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Percutaneous Osseointegrated Prostheses for Amputees: Limb Compensation in a 12-Month Ovine model

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Abstract

Percutaneous osseointegrated prostheses are being investigated as an alternative strategy to attach prosthetic limbs to patients. Although the use of these implants has shown to be promising in clinical trials; the ability to maintain a skin seal around an osseointegrated implant interface is a major challenge to prevent superficial and deep periprosthetic infections.

The specific aim of this study was to establish a translational load-bearing ovine model to assess postoperative limb compensation and gait symmetry following a percutaneous integrated implant. We tested the following hypotheses: (1) the animals would return to pre-amputation limb loads within 12-months; (2) the animals would return to a symmetrical gait pattern (stride length and time in stance) within 12-months.

The results demonstrated that one month following surgery, the sheep loaded their amputated limb to a mean value of nearly 80% of their pre-amputation loading condition; by 12-months, this mean had dropped to approximately 74%. There were no statistical differences between the symmetry of the amputated forelimb and the contralateral forelimb at any time point for the animals stride length or the time spent in the stance phase of their gait cycle. Thus, the data showed that while the animals maintained symmetric gait patterns, they did not return to full weight-bearing after 12-months. The results of this study showed that a large animal load-bearing model had a symmetric gait and was weight bearing for up to 12 months. While the current investigation utilizes an ovine model, there data show that osseointegrated implant technology with postoperative follow-up can help our human patients return to symmetric gait and maintain an active lifestyle, leading to an improvement in their quality of life following amputation.

Keywords

Percutaneous; osseointegrated; gait; amputation; ovine

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Introduction

Limb amputation is a devastating outcome for those who experience severe traumas, survive certain cancers, or have certain congenital abnormalities. Furthermore, the number of patients afflicted with diabetes continues to rise, leading to a concomitant increase in the number of amputations related to diabetes (1998; 2001; Cowie et al. 2009; Cowie et al. 2010; 2011). Finally, as the number and severity of political conflicts increases worldwide, so does the number of combat-related amputations (Fischer 2009). With the increasing number of amputations, it is important to continue to explore potential improvements in the advancement of patient care with advanced prosthetic technology.

Socket-type attachment of an exoprosthesis is the standard of care for these patients, but is not always suitable for all patients. The technology fails when applied to limbs of limited length, especially in patients with multiple short residual limbs. Proper socket fit can be difficult to achieve and poor socket fit directly affects the activity level and satisfaction of the patient. These on-going limitations of the residual limb require repeated socket adjustments due to scarring, neuromas and fluctuations in the volume and/or length of the residual limb.

Even patients that are fitted with socket-type attachments can be dissatisfied since they frequently experience pain from persistent skin deterioration of the soft tissues resulting from poor socket fit (DesGroseilliers et al. 1978; Ehde et al. 2000; Dillingham et al. 2001; Hagberg and Branemark 2001; Mak et al. 2001; Marshall et al. 2002).

Finally, heterotopic bone formation can be induced by surgery or by trauma and can grow exuberantly into the soft tissues of the residual limb (Henrot et al. 2000; Potter et al. 2006; Potter et al. 2007) causing significant disability and limited range of motion. When load is applied through the socket to this underlying heterotopic bony mass, pressure damage occurs from necrosis as the skin and soft tissues are trapped between these hard surfaces (Henrot et al. 2000).

Percutaneous osseointegrated prostheses (POP) used as a docking system, is an alternant technology to sockets. These POP devices, also known in the literature as osseointegrated (Albrektsson et al. 1981; Branemark 1983; Hagert et al. 1986; Branemark 2003; Brånemark et al. 2005; Webster et al. 2009; Chou et al. 2010; Isaacson et al. 2010; Jeyapalina et al. 2011; Shelton et al. 2011) and endo-exoprosthesis (Aschoff 2009; Aschoff et al. 2009), represent a relatively new technology that is presently being investigated worldwide in an attempt to obviate the multiple shortcomings of socket technology by providing direct attachment in order to secure the exoprosthetic limb. Currently, there are three primary groups working with selected human amputee volunteers with this technology – Branemark and co-workers in Sweden, Aschoff and colleagues in Germany, and Blunn and Pendergrass in England). Their patients have reported significant improvements in their functionality as evidenced by improved range of motion (Moller et al. 1999; Sullivan et al. 2003), the lack of skin or residual limb problems associated with socket prosthetic attachment (Hagberg and Branemark 2009), greater overall satisfaction with their prosthetic device function (Moller et al. 1999; Henrot et al. 2000; Sullivan et al. 2003) and the previously unrecognized benefit of “osseoperception”, the central sensory feedback from the environment through the implanted bone (Jacobs et al. 2000; Sullivan et al. 2003; Klineberg 2005; Jacobs and Van Steenberghe 2006; Hagberg and Branemark 2009). Although there are multiple significant advantages seen in these clinical populations, the patients in these trials also show problems with high infection rates at the skin-implant interface, periprosthetic osteomyelitis, implant loosening, and long rehabilitation times associated with some of the existing procedures (Sullivan et al. 2003; Hagberg and Branemark 2009). The high infection rates are challenges that could be significantly reduced or eliminated by assuring that the natural antibacterial skin barrier were maintained at the skin-implant interface. Currently, these devices are not approved for clinical use in the United States and some other parts of the world due to the reported 18-50% infection rates (Hagberg and Branemark 2001; Hagberg and Branemark 2009).

To facilitate the global approval and clinical use of these osseointegrated percutaneous implants, we believe that a weight-bearing, large animal model needs to be established to study the efficacy of decreasing the infection rates at the skin implant interface. Previously, the ovine model has shown promise for the translational testing of bone endoprosthetic implants (Willie et al. 2004; Bloebaum et al. 2007; Pearce et al. 2007). Sheep have a body weight similar to that of most humans, have a bone morphology, structure and size appropriate for the testing of human implants (Newman et al. 1995; Willie et al. 2004) and have a bone remodeling rate similar to that of humans (Willie et al. 2004).

Gait analysis on amputees has also been performed as an important tool for assessing ambulation and weight bearing to confirm rehabilitation milestones and clinical endpoints (Kulkarni et al. 2005; Gard 2006). In quadrupeds, the analyses are complex in that animals have been reported to offload their injured limb and apply more loads to their three other limbs (Duda et al. 1998; Seebeck et al. 2005; Bockstahler et al. 2009). However, most of the quadruped gait literature deals with fracture healing events. Healing around a percutaneous, osseointegrated implant for amputees would most appropriately be compared with appositional bone formation into porous coated total joint replacements that has been well documented as appositional bone attachment (Hofmann et al. 1991; Bloebaum et al. 1992; Bloebaum et al. 1992; Hofmann et al. 1993; Bloebaum et al. 1994; Bloebaum et al. 1997; Bloebaum et al. 1998; Bloebaum et al. 2007) taking up to one year to achieve.

The specific aim of this study was to establish a load-bearing amputation animal model that could be used to evaluate percutaneous osseointegrated implant technology and to monitor the animal’s changes in gait patterns over time. The continued ambulation of the animal postoperatively would allow us to assess the effectiveness of the device, as reflected by weight bearing and gait analyses. Thus, we tested two hypotheses: (1) The animals would return to pre-amputation limb loads within 12-months; (2) The animals would return to a symmetrical gait pattern within 12-months compared to this contralateral limb.

Methods

Model Selection

Various animal models were investigated prior to this study, but sheep were chosen for this investigation because it was a large animal model with both body weights and bone remodeling rates comparable to an adult human (Willie et al. 2004; Peters et al. 2006; Bloebaum et al. 2007). Previous studies such as (Duda et al. 1998) show the efficacy of the forelimb application because the anatomical orientation of the forelimb was more vertical than the hindlimb, making it a better model for the implant design and postoperative observations and care.

Implant Design and Fabrication

The metacarpal III bones from an initial 20 mature crossbred sheep carcasses were imaged by using a clinically based CT scanner (LightSpeed VCT XT™, GE Healthcare Worldwide, United Kingdom) at a tube voltage of 100 kVp with an automatically calibrated variable current and stored digitally as DICOM files. These digital CT images were reconstructed using a commercially available software package (MIMICS, Materialise Corp., Plymouth, MI, USA), then ported to a custom analysis program for analyses (MatLab, MathWorks

Corp., Natick, MA, USA) to provide not only the anteroposterior and mediolateral dimensions, but also the three-dimensional morphology of the medullary canal at 1 mm increments throughout the length of each bone. From these data, 3 implant sizes and surgical broaches, corresponding to the 25th, 50th, and 75th percentiles, were designed (Intelligent Implant Systems, LLC, Charlotte, NC, USA) and fabricated (IMDS Co-Innovative, Logan, UT, USA) from the medical grade Ti_6Al_4V titanium alloy.

The intramedullary portion of each implant was textured by grit blasting to facilitate immediate bone attachment and to achieve bone/implant integration. The subdermal barrier and the most distal portion of the stem were coated with a 500-750 micron thick commercially pure titanium porous coating (P^2 type, Thortex Corp., Portland, OR, USA) with a porosity of 52 ± 12%. All of the implants were passivated following ASTM standard B 600 - 09, then sterilized using high pressure saturated steam at 121 C for around 20 minutes using an autoclave.

Surgery

Following an institutionally approved protocol, the right Metacarpal III bone of nine skeletally mature female sheep of mixed breeds (Rambouillet, Targhee, Suffolk, Crossbred, Polypay), aged 2-4 years, and weighing 80-95 kg were fitted with percutaneous osseointegrated implants. Each animal underwent a screening process prior to surgery to ensure they were healthy and the metacarpal was sized for implant selection radiographically. Next, the animals were anesthetized and prepared for surgery. An anteriorly based skin flap was made on the distal end of the right forelimb and the dewclaws were excised posteriorly. Care was taken to preserve the blood supply to the skin. The distal portion of the third metacarpal was transected at the metaphyseal flare and the medullary canal was reamed and a porous-coated (on the distal end), titanium implant was pressed and malleted into place. The fit and fill of the implant within the medullary canal was verified using intraoperative radiography. A central longitudinal “stab” wound was made in the skin flap and the flap was pulled over the Morse taper extending from the end of the implant. A Delrin® /polyurethane exoprosthetic limb, designed to weigh approximately the same as the amputated limb, was attached using a titanium adapter attached to the implant via the Morse taper protruding through the skin (Figure 1). Subjects were given 100-mcg fentanyl patch 12 hours prior to surgery and ketoprofen and buprenorphine immediately before surgery. Ketoprofen was administered for 7 days post-op and fentanyl patches were replaced every three days for a total of nine days (including the day prior to surgery).

Gait Analysis

A commercially available pressure mat (Tekscan HR Mat, Tekscan, Inc., South Boston, MA, USA) was used as it allowed the sheep to ambulate freely across the transducer while peak vertical forces (PVFs) were recorded from each limb as the animal moved through the gait cycle (Figure 2 right). The mat (width=0.45m, length=1.5m) was placed in the straight edge of an enclosed metal elliptical walkway (Figure 2 left). The sheep maintained a walking speed throughout the testing by the presence of a caretaker following them around the walkway. The walkway was approximately 0.6 m in width while the enclosure was 10 m in length, 4 m in total width, and 1 m high. A 3 mm thick outdoor carpet was placed over the sensor as a shim to prevent the animals from slipping and to protect the sensors and to avoid shying of the sheep as has been done in previous sheep studies (Seebeck et al. 2005). Force calibration was performed with the shim in place before each testing session.

The PVFs, the stride lengths, and the stance phases as a percent of the gait cycle were recorded for each animal before amputation (Time 0) and at 1-, 2-, 3-, 6-, 9-, and 12-months following amputation. During each recording session the animals walked across the sensor at least five times while data were recorded from each of the four limbs and synched with digital video images at a sampling rate of 30 Hz. This frequency was selected as it was the sampling rate of the digital images, ensuring that one frame from the pressure mat corresponded to one frame from the video recordings, allowing each limb strike to be analyzed correctly. The rationale for the frequent time periods chosen in this investigation was based on the endosteal bone response to endoprosthesis (Bloebaum et al. 1994; Hofmann et al. 1997; Willie et al. 2004). The fracture healing model time periods previously used (Duda et al. 1998) did not allow for the longer term 12-month follow up used in this study.

Once PVFs were obtained from each limb, the PVF weight distribution for each limb was obtained, as has been done with previous ovine studies (Kim and Breur 2008) using the following equation:

$$\text{PVF Distribution}=\frac{\text{PVF}^{\text{RF}}}{\text{PVF}^{\text{RF}}+\text{PVF}^{\text{LF}}+\text{PVF}^{\text{RH}}+\text{PVF}^{\text{LH}}}$$

where the superscript PVF^{RF}, PVF^{LF}, PVF^{RH}, and PVF^{LH} indicate the peak vertical forces for the Right Forelimb, Left Forelimb, Right Hindlimb, and Left Hindlimb respectively. The advantage of using the PVF Distribution over other measures is that it minimizes the influence of both the weight and the velocity of the animal. The postoperative PVF distribution for each limb was compared to the preoperative PVF distribution for each limb using a Two-Tailed Paired t-Test using commercially available software (Microsoft Excel, Microsoft Corporation, Redmond, WA, USA), and then adjusted for multiple comparisons using the Hochberg multiple comparison procedure.

Stride length was calculated as the distance from hoof strike to hoof strike, from the same limb, while stance phase as a percentage of the gait cycle, was taken as the time the animal was in stance phase divided by the time it took to complete one gait cycle. Temporospatial parameters, such as these, can be used to measure lameness in quadrupeds (Breur and Kim 2008; Sanchez-Bustinduy et al. 2010). The stride length and stance phase as percentages of the gait cycle from the amputated right forelimb were compared to the contralateral left forelimb at each time point to determine if the animals had a symmetrical gait. Statistical significance was determined using a Two-Tailed Paired t-Test (Microsoft Excel, Microsoft Corporation, Redmond, WA, USA) with the p-values adjusted for multiple comparisons using the Hochberg multiple comparison procedure. Data are displayed as means and 95% confidence intervals.

Results

Peak Vertical Forces (PVFs)

Preoperatively, the forelimbs of the sheep were loaded with approximately 33% more weight than the hindlimbs. This back-to-front load distribution was similar in trend with work previously reported in other ovine studies (Kim and Breur 2008). One month following surgery, animals loaded their amputated right forelimb with 80.4 ± 2.5% of the preoperative load ($p<0.05$) (Figure 3). The PVF distribution remained relatively constant for the next two months. However, between months 3 and 6, the value dropped significantly ($p=0.011$) to 78.6 ± 4.8% of the preoperative PVF distribution. By the end of the 12-month study, the PVF distribution had continued to decrease to 74.4 ± 4.0% of the preoperative value ($p<0.05$).

At 12-months, the animals were applying greater loads to the non-amputated left forelimb yielding a PVF distribution 15.3 ± 5.7% greater than the pre-amputation condition ($p<0.05$) while the left and right hindlimbs respectively had a PVF distribution of 8.2 ± 7.4% ($p<0.05$) and 10.1 ± 7.1% ($p<0.05$) greater than their pre-amputation condition (Figure 4). This shows that the sheep were applying more loads to the other three limbs and that less load was applied to the amputated right forelimb.

Stride Length

The stride length was approximately 1 m for all four limbs preoperatively and there was no statistical difference measurable in stride length between the forelimbs or the hindlimbs ($p>0.05$). One month following amputation, and throughout the remainder of this 12-month study, the amputated right limb and non-amputated left limbs were consistent with a stride length around 1 m. There was no statistical difference ($p>0.05$) measurable between the right and left forelimbs at any postoperative time point, indicating a symmetrical stride length between the amputated right forelimb and contralateral left forelimb.

Stance Phase as a Percent of Gait Cycle

Before surgery, the stance phase for each limb was between 54-60% of the total gait cycle. Preoperatively, there was no statistical difference measurable between the forelimbs or the hindlimbs ($p>0.05$). Over the course of the 12-month study, the animals spent approximately 60% of their gait cycle in stance phase. There was no statistical difference measurable ($p>0.05$) between the right forelimb and left forelimb at any postoperative time point. This shows that the sheep spent an equal amount of time, on each forelimb, at each time point throughout the study and supports the observation that there was no measureable gait asymmetry.

Discussion

This investigation confirmed that an amputation model was load bearing and would allow the assessment of percutaneous osseointegrated implant function and the ability to test the efficacy of the device. One month postoperative, the animals loaded their prosthetic limb less than they had preoperatively and their PVF distribution was never restored to pre-amputation loads disproving Hypothesis 1. The sheep had a physiologically symmetrical stride length and uniform time in stance phase, over the 12-month evaluation period, supporting Hypothesis 2.

Although the sheep never returned to their preoperative load status, the results of this study are promising as they conclude that an adequate skin seal was maintained preventing infection and allowing them to resume symmetrical gait patterns. For the first three months following surgery, the PVF distribution was approximately 80% of the preoperative value. Despite being load with less weight, these load amounts indicate a good initial fit showing implant stability and maintained skin seal. One very possible explanation for altered loading of the implant one month postoperatively could be the changed proprioception with the artificial implant. The Delrin/polyurethane exoprosthetic limb could have altered the feeling of balance and grip with the surface. However, one would expect that over time, the animals would have acclimated to the shortcomings of the exoprosthetic limb. Instead, over the 12-month period, the applied loads decreased to nearly 74% of the preoperative value. We believe that the decrease in loading over time could be due to stress shielding of the bone by the implants with resorption of the stress shielded bone and a subsequent decrease in cortical bone strength (Chou and Bloebaum 2008). Finite element models have shown that percutaneous, osseointegrated endoprosthetics can significantly change the stress and strain energy density levels in bones due to both the implant and altered loading conditions, providing another explanation for the decrease over time (Tomaszewski et al. 2010). Based upon the radiographic findings, all of the animals exhibited at least some distal resorption of the implanted third metacarpal, and this loss of bone may explain the change that occurred in the forelimb loading conditions over the 12-month study. This bone loss could be diminished by an implant design that would provide more uniform distal stress distribution along the bone-implant interface (Van Rietbergen et al. 1993; Aamodt et al. 2001; Swider et al. 2006; Xu and Robinson 2008). Given our present system design, it is unknown what would occur to the prosthetic limb loads after 12-months. A longer term study would be needed to determine if loads would continue to decrease, remain the same, or improve over time, as the bone continues to remodel around the implant. To compensate for the decreased load on the amputated limb, the animals applied a greater load to the other three limbs, with the greatest shift to the contralateral left forelimb.

Although animals loaded their prosthetic limb less throughout the 12-months study, they exhibited a symmetrical gait with regards to both stride length and time in stance phase throughout the study. These findings are supportive of the observation that lameness, caused by pain or discomfort (Breur and Kim 2008; Sanchez-Bustinduy et al. 2010) was absent, also reflecting the maintenance of skin seal in this investigation. Studies on unilateral above-knee amputees' show a 20% offload between the amputated and non-amputated limbs (Summers et al. 1987; Gauthier-Gagnon et al. 2000). However, these patients display an asymmetrical gait, especially with regards to time spent in stance phase (Jaegers et al. 1995; Nolan et al. 2003).

One possible limitation of this study was the potential saturation of individual elements on the pressure mat (sensels) with the exoprosthesis. The exoprosthesis had a smaller surface area than the hoof so there was the risk of some sensels becoming saturated during a limb strike; however, the number of saturated sensels was small and would not account for the 20-26% difference in postoperative PVF distribution from preoperative conditions. The accuracy might be improved by designing an exoprosthetic foot with a surface area similar to the hoof size of a sheep and by using a different shim material; although, only 2-3% error was noted suggesting good precision in the measurement system.

In conclusion, the ovine amputation model seems to be an effective load-bearing model at the 12 month time period which would allow continued investigations of developing a permanent skin seal for the prevention of high infection rates currently being promoted in clinical studies (Aschoff et al. 2009; Hagberg and Branemark 2009). Although our sheep did not return to preamputation loading conditions within 12-months, they were viable and active within the first month following amputation surgery and appeared to reach load bearing levels of 80% similar to patients with above human knee amputations. This model may be used with future amputation studies as a means to assess various implant designs that could lead to a better understanding of the stress needed to encourage bone remodeling and maintenance. A valuable application of this knowledge could be in the prevention and/or reversal of osteoporosis and osteopenia seen in the residual limbs of patients with amputations; conditions that persist with conventional socket technology (Rush et al. 1994; Kulkarni et al. 1998).

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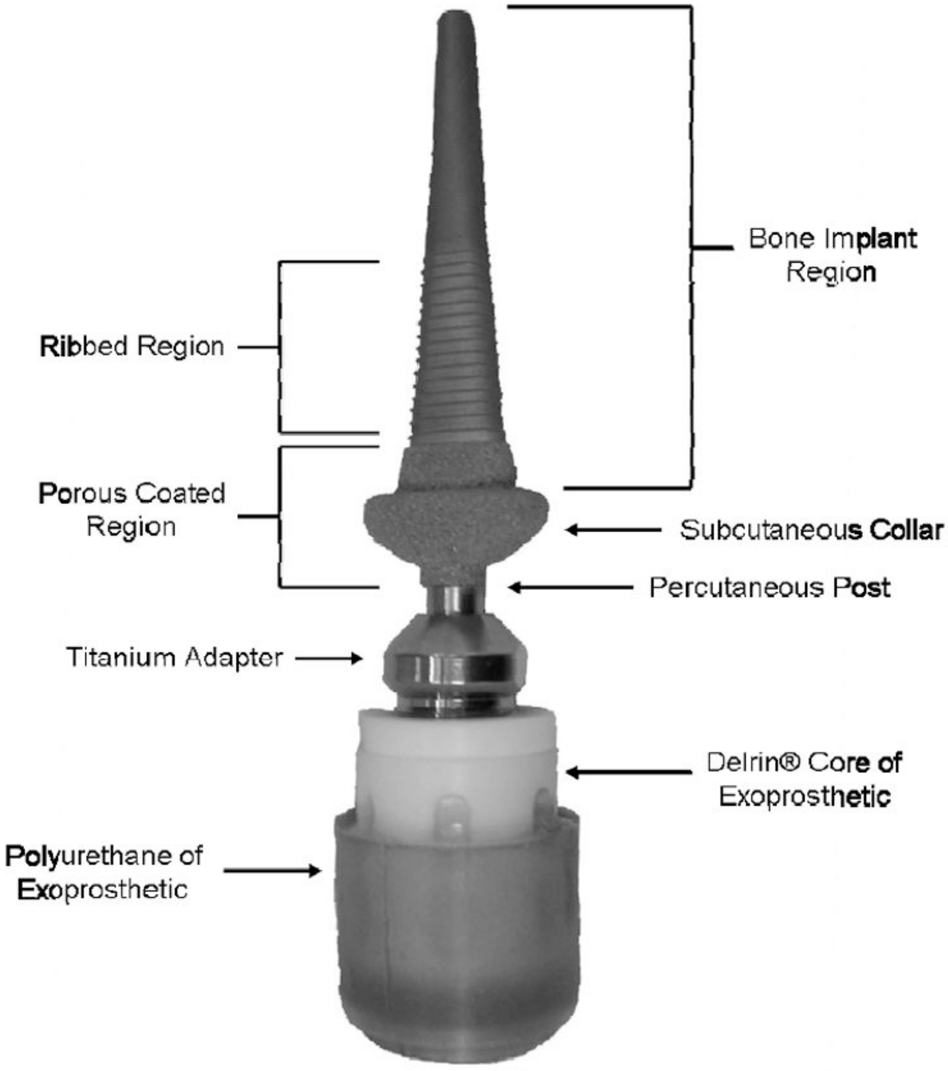

Figure 1.

Photograph of the percutaneous, osseointegrated implant used in the study showing the bone implant region, ribbed region, porous coated region, titanium adapter, and exoprosthesis.

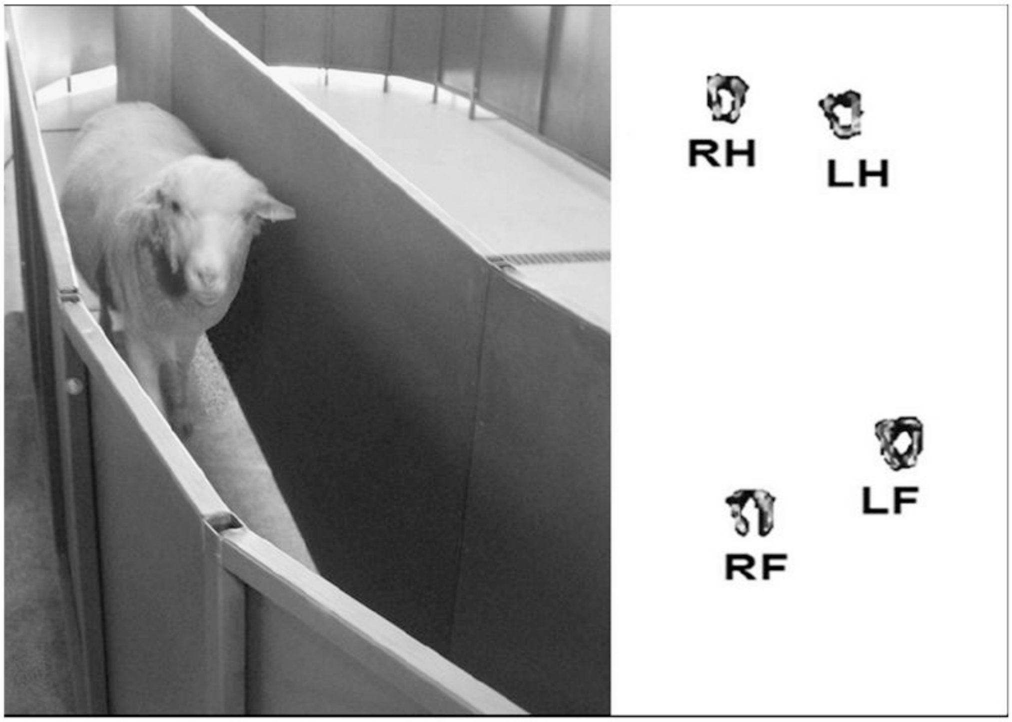

Figure 2.

(Left) Photograph of a sheep standing on the pressure mat within the enclosure. (Right) Output of the pressure sensing mat showing the Right Hindlimb (RH), Left Hindlimb (LH), Right Forelimb (RF), and Left Forelimb (LF).

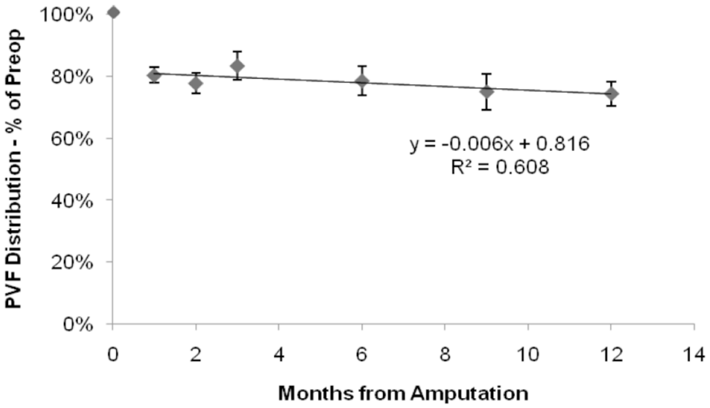

Figure 3.

Percent of preoperative PVF Distribution for the right (amputated) forelimb showing the amputated limb was loaded less after surgery for all time points, obtaining a value nearly 74% of the preamputation value.

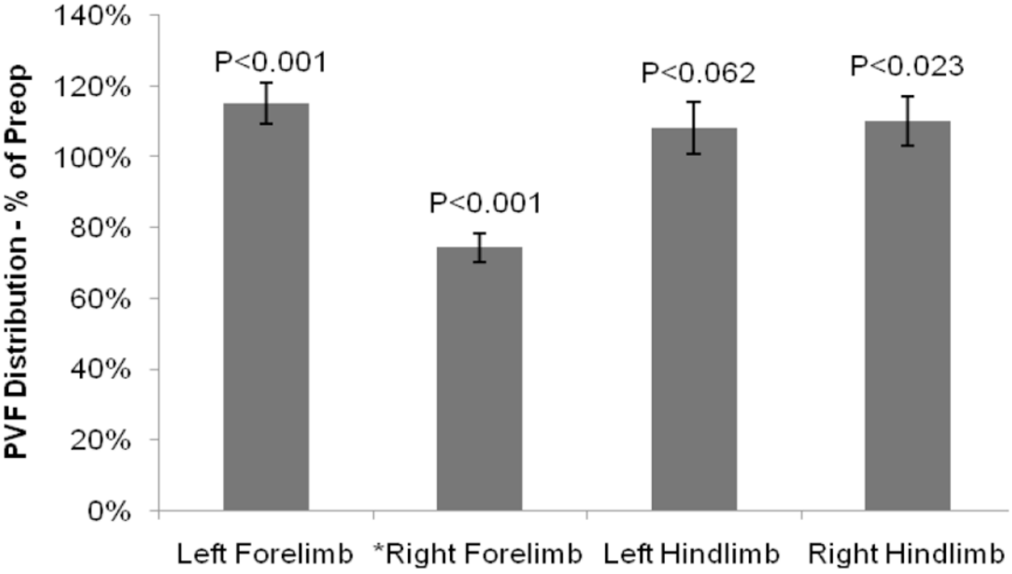

Figure 4.

Percent of preoperative PVF Distribution for the left forelimb, left hindlimb, and right hindlimb at 12-months postop, demonstrating that the three untreated limbs had a higher PVF Distribution following surgery to compensate for the decreased load on the right forelimb.