Objective and quantitative techniques to assess gait abnormalities in guinea pigs with primary and progressive osteoarthritis (OA).

Honors Research Thesis

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Abstract

Osteoarthritis is a painful, debilitating disease caused by the breakdown of cartilage in the joints. It is a chronic, progressive condition and is the leading cause of long-term disability in developed nations. The Dunkin-Hartley (DH) guinea pig is a naturally occurring model of OA that spontaneously develops the disease at around 3 months of age. DH guinea pigs experience histological changes in the development and progression of OA in their knee joints that is similar to humans. The CatWalk® gait analysis system is a computer-aided, video based apparatus, used to assess gait abnormalities in small animals. For this experiment, we looked at the effects of OA on the gait of the DH guinea pigs, as well as a control guinea pig strain, using the CatWalk®. We also assessed gait using a more traditional method called ink-blotting. We then treated the animals with a nonsteroidal, anti-inflammatory agent (NSAID) and studied its effectiveness at influencing gait parameters using the CatWalk®. We concluded that the CatWalk® was an effective technique to detect gait abnormalities between guinea pig strains with varying degrees of disease progression. We also demonstrated that treating the DH guinea strain with an NSAID improved several gait abnormalities brought about by OA, including an increase in the walking velocity, base of support, print area, stride length, and swing speed.
Introduction

Articular cartilage is composed of chondrocytes embedded in an extracellular matrix (ECM) of collagen, proteoglycans, and noncollagenous constituents. Chondrocytes normally support a steady-state equilibrium between anabolic and catabolic activities that maintains the structural integrity of the ECM (Goldring & Goldring, 2004). Circumstances that impair the biochemical and biomechanical properties of cartilage can disrupt this balance, which results in a net loss of cartilage and causes a decrease in joint function (Trippel et al., 2004). Continued degeneration of cartilage ultimately leads to remodeling of subchondral bone and the formation of osteophytes at joint margins – representing hallmark radiographic signs of osteoarthritis (OA) (Malemud & Goldberg, 1999). Although cartilage is the principle site of injury, OA also involves a transitory and potentially episodic inflammation of the synovium that contributes to deterioration of the joint (Poole, 1999).

OA is a chronic, progressive, and degenerative articular disease that is common in weight-bearing joints (Miller & Clegg, 2010), particularly the hip or knee (Jansen et al., 2011). It is believed to be a consequence of mechanical and biological events that destabilize the normal coupling of degradation and synthesis within articular joint tissues (Fernandes et al., 2002). OA is considered one of the major concerns in human health care because of the vast number of people involved and the severe impact this sometimes crippling disease can have on quality of life (van Weeren & de Grauw, 2010). To date, there is no cure for OA. The only available treatments aim at reducing symptoms, including pain and inflammation, to maintain joint mobility and limit the loss of function (Henrotin et al., 2011).
Dunkin-Hartley (DH) guinea pigs show mild cartilage degeneration at about 3 months that becomes progressively worse with advancing age. They exhibit peripheral sensitization such that joint movements, even in the normal working range, elicit burst activity of primary afferent neurons and pain (Schuelert et. al, 2010). Compared to other laboratory models of experimental OA, the DH guinea pig model of naturally occurring OA is more attractive from the standpoint of clinical relevance since there is no artificial derangement of the joint (McDougall et. al, 2010). These animals develop OA of the knee that bears histological and biochemical resemblance to human OA with lesions appearing predominantly on the medial side of the joint (Aaron et. al, 2007). In addition to the use of DH guinea pigs, an OA-resistant strain, Strain 13, has been established for comparison purposes.

Gait disturbance is identified as a breakdown in performance and gait analysis provides insight into the underlying OA progression (Ferland et. al, 2011). The CatWalk® by Noldus, is a gait analysis method that allows easy quantification of a large number of locomotion parameters during walkway crossing (Koopmans et. al, 2005). With this computer-assisted method of locomotor analysis, it is possible to objectively and rapidly quantify several gait parameters (Vrinten & Hamers, 2003) that are both dynamic and static, and is capable of taking into account the animal’s speed and weight distribution. The Catwalk® was originally designed by Hamers et. al, (2001), to assess spinal cord injuries in rats. It has also been used to study diseases and injuries to the nervous system, such as Parkinson’s (Vlamings et. al, 2007) sciatic nerve injury (Bozkurt et. al, 2008), spinal lesions (Gorska et. al, 2008), as well as joint injuries resulting from monoarthritis (Ängeby-Möller et. al, 2008), rheumatoid arthritis (Simjee et. al, 2007),

and osteoarthritis (Ferland et. al, 2011). While the Catwalk® has been used to study the role of secondary OA in gait, it has not been used in a naturally occurring OA model, such as the DH guinea pig.

Prior to the development of the Catwalk®, one primary means of assessing an animal’s gait was by collecting images of its footprints, a process dubbed “ink blotting”. The anatomical landmarks on the feet are smeared with non-toxic paint or ink and the animal is then allowed to walk down the track, leaving its footprints on normal paper (Dijkstra et. al, 2000). It is convenient to visualize the paint on the plantar surface before walking an animal, ensuring that all the important anatomical structures may be represented on the print (Johnston et. al, 1991). Footprint analysis was often used because it can be performed quickly; is economical; is quantitative and objective; allows visualization of uneven weight-bearing distribution or pressure areas, of toe drag, and of asymmetry of anatomical structures; and serves as a permanent record for later comparison and for motivating the patient to walk more effectively (Shores, 1980). Once imprinted on the sheet, the footprints are then manually measured with a standard ruler.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are one of the most commonly used drugs due to their analgesic, antipyretic, and anti-inflammatory properties (Johnson & Day, 1991). In particular, these medications are useful in treating musculoskeletal problems such as OA (Goodrich & Nixon, 2006) because they are thought to be able to relieve some of the discomfort associated with the disease. To date, few studies have been reported that monitor gait changes in laboratory animals following administration of NSAIDs.

For the present study, three primary aims were investigated: 1. to compare the
effectiveness of the Catwalk in assessing gait versus the traditional method of ink-blotting; 2. to determine how OA affects joint movement by assessing several dynamic and static parameters in disease-prone and resistant guinea pigs via the CatWalk®; and 3. to assess the effectiveness of flunixin meglumine in influencing CatWalk®-determined gait parameters in the Hartley guinea pig model of OA.

Materials & Methods

All procedures were approved by the university’s Institutional Laboratory Animal Care and Use Committee and performed in accordance with the NIH Guide for the Care and Use of Laboratory Animals. Four Hartley guinea pigs were obtained from Charles River Laboratories (Wilmington, MA) and four Strain 13 animals from the U.S. Army Medical Research Institute of Infectious Diseases (Fort Detrick, MD) for data collection at 480 days of age. Animals were housed in groups of two in solid bottom cages and allowed ad libitum water and guinea-pig chow (Harlan Teklad 7006) containing vitamin C (800 mg/kg) and vitamin D3 (2.4 IU/g). Body weight (grams) was monitored throughout the study.

Animals were acclimated to both the ink blot technique and the Noldus Catwalk® 7.1 (Leesburg, VA) over the course of one week; training and eventual data collection were all performed during the same period of the day (10AM to 4PM) and consistently involved the same four individuals. Animals were randomly selected to undergo either ink blot or Catwalk® data collection.

Following completion of the study, animals were humanely euthanized. Both knees from each animal were evaluated using the described scoring system. Whole knee
joints were fixed in 10% neutral buffered formalin and prepared for histological analysis, as previously described, with the following modifications: after a monitored period of decalcification in 8% formic acid/hydrochloric acid, joints were cut in half on a coronal plane and further decalcified in 8% formic acid/acetic acid. Decalcification was standardized within harvest age to ensure that adequate processing was attained with minimal exposure to acidic conditions. Paraffin sections (5 µm) were taken from the center of the medial tibial plateau in each joint and stained with toluidine blue or subjected to immunostaining, as described below. Two independent, blinded observers performed histological grading of serial coronal sections of each knee, using adapted Mankin criteria based upon characteristic features of OA in this species (Santangelo et al, 2011). Histological evidence of chondropathy incorporated: (1) grading of articular cartilage structure from 0-8; and (2) grading of proteoglycan loss, as determined by loss of toluidine blue staining intensity, from 0-6. Chondropathy was scored for the medial and lateral tibial plateaus; total scores ranged from 0 (normal) to 28 (severe structural damage and complete loss of toluidine blue staining),

Ink Blot Analysis – To provide a consistent length and width to the technique, ink blot analysis occurred through the tunnel provided with the Catwalk® system (described below). Six distances (Table 1) were measured from the heel of one print to the heel of the designated print of interest. Six different parameters were assessed for the ink blotting method. All footprints were measure heal-to-heal for each limb. As a statistical difference between contralateral limbs was not present, distances for front limbs and hind limbs were combined. “Stride distance” was the distance between the same limbs. This was measured for both when the limbs were together and apart. “Ipsilateral together” was
when the front and hind limb on the same side were together. “Ipsilateral apart” dealt
with the front and hind limb were apart on the same side. “Contralateral distance” was the
distance between either both hinds or both fronts. It was also measured when the limbs
were apart and together. All distances were measured in centimeters (Figure 1).

CatWalk® Analysis – All procedures were executed in the dark (except for light
emitting from the nearby computer screen) to enhance the contrast of the paw print
images; this was also the environmental condition in which animals were most
comfortable walking on the elevated platform. The Catwalk® system of automated gate
analysis has been previously described (Mogil, 2010). Subjects traversed a glass plate
walkway (100x15x0.6cm) through a 17.6cm wide tunnel. LED light entered the distal
long edge of this glass floor from an encased fluorescent lamp and was internally
reflected, scattering at points where the paw touches the glass. A high speed color video
camera was located 44cm beneath the apparatus and recorded the digitized signal for later
analysis by a computer running the CatWalk® software 7.1. Two infrared light beams
located 90cm apart were used to detect the arrival of the animal and control the start and
end of data acquisition. In addition to animal velocity (cm/s), a number of static and
dynamic, individual paw print parameters were determined by the Catwalk®. As for the
ink blot analyses, statistical differences were not present between individual, contralateral
front, or contralateral hind limbs and these data were combined. Parameters studied
included velocity, base of support of the hind limbs, base of support of the front limbs,
print area of the hind limbs, print area of the front limbs, stride length of the hind limbs,
stride length of the front limbs, swing speed of the front limbs, and swing speed of the
hind limbs. Velocity (cm/sec) was calculated by dividing the distance crossed by the
animal in the corridor with the time taken to complete the distance (Ferland et al., 2011). Base of support is the amount of pressure (units of pressure/cm²), in terms of pixels, the animal places on each limb. Print area is the total floor area contacted by the paw during stance phase; that is, the area that would be blackened if the animal’s paw had been painted with ink (Hoffmann et al., 2010). Stride length is how long each step with each limb is. The swing speed (m/s) parameter is computed by dividing the stride length by the swing phase duration (Ferland et al., 2011). For data analysis, software automatically labeled all illuminated areas containing pixels above the set threshold (7 pixels). To determine the influence of a NSAID in CatWalk gait parameters in both guinea pig strains, 5mg/kg flunixin meglumine was administered once subcutaneously between the shoulder blades. Four hours post-administration of the drug, animals were run on the CatWalk, as above, for data collection. A total of two complete, uninterrupted runs were analyzed for each animal under each experimental condition.

Statistical Analysis – Body weight and gait analysis data are represented as mean ± standard error of the mean (SEM); total tibial OA indices are shown as median ± range. Contralateral front and hind limbs were analyzed for both ink blotting and CatWalk parameters using paired t-test; as no statistical differences were present for either technique, these data were combined to allow front limb and hind limb comparisons. Body weight and individual ink blot parameters were analyzed using unpaired t-tests. Individual CatWalk parameters were analyzed using repeated measures two-way ANOVA (based on variables for guinea pig strain and application of the NSAID) followed by Bonferroni post-tests. OA indices were analyzed using the one-way analysis of variance (ANOVA), Kruskal-Wallis test, followed by Dunn’s Multiple Comparison
post-hoc test, as previously described (Santangelo, et al 2011). All statistics were performed using GraphPad Prism Version 4.0 (La Jolla, CA) with a statistical significance of p<0.05.

Results

A significant difference in body weight was not detected between Hartley (971.80 ± 64.89 grams) and Strain 13 animals (1035.00 ± 65.50 grams). As expected, a significant difference (p<0.01) in OA scoring was present between Hartley [20 (18-24)] and Strain 13 [10 (8-13)] animals.

Ink Blot Analysis – No significant differences were found in the front stride distance, hind stride distance, ipsilateral together, ipsilateral apart, or the front contralateral parameters (Table 1). A significant difference was noted, however, in the hind contralateral stance distance between the OA and OA-R groups, which indicated that the OA animals plant their hind limbs closer together when compared to the OA-R group.

CatWalk® Analysis – Figure 2 shows the results for the velocity using the CatWalk®. A significant difference was noted between the OA group verses the OA-D, OA-R, and OA-RD. No significant differences were detected between the OA-D, OA-R, and OA-RD.

For the base of support of the hind limbs (Figure 3), it was noted that the OA group placed significantly more units of pressure on the hind paws when compared with the OA-D, OA-R, and OA-RD groups. The OA-D, OA-R, and OA-RD groups were not statistically different from each other. The drug did not affect the amount of pressure
placed on the hind limbs of the OA-R and OA-RD groups; however, OA-D had a significantly decreased base of support compared to that of the OA-R and OA-RD groups.

The base of support for the front limbs (Figure 3) shows that a statistical difference was found between the OA group and the OA-D group. No statistical difference was found between the OA, OA-R, and OA-RD groups. There was also no difference detected between OA-D, OA-R, and OA-RD. The OA-D group puts significantly more pressure on their front paws when compared with the OA group.

Figure 4 displays the data for the print area of the front limbs. The OA-D group had a significantly larger print area when compared with the OA, OA-R, and OA-RD groups. It can be noted that OA alone does not influence the print area of the front limbs, but print area is increased when an OA animal receives the drug. No significant differences were detected between the OA, OA-R, and OA-RD groups.

Figure 4, the print area of the hind limbs, shows that the OA-D group had a significantly larger print area when compared with the OA, OA-R, and OA-RD groups. It can be noted that OA alone does not influence the print area of the hind limbs, but the print area is increased statistically when the OA animal receives the drug. No significant differences were detected between the OA, OA-R, and OA-RD groups.

For the stride length of the front limbs (Figure 5), a significant difference was found between OA and OA-R groups. No significant differences were detected between the OA, OA-D, and OA-RD groups. Significant differences also were not found between the OA-R, OA-D, and OA-RD groups. OA guinea pigs have a significantly shorter stride length than OA-R guinea pigs, however the OA-D group did not have a stride length that
increased significantly from the OA group to the OA-R group.

The stride length of the hind limbs (Figure 5) shows a significant difference between the OA and OA-R groups. No significant differences were found between the OA, OA-D, and OA-RD groups, nor were they noted between the OA-R, OA-D, and OA-RD groups. OA significantly shortened the stride length, but the OA-D did not see enough of an increase in stride length to be statistically significant from the OA group.

As seen in Figure 6, the swing speed of the front limbs of a guinea pig with OA is significantly less that of the OA-R and OA-RD. However, the OA-D group has a significantly faster swing speed than either the OA-R or OA-RD groups. No significant differences were found between the OA-RD or OA-R groups.

The results of the swing speed of the hind limbs (Figure 6) shows a significant difference between the OA and OA-R and OA-RD groups. The OA-D group also shows a large statistical difference when compared to the OA-R and OA-RD groups. No other significant differences were found.

Discussion

Because of the vast variety of parameters the Catwalk® was able to detect in an efficient and timely manner, we have concluded that this method is preferable to the traditional ink-blotting method. In particular, ink-blotting cannot factor in the animals’ speeds or weight distributions. The animals also tended to drag their feet, leaving smears across the paper that were difficult to measure. Ink-blotting was also unable to detect significant differences in stride length, a parameter of note in which the CatWalk® was, indeed, able to detect significant differences between the OA-prone and OA-resistant
guinea pig strains. In addition, the animals tended to pause within the tunnel, creating lines that oftentimes were not straight enough to measure. With the CatWalk®, data are only analyzed when the animal completes an uninterrupted run in a straight line. Ink-blotting was also challenging because the first few steps often appeared smeared because of excessive paint, while the final steps were often incomplete because most of the paint had already worn off. Manually measuring each individual parameter with a ruler ended up being tedious and far more time consuming than the CatWalk®. The ink-blotting method was only able to detect a statistically significant difference in gait for one parameter, while the CatWalk® was capable of assessing statistical differences in a wide variety of parameters.

Ink-blotting was, however, able to study one parameter that the CatWalk® was unable to detect. Ink-blotting is capable of measuring contralateral distances between limbs. Given that ink-blotting was able to detect statistical differences in the hind contralateral parameter, it remains a potentially valuable means of gait analysis.

When the OA animals were given a NSAID, they reached velocities that were not statistically different from that of the OA-R and OA-RD animals. We can conclude from this that the walking speed of OA-prone animals was influenced by treating with an NSAID. Ferland et. al, (2011), studied the effects of OA on the velocity of rats in experimental models of OA using the CatWalk®, but results did not yield any significant findings for this parameter. It may be worthwhile to investigate the effects of NSAIDs in these same models to see if a difference in walking velocity can be detected in these animals.

Guinea pigs with OA placed significantly more pressure on their hind limbs when
compared to the OA-R and OA-RD groups. When given the anti-inflammatory agent, however, they were able to decrease their base of support to that of an OA-resistant animal, potentially related to the increased walking velocity of these animals. For the base of support of the front limbs, the OA group did not place a significantly different amount of pressure on their hind limbs when compared with the OA-R and OA-RD groups. However, they did manage to put significantly less pressure on their front limbs when compared to the OA-D group. Given that the velocity of this group has increased, it is plausible that the drug allows them to place more pressure on their front limbs to compensate for the fact that they are placing less pressure on their hinds. To date, there is no other scientific literature available that looked at the effects of joint disease on the base of support using the CatWalk®. However, Ferreira-Gomes et. al, (2008), noted that OA animals minimize contact with the floor and exert less pressure on the painful limb during walking, thus showing a decreased weight bearing in the osteoarthritis limb (Ferreira-Gomes et. al, 2008). Angeby-Moller et. al, (2008), also made note of this using in rats with monoarthritis.

The print area of the front limbs did not differ between the OA and OA-R and OA-RD groups. However, when given an NSAID, the OA group statistically increased the print area of their front limbs. It is possible that this increase is directly related to the increased base of support as a result of increased walking velocity. In other words, the OA guinea pigs had an increased print area because there was an increased amount of pressure on each of their front limbs to compensate for their increased velocity. For the print area of the hind limbs, the OA-D group had a much larger area when compared to the other three groups. Like the front paws, this is probably due to a change in their base
of support. However, since the base of support of the hind paws decreased following treatment with an NSAID, it is presumed that the print area is increased while the intensity of the pixels, interpreted as base of support, is decreased. Interestingly, Masocha & Pavarthy, (2009), did not detect any differences in the print area of the hind limb when using the CatWalk® to assess for gait differences in mice with monoarthritis. Hoffmann et. al, (2010), also did not detect any differences in print area during their study with rheumatoid arthritis and rats.

The stride length of both the front limbs and hind limbs was significantly longer in the OA-R group when compared with the OA group. However, when given the NSAID, the OA-D group did not end up having a stride length that was significantly different from the OA group. There were also no significant differences between the OA-D and the OA-R and OA-RD groups. This suggests that, although walking velocity is increased in OA animals receiving an NSAID, this increased speed is not related to an increase in stride length.

For the swing speed of the front and hind limbs, the OA group was significantly slower when compared to the OA-R and OA-RD groups. When given an NSAID, however, the OA-D group had an increased swing relative to the OA-R and OA-RD group. It is plausible that treating with an NSAID may allow OA animals to overcome shortcomings in limb movement brought about by the presence of disease. For the swing speed of the hind limbs, the OA-D group moved significantly faster than the OA-RD and OA-R groups.

In summary, this is the first work to evaluate the CatWalk® Gait Analysis system in a guinea pig model of naturally-occurring disease. This study is also the first to study
the effects of a NSAID on parameters related to movement afflicted by disease progression. Given that the DH guinea pig has histological changes similar to those seen in joint disease in humans, this animal model may be a better choice for screening of future experimental drugs aimed at modifying the symptoms and pathology related to OA.
References


Mogil JS, Graham AC, Ritchie J, Hughes SF, Austin JS, Schorscher-Petcu A, Langford DJ, Bennett GJ (2010) Hypolocomotion, asymmetrically directed behaviors (licking, lifting, flinching, and shaking) and dynamic weight bearing (gait) changes are not measures of neuropathic pain in mice. Molecular Pain 6(6): 34.


Figure 1. Representative ink blotting trial (A) and a schematic (B) of four of the parameters of interest that may be measured by this technique.
Table 1. Results from the six gait parameters measured via the ink-blotting technique

<table>
<thead>
<tr>
<th>Parameter</th>
<th>OA Group (N=4)</th>
<th>OA-R Group (N=4)</th>
<th>p-value (OA vs. OA-R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipsilateral apart</td>
<td>9.74 ± 0.91</td>
<td>8.86 ± 1.53</td>
<td>0.5637</td>
</tr>
<tr>
<td>Ipsilateral together</td>
<td>3.21 ± 0.79</td>
<td>2.90 ± 0.82</td>
<td>0.6070</td>
</tr>
<tr>
<td>- mean ± SD</td>
<td>2.94 [2.64 – 3.78]</td>
<td>2.81 [2.22 – 3.59]</td>
<td></td>
</tr>
<tr>
<td>- median [IQR]</td>
<td>2.94 [2.64 – 3.78]</td>
<td>2.81 [2.22 – 3.59]</td>
<td></td>
</tr>
<tr>
<td>Front contralateral</td>
<td>1.84 ± 0.19</td>
<td>2.29 ± 0.59</td>
<td>0.1993</td>
</tr>
<tr>
<td>- mean ± SD</td>
<td>1.90 [1.70 – 1.99]</td>
<td>2.13 [1.83 – 2.75]</td>
<td></td>
</tr>
<tr>
<td>- median [IQR]</td>
<td>1.90 [1.70 – 1.99]</td>
<td>2.13 [1.83 – 2.75]</td>
<td></td>
</tr>
<tr>
<td>Hind contralateral</td>
<td>2.98 ± 0.57</td>
<td>4.00 ± 0.34</td>
<td>0.0221**</td>
</tr>
<tr>
<td>Front stride distance</td>
<td>13.44 ± 1.38</td>
<td>10.95 ± 2.18</td>
<td>0.1009</td>
</tr>
<tr>
<td>Hind stride distance</td>
<td>12.69 ± 1.09</td>
<td>11.50 ± 1.39</td>
<td>0.2258</td>
</tr>
</tbody>
</table>

t test was used for the two-group comparison.

** statistically significant difference, p<0.01.
Figure 2. Velocity (cm/sec) of guinea pigs prone and resistant to osteoarthritis (OA) as determined using the Noldus CatWalk Gait Analysis System. The velocity for the OA group was significantly less than the other groups, for which no statistical difference was detected.

OA= Dunkin-Hartley (DH) guinea pig group
OA-D= DH guinea pigs receiving a NSAID
OA-R= Strain 13 guinea pig group
OA-RD= Strain 13 guinea pigs receiving a NSAID
* = statistically significant difference, p value <0.05
** = statistically significant difference, p value <0.01
Figure 3: Base of Support of the hind and front limbs (units of pressure/cm²) of guinea pigs prone and resistant to osteoarthritis (OA) as determined using the Noldus CatWalk Gait Analysis System.

OA= Dunkin-Hartley (DH) guinea pig group
OA-D= DH guinea pigs receiving a NSAID
OA-R= Strain 13 guinea pig group
OA-RD= Strain 13 guinea pigs receiving a NSAID
*
**= statistically significant difference, p value <0.05
**= statistically significant difference, p value <0.01
Figure 4: Print Area of the hind and front limbs (mm²) of guinea pigs prone and resistant to osteoarthritis (OA) as determined using the Noldus CatWalk Gait Analysis System.

**OA**= Dunkin-Hartley (DH) guinea pig group  
**OA-D**= DH guinea pigs receiving a NSAID  
**OA-R**= Strain 13 guinea pig group  
**OA-RD**= Strain 13 guinea pigs receiving a NSAID  
* = statistically significant difference, p value <0.05  
** = statistically significant difference, p value <0.01
Figure 5. Stride Length (mm) of guinea pigs prone and resistant to osteoarthritis (OA) as determined using the Noldus CatWalk Gait Analysis System.

OA= Dunkin-Hartley (DH) guinea pig group
OA-D= DH guinea pigs receiving a NSAID
OA-R= Strain 13 guinea pig group
OA-RD= Strain 13 guinea pigs receiving a NSAID
 *= statistically significant difference, p value <0.05
 **= statistically significant difference, p value <0.01
Figure 6. Swing Speed (m/sec) of guinea pigs prone and resistant to osteoarthritis (OA) as determined using the Noldus CatWalk Gait Analysis System.

OA= Dunkin-Hartley (DH) guinea pig group  
OA-D= DH guinea pigs receiving a NSAID  
OA-R= Strain 13 guinea pig group  
OA-RD= Strain 13 guinea pigs receiving a NSAID  
* = statistically significant difference, p value <0.05  
** = statistically significant difference, p value <0.01