, Black, & McIlroy, 2010). The poor to moderate discriminative ability of the symmetry ratio in the face of high reliability may be due to the fact that spatiotemporal symmetry does not provide a fair assessment of overall gait symmetry (Roerdink, Roeles, van der Pas, Bosboom, & Beek, 2012). Therefore, as a global symmetry index, the LGGA may be more sensitive to differences in symmetry among individuals, despite its greater portion of error variance (i.e. lower ICC value). In terms of agreement, the differences in symmetry between sessions in LGGA were much lower and more consistent among participants. Consequently, the 95% LOA, SEM and MDC values obtained for the LGGA were generally lower than those obtained for both the GGA and the AsymGPS. These results indicate that the LGGA has higher agreement, and therefore is more appropriate to assess changes in symmetry over time. The higher measurement errors demonstrated by the GGA and the AsymGPS represented a greater portion of total variance, thus explaining their considerably lower reliability. Still the LGGA showed lower agreement than the symmetry ratio (Lewek & Randall, 2011), but again this should be considered with caution given their questionable methodology and the limitations of the symmetry ratio. Longitudinal studies are needed to assess if change in LGGA reflect true changes in symmetry as a result of injury or rehabilitation.

Unexpectedly, this study also showed that the AsymGPS was even less repeatable than GGA. The main differences between the two scores are the angular kinematics included in the calculation and the mathematical equation. Based on our previous exploratory analysis we believed that the angular kinematics had a higher impact on the score's repeatability than the mathematical equation. Hence, our expectation was that, independently of the mathematical equation, the removal of the least reliable kinematics would improve the score's repeatability. But it is possible that by leaving one of the least reliable kinematics (hip rotation (McGinley et al., 2009)) the score's repeatability remains low. Nonetheless, considering that there were less unreliable variables in AsymGPS, its lower repeatability can only be explained by the formula used for the AsymGPS (RMSE). Specifically, because the squared bilateral differences are averaged inside the square root, the AsymGPS may give more weight to larger absolute differences (Chai & Draxler, 2014). The higher bilateral differences are typically found on the coronal and transverse planes, which happen to be the most affected by marker placement inconsistency (Della Croce et al., 1999; McGinley et al., 2009). Therefore, despite having less variables in the less reliable planes, the AsymGPS seems to artificially inflate asymmetry, which in turn may result in higher measurement error and lower agreement between sessions.

Overall, this study shows that global symmetry indices based on joint angles are not repeatable, and that the mathematical formula used in the global index may affect its psychometric properties. These findings represent a significant contribution to the limited knowledge that currently exists in this area, and highlight the importance to continue this work in these and other symmetry indices.

Study 4 - Global gait asymmetry of knee osteoarthritis patients in comparison to healthy adults

Given that the LGGA is reliable and has acceptable measurement error, study 4 compared different groups of individuals. These comparisons are essential to further investigate the relationship between gait asymmetry and the development/progression of pathologies as well as the effectiveness of interventions. To achieve this, the LGGA must be sensitive to clinically relevant differences in symmetry. As such, the final study (Chapter 5) was conducted to analyse if the LGGA could detect real symmetry differences between healthy individuals and those with a pathology typically associated with asymmetry. To achieve this goal, the LGGA scores of a group of individuals with KOA were compared to those of a group of healthy individuals. As expected, the LGGA scores were significantly higher in the KOA group (indicating greater asymmetry), and according to the previous study, this difference was above measurement error (difference between median LGGA scores: 0.55; MDC: 0.45). Although the two groups presented different characteristics (healthy individuals were younger, taller and had lower body mass and BMI), there is no evidence to suggest that these characteristics had an influence in the symmetry scores. Furthermore, gait speed and the bilateral differences in segment geometry (potential confounding variables) were similar between the two groups, suggesting that the increased asymmetry found in the KOA group was representative of truly asymmetric gait patterns. Moreover, this increase in asymmetry is supported by the literature (Asay, Mündermann, & Andriacchi, 2009; Bejek, Paróczai, Illyés, & Kiss, 2006; Christiansen & Stevens-Lapsley, 2010; Creaby, Bennell, & Hunt, 2012; Mills, Hettinga, Pohl, & Ferber, 2013; Turcot, Sagawa, Hoffmeyer, Suvà, & Armand, 2015; Viton et al., 2000), giving us confidence that the LGGA is capturing the asymmetrical gait pattern of these patients. Nevertheless, these group differences present a limitation. Furthermore, this study should not be taken as proof of validity (even though the results compared favourably with expectations) as this demands further testing and the use of different analyses (Terwee et al., 2007).

2. Conclusion

The work in this thesis consists of preliminary steps in the development of a global index that can be used, as real time feedback, in gait retraining programs to restore gait symmetry. The present series of studies showed that the initially proposed index (GGA) was able to comprehensively represent overall gait symmetry, being sensitive to changes that occurred within the same session, but unfortunately could not provide consistent measurements in different sessions. This poor repeatability, which was shared with another global index, was shown to be associated with the great sensitivity of joint angles to inaccurate estimations of the segments' pose. As a result, the GGA was modified into LGGA. This new index presented superior and acceptable intersession agreement and reliability, in a group of healthy individuals, and was able to capture the increase in gait asymmetry typically found in patients with KOA.

The LGGA presents several advantages over the currently existing measures of symmetry. Namely, as a global symmetry index, it provides a more comprehensive assessment of overall gait symmetry, without hiding compensation strategies among the different segments. Its global nature is not only beneficial from an assessment perspective, but also from a learning point of view. Furthermore, the LGGA overcomes limitations that were common among other symmetry indices, particularly the potential for artificial inflation. On the other hand, these characteristics prevent the inclusion of variables with different physical quantities into the score, and the assessment of the direction of symmetry, which may be clinically relevant. Specifically, the LGGA was intentionally designed to increase successively with bilateral absolute differences so that asymmetries with different directions are not cancelled out, as this would result in an underestimation of asymmetry. This means that the LGGA will always change with the magnitude of the asymmetry, but will not be sensitive to changes in the direction of symmetry for the same magnitude of asymmetry. Nevertheless, as a symmetry measure, the LGGA can complement, rather than replace, the information obtained from a three-dimensional gait analysis. As such, it provides an objective summary measure of gait symmetry, but the information regarding the mechanism behind the level of symmetry must be obtained from the remaining data.

3. Methodological considerations

Symmetry calculation

The choice for the mathematical formula for our global index originated from GASI (Hoerzer et al., 2012), which was, at the time, the only global symmetry index that produced a single metric. Based on this index, but leaving out the PCA analysis, our global index was designed as the magnitude of a difference vector between the bilateral gait curves. However, we chose not to normalise the differences or the variables included in the vector to avoid the risk for artificial inflation. When variables or differences in variables that are more prone to error (i.e. those in the transverse and coronal plane) are divided by smaller values (i.e. their range), their asymmetry is artificially inflated (Herzog, Nigg, Read, & Olsson, 1989). Moreover, the existence of other global gait indices (i.e. the GPS (Baker et al., 2009)), which also did not normalise the gait variables, further supported our decision. Nevertheless, to allow this to be explored later on, the equation was slightly changed. Hypothesising that the attribution of different weights to each variable could be a better normalisation alternative, we chose to have a difference vector per variable (and sum them to obtain a single score), rather than a long difference vector that included all the variables. This would also allow the index to be decomposed to provide a better understanding of which variables contribute more to the overall score. By choosing out of the normalisation, the index could no longer accommodate variables with different physical quantities (angles, moments of force, etc). Thus, considering our long term goal to use the index in gait retraining and that instrumented treadmills are considerably more expensive, we chose to include only joint angles (or, later on, the linear distances between the "joint centres" and the centre of the pelvis). Finally, in contrast to what is done in other symmetry indices, we chose to calculate symmetry between each two consecutive gait cycles, rather than between the mean curves of each side. This may provide a more accurate representation of gait symmetry (Vagenas & Hoshizaki, 1989), particularly when assessing variables or populations with greater intra-limb variability (Zifchock & Davis, 2008). Although a previous study has found similar results in running symmetry when the Symmetry Angle was calculated using consecutive and non-consecutive steps, these findings may not generalise to walking or to other symmetry indices and variables (Zifchock & Davis, 2008).

Marker set and modelling

Three-dimensional motion analysis requires the determination of the instantaneous pose (position and orientation) of segments (Cappozzo, Catani, Leardini, Benedetti, & Della Croce, 1996). The quality of the results depends on the chosen marker set and the pose estimation algorithm, and on the conventions to represent model based items (i.e. joint angles). Although the use of conventional gait models is more appealing to clinical practice due to the reduced number of markers and cameras needed (Richards, 2008), these models are more prone to error. Namely, given their use of direct pose estimation methods (non-optimal), the segments' coordinate systems are computed at each frame of the motion trial as they are in the static calibration trial, thus making no assumption about the rigidity of the bodies. Consequently, these models have a minimal ability to compensate for soft tissue artifact, as an error in the position of a marker results in a direct error in the estimation of the segment's coordinate system (Robertson, Caldwell, Hamill, Kamen, & Whittlesey, 2014). Furthermore, the coordinate system of the distal segment is computed using a virtual joint centre that is created with reference to the proximal segment, which means that errors in the pose of the proximal segments propagate to the distal segments (Robertson et al., 2014). Finally, using this shared virtual joint centre and constraining the translational degrees of freedom may introduce unnecessary errors in the angular kinematics (Cereatti, Camomilla, Vannozzi, & Cappozzo, 2007; Schmitz et al., 2016). While six degrees of freedom models are still affected by soft tissue artifact and marker placement imprecision, they overcome the theoretical limitations of conventional gait models and are highly reliable (Collins et al., 2009).

Taking this into account, the marker set and model used in this thesis were based on the calibrated anatomical system technique (CAST) (Cappozzo, Catani, Croce, & Leardini, 1995). Explicitly, the model was composed of 8 independent rigid segments (trunk, pelvis, thighs, shanks and feet). The pelvis was created based on the CODA pelvis model (Robertson et al., 2014). The remaining segments were created so that their frontal planes were defined by the medial and lateral markers at the distal extremity and by the midpoint between the markers at the proximal extremity (or by the proximal virtual joint centre, in the case of the thigh). Additionally, the longitudinal axis is created from the midpoint between the aforementioned markers of the distal extremity to the midpoint (or virtual joint) at the proximal extremity (the origin). Subsequently, the anterior-posterior axis is created using the cross-product between the longitudinal axis and the frontal plane, and finally the medial-lateral axis is created from the cross-product between the longitudinal and the anterior-posterior axes. These coordinate systems are therefore orthogonal, right-handed and distally biased, with the medial-lateral axis pointing to the right.

In the first three studies, the joint angles were calculated into the joint coordinate system (Grood & Suntay, 1983) due to its wide use in biomechanics and its ability to provide rotations with a functional and anatomical meaning (Robertson et al., 2014). For the knee joint angle, we created a second coordinate system that was proximally biased, by defining the frontal plane with the markers at the medial and lateral femoral condyles and the midpoint between the medial and lateral malleoli (Robertson et al., 2014). This decision was made to reduce the effect of potential structural asymmetries (i.e. tibial torsion) in the overall GGA score.

Choice of reliability and measurement error parameters

The ICC is the most commonly used reliability parameter for continuous measures (Terwee et al., 2007). According to Weir (2005) there are ten ICC models in total, and the choice for the appropriate model requires the consideration of four issues: (1) one-way or two-way models, (2) fixed or random effects, (3) single or average scores, and (4) inclusion or exclusion of systematic error.

(1) One-way models collapse the systematic and random variability (error) together, and assume that different subjects may be assessed by different raters (in other words, each rater does not need to assess all subjects). Conversely, two-way models allow the partitioning between systematic and random error, and assume that all subjects are assessed by the same rater (or group of raters). The design of test-retest repeatability studies mandates that all subjects are assessed by the same rater in different occasions, therefore requiring the use of 2-way models.

(2) A factor is fixed when all its levels are included in the analysis, contrasting with random factors in which the levels are only a sample of possible (random) cases, and the resultant analysis can be used to generalise to other levels. Again, in the case of our repeatability studies, the subjects constitute a random factor, since they are only a sample of possible cases, but the single rater, which is the only rater of interest, constitutes a fixed factor. As such, the most appropriate ICC model is one with mixed effects.

(3) ICC models can be applied to either single measurements (i.e. a single GGA score obtained from one cycle) or average measurements (i.e. the average of x GGA scores obtained from x cycles). Although their interpretation is different, mathematically the ICCs for single measurements are just a special case of ICCs for the average of x scores.

(4) Systematic error is one that results in unidirectional changes in the scores of repeated measures, such as learning or fatigue. Random error, on the other side, randomly increases or decreases the scores of repeated testing (i.e. normal biological variability). Although some authors defend that systematic error should be included in the analysis of measurement error (Terwee et al., 2007), it has also been argued to be a natural phenomenon and not a contributing factor to reliability in test-retest situations (Weir, 2005). Since our repeatability studies were carefully designed, the systematic error was expectedly small. This expectation was confirmed in exploratory analyses, where a

two-way mixed-effects ICC model that includes systematic error provided strikingly similar reliability results.

Taking this into consideration, we chose to use the two-way mixed-effects model, $ICC_{C,k}$ (McGraw & Wong, 1996) or $ICC_{3,k}$ (Shrout & Fleiss, 1979), in our repeatability studies.

It is well know that the ICC values can be influenced by the variability between subjects in the sample. Specifically, a large ICC (high reliability) can be obtained when the variability between subjects is large, despite poor inter-trial consistency. Conversely, even when inter-trial consistency is high, the ICC may be lowered by the homogeneity in the sample, making the differentiation of subjects difficult. Therefore, the interpretation of the ICC should be done in conjunction with the examination of the measurement error (Weir, 2005). The SEM is an adequate representation of measurement error (Terwee et al., 2007). Contrarily to ICC, the SEM is a fixed characteristic of a measure and does not depend on the sample's heterogeneity. But like ICC, the SEM can either include or exclude the systematic error. In order to be consistent with the chose ICC model, and considering that systematic error was small, we chose to calculate $SEM_{consistency}$, which does not take systematic error into account.

There are three ways to calculate $SEM_{consistency}$ (de Vet, Terwee, Knol, & Bouter, 2006): (1) as the square root of the mean of squares of the residual, which is obtained from the ANOVA table ($SEM = \sqrt{\sigma_{residual}^2}$), (2) by dividing the SD of the mean differences between the two measurements by the square root of two ($SEM = SD_{diff}/\sqrt{2}$), and (3) or by transforming the ICC formula into $SEM = \sigma\sqrt{(1-ICC)}$, where σ is the total variance. The use of the latter formula is discouraged because the choice of the ICC model, and its dependence on sample heterogeneity, can affect the size of the SEM (Weir, 2005). Thus, given that the first two formulas provide equivalent results we chose to calculate SEM in our studies as $SEM = \sqrt{\sigma_{residual}^2}$.

Symmetry indices for other motion capture technologies

Throughout the introductory chapter, we presented several symmetry indices and how they evolved from using a single biomechanical parameter at a specific point of the gait cycle to using multiple biomechanical parameters throughout the entire gait cycle. To collect the amount and type of data used in the latter indices, optoelectronic systems were often used (Hoerzer, Federolf, Maurer, Baltich, & Nigg, 2015; Lundh et al., 2014; Nigg et al., 2013). However, given the cost and the training associated with these systems, others (mentioned below) have developed symmetry indices specifically to use with accelerometry data. In these indices the biomechanical parameter is again reduced to one or two, but the entire acceleration signal is used (although it is not clear if the analysis is done for each gait cycle or for a series of gait cycles). Namely, Kobsar et al (2014) and

Yoneyama (2013) proposed different methods to calculate symmetry from a single accelerometer attached to the lumbar spine, and Sant'anna and Wickström (2010) proposed another method that used two accelerometers attached to each lower leg. Kobsar et al (2014) first calculated the step and stride regularity as the autocorrelation between the original signal and the same signal shifted by the average step and stride duration, respectively. Symmetry was calculated as the percent difference in these two parameters for each of the three signal components (vertical, medio-lateral and antero-posterior). Yoneyama (2013) first integrates the acceleration signals and then calculates and represents visually a 3D autocorrelation spectrum and a 3D biphasicity score. Finally from these visual representations two symmetry indices are calculated as the unit vector along the axle (axis of the minimum score) and as the angle formed by this axle and the x-axis. Lastly, Sant'anna and Wickström (2010) used an abstract method to calculate symmetry through the symbolisation of the acceleration signals. Other cost-effective alternatives that are currently emerging are the methods proposed by Auvinet et al (2015) and Moevus et al (2015) using depth cameras.

Some of these indices were not known when we initiated the development of our global index, and those that did, were not initially considered due to their specificity with regards to the technology used. Although we recognise that optoelectronic systems may be expensive, they are already available in many gait labs, and are becoming more affordable. Additionally, we believe it is important to first develop and test the index with the best data available, and only then find or develop more affordable surrogate measures. Moreover, the index developed in this thesis can be applied to other technologies that provide the 3D positions of segments' extremities. The aforementioned indices are interesting options, but further testing and knowledge of their psychometric properties is essential before they can be applied in a clinical context.

4. Recommendations for future research

Even though the present thesis shows that the LGGA is repeatable and sensitive to the higher level of asymmetry of KOA patients, further studies should be conducted to learn more about the psychometric properties of the LGGA, before it can be used in a clinical context. In terms of validity, in the absence of a gold standard, the relationship between LGGA scores and the degree of deviation of various bilateral biomechanical parameters from normality should be analysed. Additionally, the ability of the LGGA to discriminate individuals with a clinically relevant asymmetry should be objectively quantified. In these analyses, the potential normalisation of the index to height should also be addressed, to see if it would improve or worsen the validity of the index. The repeatability of the LGGA should also be further explored. Specifically, future repeatability studies should be extended to clinical populations and should also assess the inter-assessor agreement and reliability. Finally, longitudinal studies should be conducted to assess the responsiveness of the LGGA to clinical interventions that are known to be effective and to lead to improvements in gait symmetry.

At last, once the results from the aforementioned studies are satisfactory, the efficacy of gait retraining using LGGA as augmented feedback should be investigated, by exploring if the expected gait adaptations occurred acutely and persisted in the long term, and by analysing their associated long term effects. This application was the initial motivation for this thesis. Nonetheless, similarly to gait indices, the LGGA can complement the standard gait report by providing an objective summary assessment of the patient's overall gait symmetry.

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Thesis related outcomes

First author papers in scientific journals

Published

Cabral, S., Resende, R. A., Clansey, A. C., Deluzio, K. J., Selbie, W. S., & Veloso, A. P. (2016). A Global Gait Asymmetry Index. Journal of Applied Biomechanics, 32(2), 171–177

Submitted

Cabral, S., Fernandes, R., Selbie, W. S., Moniz-Pereira, V., Veloso, A. P. (April, 2016). Inter-session agreement and reliability of the Global Gait Asymmetry index in healthy adults. Gait and Posture.

Cabral, S., Fernandes, R., Selbie, W. S., Moniz-Pereira, V., Veloso, A. P. (July, 2016). Comparison of inter-session agreement and reliability among three global gait symmetry indices in healthy adults. Journal of Biomechanics.

Cabral, S., Fernandes, R., Moniz-Pereira, V., Yázigi, F., Selbie, W. S., Espanha, M., Veloso, A. P. (August, 2016) Global gait asymmetry of knee osteoarthritis patients in comparison to healthy adults. Archives of Physical Medicine and Rehabilitation.

Podium presentations

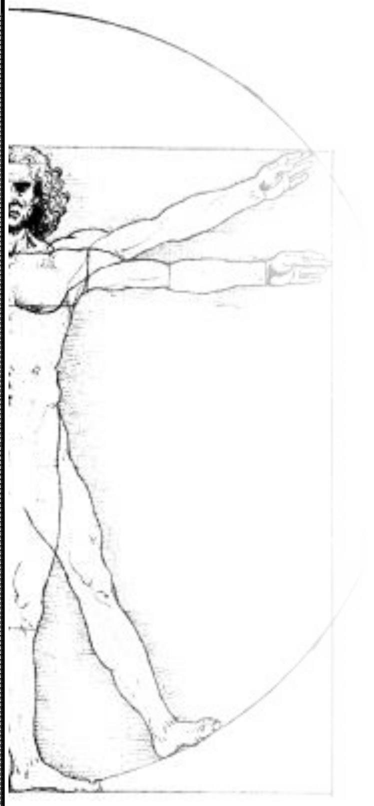
Cabral, S., Selbie, W. S., Fernandes, R., Yázigi, F., Moniz-Pereira, V., Armada-da-Silva, P., Espanha, M., Veloso, A. P. (2015). Differences in global gait asymmetry between knee osteoarthritis patients and healthy adults. 25th Congress of the International Society of Biomechanics, Glasgow, UK.

Cabral, S., Resende, R., Clansey, A. C., Selbie, W. S. and Veloso, A. P. (2015) Desenvolvimento de uma medida global de assimetria da marcha. 6º Congresso Nacional de Biomecânica, Monte Real, Leiria, Portugal.

Poster presentations

Cabral, S., Resende, R., Clansey, A. C., Selbie, S. W. and Veloso, A. P. (2014). Development of a global gait asymmetry score. 7th World Congress of Biomechanics, Boston, MA, USA.

Appendix



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Compilation authorization

We, the co-authors of the article "A global gait asymmetry index", published in 2016 in the Journal of Applied Biomechanics, volume 32, pages 171-177, hereby authorize its inclusion in the thesis "Development of a global gait symmetry score using biomechanical parameters", submitted by the PhD candidate Sílvia Arsénio Rodrigues Cabral.

Cruz-Quebrada, 25th August, 2016

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(Sílvia Cabral)

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(Renan A. Resende)

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(Adam C. Clansey)

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(Kevin J. Deluzio)

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(W. Scott Selbie)

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Compilation authorization

We, the co-authors of the article “Inter-session agreement and reliability of the Global Gait Asymmetry index in healthy adults”, submitted to the journal Gait & Posture, hereby authorize its inclusion in the thesis “Development of a global gait symmetry score using biomechanical parameters”, submitted by the PhD candidate Sílvia Arsénio Rodrigues Cabral.

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(Flávia Yázigi)

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