Chapter 10

Use of Natural Latex as a Biomaterial for the Treatment of Diabetic Foot — A New Approach to Treating Symptoms of Diabetes Mellitus

Suélia de Siqueira Rodrigues Fleury Rosa, Maria do Carmo Reis,
Mário Fabricio Fleury Rosa, Diego Cólon, Célia Aparecida dos Reis and
José Manoel Balthazar

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/59135

1. Introduction

Diabetes mellitus (DM) is one of the most investigated health issues today, and it is becoming a major concern for academicians and decision makers in Public Health, mainly due to its complications, which are associated with high rates of morbidity and mortality. This disease interferes with various aspects of the daily lives of the individuals affected and imposes various lifestyle restrictions. Some of its chronic complications are the most common causes of non-traumatic lower-limb amputations. In most cases, amputation is initially preceded by an ulcer on the foot. The diabetic foot, as defined by the World Health Organization (WHO), is a foot with an infection, ulceration, and/or destruction of deep tissue associated with neurological abnormalities and various degrees of peripheral vascular disease in the lower limbs. The various socioeconomic impacts of this disease in its more advanced stages, which result from prolonged hospitalization, rehabilitation, and the great needs for home care and social assistance, provide motivation for public health policies and research for new ways to prevent and treat the diabetic foot from a multidisciplinary perspective [1, 4]. In this chapter, we present the results of a study on factors that contribute to the prevention and treatment of diabetic foot ulcers using natural latex biomaterials made from *Hevea brasiliensis*, in the form of biomaterials applied to humans (in this case, in direct contact with the human skin). The chapter is organized in the following way: in section 2, it is defined what a diabetic foot is, to provide the context for addressing the problem. The use of natural latex biomaterials made from *Hevea brasiliensis* is discussed in the context of biotechnology, wherein *Hevea brasiliensis* is used as a raw material in the prevention and treatment of diabetic foot. In section 3, the diabetic foot is described by a mathematical model and it is presented how the use of biomaterial latex acts as modifier of the dynamics of the system to believe this application as a minor theory and/or auxiliary hypothesis in the biotechnological process as it applies to humans. In section 4 and 5 the chapter closes with a presentation of a "natural latex insole" prototype capable of preventing and treating diabetic foot ulcers.

2. International consensus on the diabetic foot

Among the consequences of DM are the increased incidences of amputation of the lower limbs and mortality. Many scientific studies have been conducted to increase understanding of diabetes and established a general framework for its treatment, prevention, and assistance. In light of these and other needs, the Brazilian Federal Government launched on December 17, 2011 a major public health policy, which is the National Plan on the Rights of the Disabled Person, or as it is more commonly known, the *VIVER SEM LIMITES (living without limits)*. The main objective of this initiative was to establish new fronts and intensify actions that were already being developed by the Government and/or the private sector for the benefit of persons with disabilities. This initiative established a set of public policies that were articulated along four axes: (1) access to education, (2) social inclusion, (3) health care, and (4) accessibility. These public policies were established by means of a plan of action that articulated and organized innovative initiatives in multiple subject areas designed to make it possible to achieve improvements in the quality of life, dignity, and rights of persons with disabilities. The research presented in this chapter fits into the context of this policy, as it is being conducted within the Center for Research, Development, and Innovation in Assistive Technology and Accessibility at the University of Brasilia (UnB), in partnership with the Engineering and Biomaterials Laboratory—BioEngLab®, Faculdade Gama (FGA), University of Brasília (UnB), which gives priority to the multidisciplinary asymmetry upon which this study is based. Diabetes mellitus is classified among the chronic diseases that are mostly asymptomatic or almost asymptomatic. These are diseases that do not endanger the life of a person in the short term. Shown by many researchers to be very costly, not only to the affected individuals and their families but also to national governments, it is the sixth most common cause of primary diagnosis in hospitalizations [1-6]. In Brazil, the prevalence of DM is approximately 15% in the age group above 35 years, according to [5]. In a perspective analyses, some studies [7-11] have reported that approximately 50% of patients are unaware of the diagnostics and that 24% of patients known to be diabetic make use of no treatment. This causes a variety of complications, among which the diabetic foot is notable, as it is considered a serious problem with often devastating consequences (the related ulceration, which can involve amputation of the toes, feet, or legs). Diabetes has been associated with several structural and functional alterations of the feet that can result in higher plantar pressures, anatomical deformities (claw toes, charcot neuro-osteoarthropathy), limited joint mobility, and skin changes (callus formation) [12]. The diabetic foot exhibits morphological alterations, and its distribution of the various tissues influences its functioning, resulting in a set of changes in the patient. This study focuses on biomechanical changes, with emphasis on the vertical ground reaction force involved. In [13], that is a major study of the biomechanics of gait analysis, the vertical ground reaction force was measured and the movement of the ankle joint was filmed in patients with diabetic neuropathy. That study showed that the values of the 1st and 2nd vertical ground reaction force peaks are greater in patients with diabetic peripheral neuropathy. The vertical ground reaction force was found to have different characteristics among the different groups studied; thus, methods to reduce the vertical ground reaction force are required to decrease the likelihood of developing plantar ulcers. In Brazil, because of the tropical climate and cultural norms, walking barefoot and using inappropriate or insufficient diabetic foot care (lack of good hygienic habits, hydration, transport type, etc.) are common [14]. According to the literature [15-17], the causes of foot injuries are strongly related to increased pressure in certain areas and deformities of the feet and toes. This is because of diabetic neuropathy (DN), which is considered to be the main permissive factor for developing foot ulcerations in diabetic patients. Lesions are generally caused by unanticipated and undesirable events that are complicated by possible gangrene and infection, because of deficiencies in the healing process, which can lead, in extreme cases, to amputation. It is known that ulcerations may lead to a decrease in the quality of life, prolonged hospitalization, consequent absenteeism, early retirement, and high economic costs associated with treatment and reduced working capacity of individuals of productive age. Recent studies provide information pertaining, in greater quantity and accuracy, to dramatic changes. In elderly patients affected by the disease, foot abnormalities can result in loss of stability that can lead to falls and consequently to death. Previous studies have used various tests, such as capturing a controlled gait, foot anthropomorphic measurements, and clinical examinations, to understand these changes. The results of previous studies have shown that pressure and shear stress variables are applied at distinct points and affect the frontal regions of the foot (the forefoot) more than the heel regions [18-22]. Among the changes that occur are reduced sensitivity to pain, vibration, and temperature; hypotrophy of small muscles; distention of the dorsal veins in the feet; and decreased postural sensitivity, which results in changes in gait and contributes to the formation of calluses [23, 24]. As some studies [4,5, 16, 17-21] have reported, these changes indicate that the feet of diabetic persons must be well cared for, protected, and accommodated accordingly, because of the risk of ulcers developing as result of repetitive trauma or, for instance, the presence of foreign objects inside footwear and/or inadequate accommodations. Another important factor involving the diabetic foot is that motor neuropathy also leads to muscle weakness and subsequently to intrinsic muscle atrophy of the feet. These changes result in deformities, such as claw and hammer toes (dominance of the flexors over the extensors), foot cavus (pronounced curvature of the foot), and pressure points in some areas of the feet (mainly in the metatarsal head, plantar, and dorsal regions of the feet), which change the normal gait pattern when walking [25]. Autonomic neuropathy leads to the reduction or total absence of sweat secretion, making the foot dry and the skin more susceptible to breakage than normal. Skin dryness favors the formation of fissures and cracks that, if not treated properly, can develop into ulcers with or without infection. Natural protection and skin integrity become less efficient, exposing the foot to the risk of mechanical lesions [26, 27]. It is evident that intrinsic and extrinsic factors contribute to abnormal pressure on the foot and the possible stress of accommodation. This chapter presents a new contribution to DM treatment and more specifically the diabetic foot problem. This contribution was developed by examining some of the extrinsic factors that contribute to the emergence of injuries that affect the diabetic foot and asking: how can these extrinsic factors be changed. This is the question that guided this research, which mobilizes a multidisciplinary group of researchers (in the areas of engineering, health, and human sciences) who believes that this study will contribute to customized biomechanical and behavioral changes. The following changes can be made with the proposed approach: decreasing the ground reaction force, increasing foot moisture, protecting against foreign objects, and modifying the DM gait performance index. Studies conducted in [28-34] to assess high-risk diabetic individuals have reported lower recurrence of ulcerations in groups given specially made shoes. These studies have also reported that special footwear can be beneficial to patients without expert foot care assistance and to those with severe foot deformities [28-34]. For this reason, to devise a treatment for ulcerated diabetic feet, it is vital to identify the worst-affected areas of the foot before pressure ulcers develop, using pressure gauges to establish the likelihood of preventing foot injuries through the use of customized insoles that redistribute pressure in high-pressure plantar regions during patient gait. The use of latex biomaterials in customized shock-absorbing insoles that are intended to prevent the emergence of diabetic foot ulcers constitutes a potential new contribution to diabetic foot treatment, as described in this chapter. The authors have questioned the usefulness of high foot plantar pressure in identifying neuropathy and consequent ulceration, because of the high coefficient of variation of plantar pressure. However, several other studies [35-33] have confirmed the role of mechanical stress on the development of ulceration, as well as the importance of relief of mechanical stress in the treatment of the neuropathic diabetic foot. Once patients are affected by DM, the ulcers and subsequent infection are its main complications [36]. Unless diabetic foot ulcers are properly diagnosed and treated, amputation is a frequent outcome. Other predisposing factors that have been identified as being related to increased plantar pressure include body mass, sensory deficit, and the presence of foot deformities [37]. Although diabetic patients are usually obese, body mass is a factor that can be related to the appearance of high plantar pressures and ulcers even if not combined with other factors (neuropathy, deformity). Diabetic foot treatment depends on the degree of commitment of the limbs, taking into consideration the presence and/or severity of ischemia and/or infection. Currently, there are a few options for the treatment of lesions, such as wound dressings (for which various types of bandages are available on the market), debridement of devitalized tissue, revascularization, local application of growth factors, oxygen therapy, human dermis (Dermagraft®), and amputation of extremities, the last of these being the option most frequently adopted [38-42]. Considering that diabetic foot patients are affected by serious shortcomings in scar healing, this process has been widely investigated [43-45]. Optimization of the tissue regeneration process has been studied and discussed in various lines of research, covering aspects such as pathophysiology, risk factors, anti-inflammatory drugs, and chemical substances that may influence the healing process [46-50]. Among the resources that have been proposed, low-intensity light-emitting diode (LED) therapy and the use of natural latex derived from the *Hevea brasiliensis* [50] rubber tree are noteworthy. The authors believe that this biotechnology association offers the potential for a new treatment approach, involving the use of a latex insole with LED light emission, through which healing can be induced. This treatment approach was developed by making use of the results obtained in the construction phase of the first shock-absorbing insole.

3. Participants, experimental set-up, and definitions

To ensure the suitability of the assumptions and methodological procedures pursued by the developers of the aforementioned treatment approach, the approval of the Research Ethics Committee of the State Secretariat for Health of the Federal District – Brazil (SES/DF/BR) was requested. This request was approved under Protocol 428/11. To carry out the data collection for testing and treatment in humans, two DM patients were selected, one of whom presented foot ulcerations and the other of whom did not. Both signed an Informed Consent Form (ICF), supported by a correlational descriptive and qualitative study of the relationship between the systematic collection of data and the immersion of the researcher in the context being studied [51]. The two individuals were personally contacted and invited to participate in the research. The instrument for obtaining data was a structured questionnaire with closed-ended questions and history taking (date of birth, sex, date of diagnosis, type of medicine, DM type, among other items) and application of the Michigan Neuropathy Screening Instrument questionnaire (a tool to assess symptoms related to diabetic neuropathy). The research group enrolled a patient without ulcers (who had never exhibited any ulceration) but who had pressure peaks, to test the first proposed method for correcting the performance indexes through the use of a shock-absorbing insole. We also enrolled a patient with an established ulcer who had not received prior treatment, to test for wound healing (scarring) through the use of a healing insole with red LED light.

3.1. Patient in need of plantar pressure correction

The first stage of the research was performed with the patient without any diabetic foot ulceration in the lower limbs. The focus of this stage of the research was on evaluating the effectiveness of the insole padding material in reducing plantar pressure. The patient was a 33-year-old female with Type 1 diabetes who had been diagnosed 24 years ago. She was married, had no children, had completed higher education and was a graduate student. She was a resident of the central region of the Federal District – Brazil, had a Class B license, was able to communicate and get around, and was an insulin pump user. Initially, an interview was conducted for data collection to characterize her gait condition, taking into consideration any gait change the patient exhibited while walking. Measurements were taken of the patient’s height, body weight, glycemic index (using an Accu-Chek active lancing device, with measuring strips and lancets), basal temporal dose, heartbeat, percentage of oxygen and anthropomorphic foot dimensions (via calipers). Subsequently, a questionnaire was administered to assess the patient’s quality of life, the patient’s mechanical activities (such as walking, climbing stairs, driving, and performing household chores), items related to financial considerations, side effects of medications, and lifestyle (overall dimensions). This patient was advised not to consume alcohol or any sort of medication for 24 h prior to the beginning of the experiment. The subject was informed about the experiment, and a trial run was conducted before the readings were taken. To determine where the latex shock absorbers should be placed in the insole that would be made for her, a pedographic test analysis was conducted. The equipment used was the emed®-n50 Novel platform (4 sensors/cm^2 resolution, frame rate of 50 Hz, dimensions of 700 x 403 x 15.5 mm, 6080 sensors, sensor resolution (sensors/cm^2) of 1 or 4/4/4, frequency of 50 Hz, pressure range of 10–1270 kPa, accuracy of ± 5% ZAS, temperature range of 10–40°C, maximum total force of 193,000 N) (emed® HMFT-novel-projects v23.3.44, © 2013 by Novel GmbH), which collects plantar pressure distribution data using sensors, data collection circuits, and appropriated software. The initial phase of the orthostatic recording was a "break-in" phase that began with the patient adopting a stable standing position in bare feet. The individual responsible for data collection then instructed the patient to remain in a standing position for 30 seconds with her eyes open for each dual-foot acquisition. She was asked to maintain the standing position and balance her body weight evenly on the right foot and left foot. This protocol was repeated three times to check whether the blood glucose checked at the time of testing (acute assessment) interfered with the results. Just before the plantar pressure assessment portion of each test, the patient's capillary glycemia was measured using a digital pulp puncture glucose meter (Accu-Chek System Active Glucose Meter, lancing device, measuring strips, lancet, and cotton). Figure 1 shows the equipment and system for the testing carried out to identify the highest pressure peak locations.

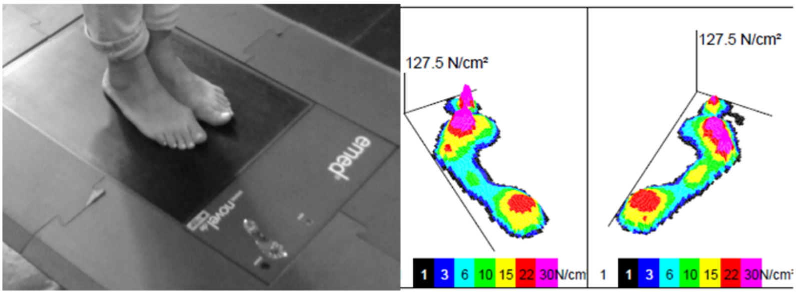

Figure 1. Photo image of the test carried out to measure foot pressure, taken by the authors with the patient's consent. The plantar pressure distribution image was produced by the emed®-n50 Novel software. The photo image highlights the frontal region of the foot as exhibiting the highest concentration of pressure. Image provided for data sample of plantar pressure: metatarsal head=MTH, hallux=toes, midfoot, and heel.

The second type of test was a static postural balance test conducted using kinetic data obtained with the AccuSway Plus force platform manufactured by AMTI. The sampling frequency was 100 Hz, and each data collection cycle lasted 30 seconds. For each cycle, four attempts were made with the patient's eyes open. The patient was asked to keep her eyes fixed on a point that was highlighted on the wall at the patient's eye level at a distance of 2.0 meters. The patient was also asked to extend her arms parallel to her body. Adhesive tape was used to mark the position where the patient should step on the platform for the four attempts. It should be noted that previous attempts were made and eliminated because of errors, such as variation of support, imbalance, arm movement, and noise in the room. To correct these errors, testing and data collection were conducted during hours with less activity/noise in the lab (saturday nights). The variables of interest that were measured were the magnitudes of the anterior–posterior (shift in y (cm)) and medial–lateral (shift in x (cm)) force centers and the average velocity of the shift from the force center (Vm in cm/s). These measurements were obtained for use in a comparative analysis with and without the patient foot insole. It should be noted that the insole selected was the one that promoted the largest plantar pressure reduction. Eight different latex insole models were made with different shock-absorbing formats, different associations, and protocols. These eight models were tested to identify the one that provided the patient with acceptable comfort, usability, and reduced pressure. The repeatability criterion was applied in the research, and the same insole model was made several times so that one from the lot that yielded the highest scores in the patient evaluation could be identified. For each insole, she completed a questionnaire, video was captured, and an evaluation was conducted by the authors. Figure 2 shows details of the test.

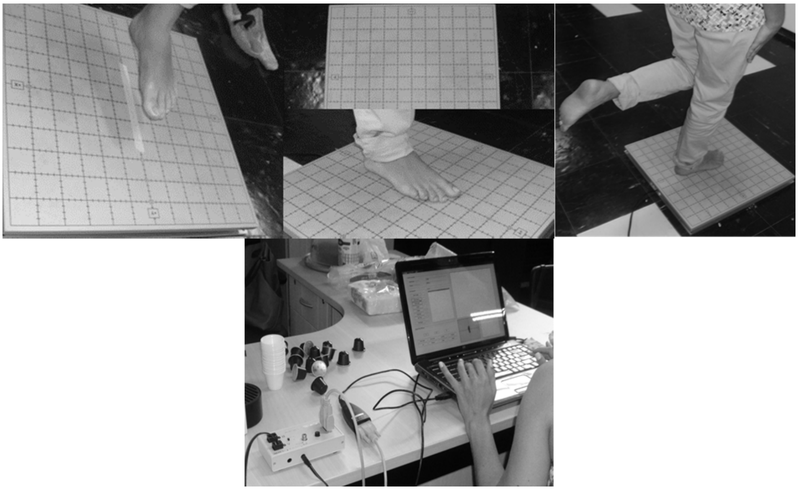

Figure 2. Pictures taken by the authors with details of the test conducted on the AccuSway Plus force platform manufactured by AMTI, with a sampling rate of 100 Hz and each collection cycle lasting 30 seconds. This platform was used to record static pressure and postural balance data, in compliance with the Nyquist criterion, with a postural static frequency value of 5 Hz.

Light Emitting Diodes (or LEDs) are semiconductor diodes that emit light when there is electrical current across them. They are manufactured in several wavelength bands (from 405 nm blue till 940 nm infrared) and in different emission patterns, that is, normal or LASER (Light Amplification by Stimulated Emission of Radiation). The LASER LED emit coherent light with a very narrow wavelength band (single color) while the ordinary LED emits in a wider band (several wavelengths). Both types of LEDs have different therapeutic purposes [49]. The blue light has renewing and anti-bacteria effects in the skin, and the red light has anti-inflammatory and scarring effect. The light intensity (emitted by the LEDs) necessary to obtain the desired therapeutic effects are lesser than LASER diodes, due to good interaction between the human skin and incoherent light (Rigau, 1996). Specifically, the blue light LED (470nm) has anti-bacteria action against *propionibacterium acnes*, by a process known as photo-inactivation (that is, the remotion of electrons from the bacteria's external citoplasmatical membrane by oxygen molecules) and the 660 nm red light also has anti-inflammatory effect and stimulate cellular multiplication. The LASER LED light has a directional effect while the ordinary LED is more spread in the area. The equipment consists of LED arrays (or cells) mounted outside and below the latex insole and they are placed only in the ulcerative regions in the feet, after a clinical examination. The light intensity is 25 J/cm² and the scarring effect is then expected. An electronic circuit controlling the LED array has a timer that terminates the process after a programmed time interval and a buzz to indicate the end.

3.2. Patient in need of established ulceration correction

In this chapter, it is presented two cases, but reference in [52], a study conducted previously have been all reported cases. The second stage of the research was conducted with the participation of the patient that had diabetic foot ulcers. This stage focused on correcting the established ulcer through the use of a healing insole associated with a red LED light. After the initial assessment, the subjects were divided into two study groups: control group (CG) and experimental group (GE). In GC: Treatment with foam dressing with silver and GE: treatment with the inducer tissue formation system.

The GC was made up of four patients and a total of five diabetic foot ulcers. These patients underwent conventional treatment for a minimum of 30 days and monitored weekly by the responsible team. A few of these patients were followed until complete healing of the ulcer. Before applying the foam dressing with silver, a nurse performed the wound debridement of devitalized tissue and hygiene with 0.9% saline and gauze. After cleaning, the ulcer had its bed dry with gauze and was found ready to receive the healing. After placing the foam with silver on the wound, gauze was placed over it and the closing was done by bandages. The exchange of this dressing was performed every 5 days at home by the patient or by its own family (except in the clinical evaluation days, where the curative was made by ambulatory nurse). Is worth mentioning that even when the dressing change was performed at home, it was necessary for the patient to carry out cleaning of the wound with 0.9% saline and gauze. The silver foam is foam made of antibacterial wound dressing impregnated with silver ions that are released continuously, to the extent that the exudate (fluid) is absorbed. The foam half silvered promotes moist environment for healing important factor.

The GE was made up of six patients and a total of nine diabetic foot ulcers. These patients underwent treatment with the healing inducer system for varying periods of tissue neoformation, and monitored weekly by the responsible team. Some of these patients used the system inducing tissue formation until complete ulcer healing. It is noteworthy that the inducing tissue formation system consists of a healing insole and an electronic circuit for tissue regeneration. After clinical evaluation to characterize the sample, it was taken the mold of the patient's foot for making the healing insole, since it is customized to each individual patient. Individuals from GE group were also monitored weekly by the responsible staff. At each time, the nurse performed the procedure debridement of devitalized tissue and cleaning the ulcer with 0.9% saline and gauze. The clinical and demographic characteristics such as age, sex, occupation, height, weight and the associated diseases in six patients belonging to the study, illnesses are listed in Table 1:

Patients and Group	age (years)	sex	height (m)	weight (kg)	occupation	Associated diseases
Patients 1 - GC e GE	46	F	1.59	98	homemaker	hypertension
Patients 2 – GE	53	M	1.75	72	Brazil server	hypertension
Patients 3 - GC e GE	57	F	1.72	87	homemaker	Nothing
Patients 4 – GE	64	M	1.78	82	businessman	hypertension
Patients 5- GC e GE	68	M	1.60	68	retired	hypertension
Patients 6 - GC e GE	62	F	1.57	60	homemaker	hypertension

Table 1. Clinical and demographic characterization of patients with diabetic foot ulcer.

Patients Group	Typeof DM	Time of Diagnosis DM	Number of ulcers already presented from the diagnosis	Number of ulcers treated in the study	Amputation (quantity and area)
Patients 1 - GC e GE	2	17	5	2	Off
Patients 2 - GE	2	12 anos	2	1	Off
Patients 3 - GC e GE	2	24 anos	6	4	two - 2nd toe (right foot) and 5th toe (left foot)
Patients 4 - GE	2	18 anos	4	1	Off
Patients 5- GC e GE	2	29 anos	3	1	two - 1st toe (hallux) and the 2nd to 5th toes (left foot)
Patients 6 - GC e GE	2	8 anos	3	2	two - the 2nd to the 5th toe, hallux and part of the foot (right foot)

Table 2. Data from patients relating to DM and diabetic foot ulcers.

Exploring the data in Table 1, it appears that patients in both groups have an average age of 58.3 years, with a minimum age of 46 years and maximum of 68 years; 50% of patients are female and 50% male; the average height of patients is 1,66m; 50% of patients have weight above average weight (77.8 kg). Regarding occupation, it was predominant householding, comprising two patients (33.3%). And 83.3% of patients, in addition to DM, also have hypertension. Is worth mentioning that, according to Table 1, among the 6 patients included in the study, 4 patients were part of both groups: experimental and control; only 2 patients were part only in the experimental group and no patients were part only in the GC. Below is the division of the total number of ulcers (11) by group: i) GC: 5 ulcers and ii) GE: 9 ulcers. In GE, among 9 ulcers, 3 were part of both groups: GC and GE. Such an occurrence is because after these 3 ulcers were accompanied by a month in the GC, they were transferred to GE, in an attempt to accelerate the healing process through the use of the inductor system tissue formation. In Table 2 it is shows the other data collected from patients regarding DM and diabetic foot ulcers.

In accordance with the Table 2, 100% of the patients show type 2 DM (the most common form of the disease); 3 patients (50%) have had a minimum of 4 ulcers since diagnosis of diabetes mellitus. The highest number of ulcers was recorded by the patient 3, who during all the time of diagnosis of DM, has recorded six ulcers. The most alarming observed data in this table is the number of amputations, as 50% of patients have two amputations caused by diabetic foot ulcers. The patient was 46 years of age, had been diagnosed with DM 15 years previously, and was a homemaker. The ulcer, which was present since two months ago, was located in region 2 (1st metatarsal head) of the right foot. This injury arose through a callus caused by mechanical stress due to the use of inadequate footwear. This patient was also more susceptible than the first patient to cracks, dry skin, fissures, and calluses, which influence the appearance of ulcers. This patient has presented five ulcers since the DM diagnosis. She is 1.59 m in height and weighs 98 kg, with illnesses associated with hypertension. This stage of the research was conducted on the premises of the Regional Hospital of Taguatinga (HRT), located in Taguatinga – Federal District-Brazil. This hospital was chosen to conduct all the steps in this stage of the study, because the medical staff included a diabetes physician who was a representative member in Brazil of the International Working Group on the Diabetic Foot, which provided support for this research and saw the potential that this study had to provide benefits to human health. Dr. Hermelinda Cordeiro Pedrosa participated in this experimental study as the main medical contributor. After the clinical evaluation conducted to characterize the patient’s ulcer, the patient's diabetic foot was prepared so that a cast mold could be taken for the production of the healing insole, which is customized and personalized for each patient. The process of taking and making the mold is explained in the sections that follow. It should be noted that the patient’s foot was cleaned and sanitized prior to being wrapped in plastic to obtain a copy of the mold. A home-use-only procedure was conducted to treat the ulcer using the tissue-healing insole. The patient first cleaned the ulcer with a 0.9% saline solution and gauze. After the cleaning procedure, the diabetic foot was ready for the insole. The patient then wore the latex insole, which was sterilized and sealed in its own packaging, and put it on by securing it with Velcro at the top. The next step was to secure the LED cell on the outside of the insole in the region of the wound, so that the light would reach the insole and the wound. In addition, the patient was advised to put a piece of plastic wrap on the LED cell to avoid contamination. The patient turned on the tissue regeneration electronic circuit using its on/off switch button and started the LED light emission in the direction of the wound, aided by the natural latex insole. During the treatment, the patient was required to stay at rest and not move the LED cell. The circuit emitted light for approximately 35 minutes. At the end of this time interval, the circuit automatically triggered an alarm. When the alarm went off, the patient had to turn off the circuit with the on/off button and remove the LED cell. After the patient removed the LED cell, gauze was placed on the outside of the insole at the wound site, using a bandage to hold the gauze in place. The gauze and bandage absorbed the discharge from the wound. The patient was advised to wear the healing insole all day or at least for a period of approximately 10 hours. The patient was also advised to make use of resting footwear along with the healing insole. Once a day, the patient repeated the entire process of cleaning the wound, replacing the insole and using the tissue regeneration electronic circuit. It should be noted that the insole was disposable and had to be replaced every day. Three times a week, the patient charged the tissue regeneration electronic circuit for a period of eight hours. It was tested for a period of two months. The patient performed the treatment with the insole and was monitored weekly by the research team. The clinical evaluation conducted by the medical team complied with the standard used in traditional methods. Figure 3 illustrates part of the procedure described above.

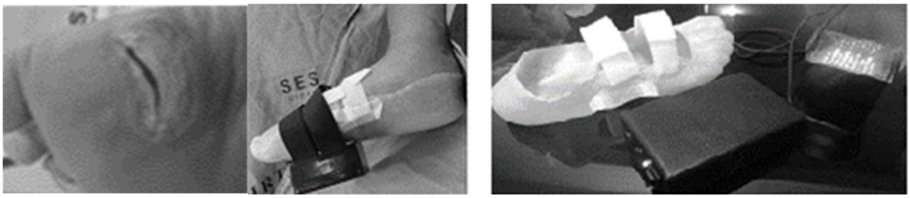

Figure 3. Photo images made by the authors of the established untreated ulcer on the patient, the system applied to the patient's foot as described for home care, and the complete system, with emphasis on the tissue regeneration electronic circuit.

3.3. Mathematical model

With the realization that injuries that occur in the diabetic foot have a mechanical etiology, many efforts have been made to achieve the stabilization and correction of these physical phenomena and correlate them to the occurrence of ulceration and the plantar pressure distribution. The pressure and shear stress variables in people with diabetes are applied at different points and produce effects in the frontal regions of the foot (forefoot) that are more pronounced than in the heel regions. The results show that the peak pressures do not all occur at the same shear stress point, a fact that underscores the need for a thorough analysis of the diabetic foot using a simple mechanical approach. To obtain a mathematical model for the system presented, we used the Bond Graph (BG) tool, which is an alternative to traditional modeling practices. The central idea of the behavioral study of the diabetic foot stance was to implement a custom-made insole derived from natural latex biomaterials to perform plantar pressure control. To accomplish this objective, the variables associated with the insole (or controller) customized design needed to be represented by the model. The use of the mathematical modeling as a biological system function representation and the use of its essential aspects to understand how it functions, based on some variables and conditions, is consistent with the production and standardization process for the technologies applied to these systems in actuality. The scenario involving biological variables and modern control systems, such as the manufacturing of latex-based shock-absorbing insoles for the prevention and cure of diabetic foot ulcers, naturally leads us to reflect upon control systems application in the area of biotechnology, in particular its use directly to control biological variables, like the plantar pressure. In this study, we suggest a control systems approach hypothesis, in which Latex materials should be used as the modifier factor of feet's system dynamics. The biotechnology revolution is based on massive scientific advances that have been made over the last sixty years. These advances have given scientists an extremely detailed understanding of life processes, have allowed life forms to be deliberately manipulated at the genetic level, and have enabled the creation of novel organisms containing genes from other species. To understand the history of the biotechnology revolution, it is useful to look at the development of the science that helped to create it. There was a significant merging of chemistry and biology (still seen by many as two distinct fields of science) in the early 1950s, as connections were made between the molecular structure of deoxyribonucleic acid (DNA) and its role in inheritance. The revolutionary techniques of genetic engineering and genome sequencing stem from this convergence [53]. Nevertheless, in the context of biotechnology, i.e., applications of science and engineering principles, materials processing, biological agents, biomaterials, mathematics, and obtaining supplies of goods and services, this study seeks to initiate discussions about derived biomaterial devices used as controllers or actuators (in the electrical engineering point of view) in the dynamics of biological systems, aiming to forge a system that best suits the linkage among engineering, biomaterials, and biological systems. For the research in question, taking into consideration that control engineering addresses the analysis and design for goal-oriented systems, in which modern control theory addresses systems that possess the qualities of self-organization, adaptability, robustness, learning, and optimality [55], use of biomaterials as a controller and / or actuator dynamics in the system presents itself as a minor theory and/ or auxiliary hypothesis possibility within the context of the paradigm [54]. From this perspective, the basic principle of mathematical modeling a physiological system is to simulate its action and thus be able to assess the parameters that may affect the system. Because of the natural aspects of the human body, which consist of many complex interactions, mathematically modeling a physiological systems allows for the development of diagnostic procedures that may be more effective in terms of the techniques applied, thus creating safer results, according to [52]. Simple mathematical models can generate complex patterns, and nature's complicated phenomena can be modeled using simple rules for generating a model for the system to assess, in this case, the insole's influence on the system parameters [56]. The challenges inherent to our proposal led us to develop various mathematical models to represent the foot dynamics. We employed the BG tool, which is an alternative to traditional modeling techniques and provides state space mathematical representations of nonlinear systems. By providing a graphical representation of a dynamic physical system, the BG tool facilitates the understanding of the influence of each element and visualization of the energy flow (gain and loss) throughout the system under study. In this respect, the BG tool differs from traditional modeling techniques. The concept on which the BG tool is based is unified representation of a dynamic system in which the elements interact with one another through ports within the system at which exchanges of energy occurs [57-58].

3.4. Static model

The first modeling procedure performed by the authors was to propose a mechanical model analogous to the diabetic foot that is capable of representing its behavior in terms of pressure variables. In formulating this analogous model, viscous and elastic elements were used in an attempt to express the structural characteristics of the pressure variables in physiomechanical terms. There are two basic component arrangements for physiological representations that are described in the literature: the Maxwell model and the Kelvin or Voight model [59]. These are viscoelastic models that represent approximations of actual material's behavior and that are sometimes combined to roughly and qualitatively represent the behavior of complex materials. The Kelvin or Voight model consists of a spring with elasticity k placed parallel to a viscous shock absorber (or damper) B. If a stress is applied at time t=0, the elongation of the spring may not be instantaneous because it may be slowed down by the shock absorber. The stress is distributed between the two components, the deformation occurs at a variable rate, and after a certain amount of time that depends on the shock absorber's viscosity, the spring approaches its maximum elongation. When the cause of the deformation is removed, the reverse process occurs: the deformation decreases over time, and the initial length tends to be restored. The Maxwell model consists of a spring and a shock absorber (damper) in series. According to this model, the material continues to deform as a constant stress is applied. The objective of the modeling is to represent important aspects of the system so that a design for a shock-absorbing insole can be developed that can govern or change the foot system response by reducing peak pressure. If we make an analogy with mathematical models, a classic example in the literature is the motorcycle and the rider; we follow the same strategy to propose a suspension derived from biomaterials, with a load distribution based on the construction of shock absorbers, i.e., generating energy loss (pressure) applied to the ground by the diabetic foot to decrease energy transfer. The representation of the diabetic foot is presented in Figure 4.

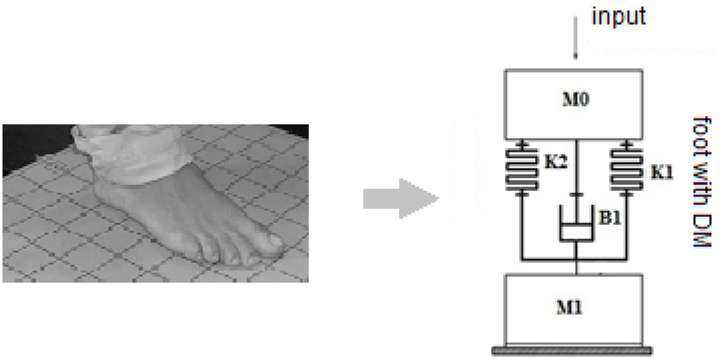

Figure 4. Photo of the foot in static position and proposal for a simple translational mechanical model.

The masses (M_0 and M_1) are the foot masses. The M_1 mass, which represents the forefoot, is connected in series with a spring (K_1) and a shock absorber (B_1). This representation shows that the force applied in passive diabetic walking has a greater impact in this region. The use of the shock absorber (B_1), which is responsible for reduced angulation and the low torque that this promotes in the system dynamics, is justified to represent the delay in activating the muscles that directly influence the pressure center (PC). Finally, for the heel region, which is responsible for driving the movement, a spring (K_2) was used. During both the compression of the spring and the movement back to equilibrium length, the force is always in the opposite direction of the displacement. Figure 5 illustrates the shock-absorbing insole system made from latex and a new model with a greater number of degrees of freedom (three in this case) and energy-damping shock absorbers that generate heat. This heat increases moisture and consequently hydration, as visually verified by the authors.

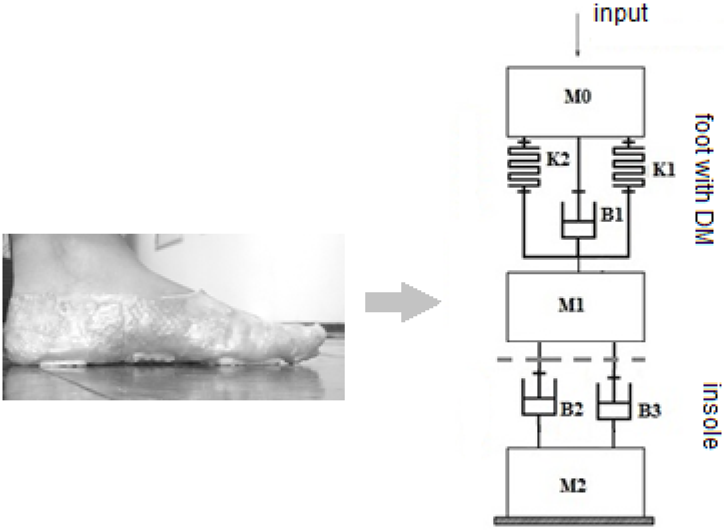

Figure 5. Photo of the foot in the static position with the insole and a proposed simple translational mechanical model with the insole element incorporated into its structure.

As explained by [60], the methodology for obtaining a model using the BG tool consists of three steps: i) specifying the analogous system based on the actual physiological model, ii) determining the energy areas, and iii) defining the simplification of the hypotheses and the input and output system variables. Following these steps to transform the analogous system into a graph of links, the following procedures were followed: 1) identification of the physical domain represented by the system and identification of the capacitive (C), resistive (R), inertial (I), sources of flow (SF) and effort (SE) elements present in the system; 2) identification of other energy variables, such as mass element velocities, and naming and assigning them type 1 junctions; 3) identification of the differences in efforts—in this case, differences in velocity, and assignment of type 0 junctions to these differences in velocity; and 4) connection of the elements identified in step 1 with their respective efforts or differences in effort, as represented by the type 1 junctions. Assignment of the causalities, automatically performed by the 20-Sim simulation software (a modeling and simulation program for mechatronic systems developed by Controllab Products). The motion equations for the systems presented in Figure 4, which represent the diabetic foot, are given by the following equations:

$$\begin{gathered} M_0\ddot{x}_1 + B_1\dot{x}_1 - B_1\dot{x}_2 + K_1x_1 - K_2x_2 + K_2x_1 - K_2x_2 = P(t) \\ M_1\ddot{x}_2 - B_1\dot{x}_1 + B_1\dot{x}_2 - K_1x_1 + K_1x_2 - K_2x_1 + K_2x_2 = 0 \end{gathered} \tag{1}$$

The parameters of the system are M_0, the foot mass; M_1, the forefoot mass; K_1, human skin elasticity in the frontal region; and K_2, human skin elasticity in the heel region. The displacements are represented by the variables x_1 and x_2. The system input is the force P(t), that is equal to the person's weight when the foot touches the ground. The motion equations for the system presented in Figure 5, which represents the diabetic foot in interaction with the insole, are the following:

$$\begin{gathered} M_0\ddot{x}_1 + B_1(\dot{x}_1 - \dot{x}_2) + K_1(x_1 - x_2) + K_2(x_1 - x_2) = P(t) \\ M_1\ddot{x}_2 - B_1(\dot{x}_1 - \dot{x}_2) - K_1(x_1 - x_2) - K_2(x_1 - x_2) = B_2(\dot{x}_2 - \dot{x}_3) + B_3(\dot{x}_2 - \dot{x}_3) \\ M_2\ddot{x}_3 + B_2(\dot{x}_3 - \dot{x}_2) + B_3(\dot{x}_3 - \dot{x}_2) = 0 \end{gathered} \tag{2}$$

The parameters of the above system are M_2, the insole mass; and B_2 and B_3, the viscous shock absorbers made of latex. The displacements are x_1, x_2, and x_3. The system input is again the force P(t). In analyzing this system, the eigenvalues of the characteristic equation were determined. Based on the consideration that a system is stable if all eigenvalues have a negative real part, the systems are asymptotically stable if and only if all eigenvalues have negative real parts, or equivalently, if all the Δ (characteristic polynomial) roots have negative real parts. Note that for systems without the insole, there is a null coefficient, and the system is critically stable, that is, may present undamped oscilattions. For systems with the insole inserted, according to the Hurwitz criterion, $M_0 > M_1$, which produces equation [3]:

$$\Delta_{foot}(s) = \left(s^4 + \left(\frac{B_1}{M_0} + \frac{B_1}{M_1}\right)s^3 + \left(\frac{B_1^2}{M_0M_1} + \frac{K_1}{M_0}\right)s^2 + \frac{B_1K_1}{M_0M_1}s - \frac{K_1K_2}{M_0^2}\right) = 0 \tag{3}$$

The terms K_1 and K_2 are spring constants that have positive values and units of N/m. The inclusion of an insole element with two shock absorbers for the proposed system changes the characteristic equation and renders the system marginally stable, a condition that is necessary and sufficient for ensuring stability in theory, according to equation [4]:

$$\begin{gathered} \Delta_{foot+insole}(s) = \left(s^5 + \left(\frac{B_1}{M_0} + \frac{B_2}{M_1} + \frac{B_2B_3}{(B_2+B_3)M_2} + \frac{B_2B_3}{(B_2+B_3)M_3}\right)s^4 + \right. \\ + \left(\frac{B_1}{M_0}\left(\frac{B_2}{M_1} + \frac{B_2B_3}{(B_2+B_3)M_2}\right) + \frac{B_1}{M_0}\left(\frac{B_2B_3}{(B_2+B_3)M_3}\right) + \left(\frac{B_2B_3}{(B_2+B_3)M_3}\right) \bullet \left(\frac{B_2}{M_1} + \frac{B_2B_3}{(B_2+B_3)M_2}\right)\right)s^3 + \\ \left. + \left(\frac{B_1}{M_0}\left(\frac{B_2B_3}{(B_2+B_3)M_3}\right) \bullet \left(\frac{B_2}{M_1} + \frac{B_2B_3}{(B_2+B_3)M_2}\right)\right)s^2 + \frac{K_2(B_2B_3)^2}{((B_2+B_3)^2M_0M_1M_2)}s\right) = 0 \end{gathered} \tag{4}$$

Making use of the mathematical and static models presented, this study seeks to evaluate whether the use of latex insole shock absorbers is able to act in the areas of major diabetic foot plantar pressure to avoid the eruption of ulcers.

3.5. Hevea brasiliensis latex biomaterials

In the process of developing the insole, only materials found in the market were considered. The most commonly used materials are silicone, polyurethane, ethylene vinyl acetate (EVA), and viscoelastic foam. Based on this review, the raw material chosen for use in this study was latex biomaterial. This biomaterial is made from the natural latex of the *Hevea brasiliensis* rubber tree, which is low cost, high in quality, highly durable, and has biocompatible physical and chemical characteristics of antigenicity, hypoallergenicity, resistance, elasticity, softness, flexibility, and strength. Recent scientific studies have shown that the materials used in insoles must have these characteristics to ensure the patient's comfort, control foot temperature, and minimize the risk of developing allergies. It is noteworthy that latex has been used to make esophageal prostheses, biomembranes, and esophageal flow controller modules. The use of latex to make insoles is extremely advantageous for the foot because it is a material that is easily moldable and has beneficial properties for the healing of wounds. The material properties of latex, which is a milky sap and a living organism prior to vulcanization, vary with temperature and so will be altered by the temperature of the foot when used in a shock-absorbing insole. At the same time, the shock absorbers are responsible for reducing pressure, which is the basis of the bioinspired system. Because the insole is a biomaterial and because of the properties of latex, it is possible to obtain a variable density through the manufacturing process, the handling, and the sourcing of the latex. Another important fact is that the viscous damping coefficient is closely related to the viscosity of the fluid, which implies that it is influenced by temperature: a temperature increase results in a decrease in the viscous damping coefficient. For this reason, we find that the higher the temperature, the "softer" the latex. In addition, the diabetic foot displays temperature and moisture changes (most often, the feet are warm and the skin is rather dry). An advantage of latex in this regard is that when vulcanized at temperatures of 35 to 45°C, it retains moisture and hydrates the patient's skin. Furthermore, latex is a non-Newtonian biomaterial, which implies that its viscosity can be controlled by factors such as geometry and temperature. Latex, which is a whitish secretion extracted from the rubber tree (*Hevea brasiliensis*), is used as biomaterial in medical devices [51]. In addition to its biocompatibility, its tensile characteristics, maximum traction force, ductility, and toughness influence the ease with which the material can be molded into complicated shapes. Latex is also being tested in humans as tissue neoformation induction material, and has been used for patients with chronic ulcers of the lower limbs and myringoplasty. Insoles are another application of latex for the treatment of diabetic foot, with or without ulceration. Research has begun into its healing effects and its suitability for use in the treatment of burns and other types of wounds.

There are several products made from biomaterials on the market for the treatment of pressure ulcers. Typically, these products come in the form of films, foams, gels, or membranes. Their fundamental characteristics are light weight, odorless application and removal, sealing against microorganisms, oxygen and water vapor permeability, ease of manufacturing, biodegradability, and biocompatibility. Among these products are the following: i) Latex biomembrane: this latex component, obtained from the polymerization of polyisoprene, induces angiogenic formation and scarring and accelerates the regenerative process of chronic wounds via chemical debridement action; ii) Aloe vera biomembrane: this product induces the formation of new blood vessels and tissue repair; iii) Hyaluronic acid: this is obtained from fermentation of gram-negative bacteria or by isolation of animal structures, such as synovial fluid, skin, and cockscomb and is used for soft tissue filling and healing functions; iv) Collagen and alginate membrane: this product, which is 90% type I and III collagen, is obtained from bovine skin or tendon and 10% alginate. From these products, a gel can be produced that provides moisture and slow dispersion of collagen in injured tissue, thereby inducing chemotaxis for granulocytes, macrophages, and fibroblasts. The raw material used in this study in the preparation of latex devices was natural latex extracted from the *Hevea brasiliensis* rubber tree, purchased on the domestic market. Some standard features, such as a low sulfur content and high viscosity, were needed for this material. A high concentration of sulfur gives latex a sticky consistency and low viscosity after vulcanization, which turns the production process into a time-consuming manufacturing process. A raw material that could met these criteria was identified: a latex extracted from rubber plantations in Florianópolis, Santa Catarina, Brazil. This latex was bi-centrifuged at 8000 xg in an α-Laval A-4.100 centrifuge with a water-cooled continuous passage. From the natural latex, the final product was prepared by mixing and resting it for two hours to produce prototypes with essential features such as elasticity, softness, strength, good texture, impermeability, absence of bubbles, and hypoallergenicity.

4. Devices developeded for diabetic foot treatment

4.1. Compound preparation— Mold-making

The development process for the insole padding material consisted of two steps: i) mold-making and ii) product preparation. The mold-making process consisted of the following steps. The mold of one foot (of average size) required 800 g of alginate and 1200 ml of water. The alginate and water were mixed well with a spoon for approximately 60 seconds until a homogeneous and creamy mixture was obtained. The mixture had to be stirred quickly to avoid consolidation (clotting) or hardening of the mixture. As soon as the mixture was ready, a foot was dipped into the container holding the material, and a setting time of approximately 3 minutes was allowed to pass. The mixture changes color when it set. After setting, the foot was removed from the container slowly and carefully. A plaster cast of the foot was then made by pouring a mixture of special plaster and water into the void where the foot had been located. This plaster mixture had to be moderately consistent. The plaster took approximately 2 to 3 hours to harden. After the plaster hardened, the mold was removed, and wet sandpaper was used to make the mold surface smoother. In the case of a patient with foot ulcers, the foot had to be wrapped with plastic wrap. This mold-making process for the insole for the diabetic foot is completely individualized and customized: the shape and proportions of the insole are dictated by the characteristics of the patient's feet. This makes it possible to provide customized comfort, softness, and well-being. It should be noted that it is a simple and quick procedure that does no harm and does not cause discomfort to the patient. This mold-making process permits molding of the entire foot or the plantar region only.

4.2. Insole preparation process

This stage of the insole preparation process consists of two main steps: preparation and characterization of the product. In this stage of the process, indispensable product requirements, such as softness, comfort, hygiene, and shock absorption, were taken into account. The mold was washed with soapy water, dried with hot air, sterilized through autoclaving, removed, and dipped into the latex and remained in the compound for 1 minute. This point represents the beginning of the polymerization that determines the final preparation of the product. The mold was then slowly and gradually removed and placed in an oven and was heated at a temperature of 70ºC (for vulcanization) at intervals of 10 minutes. The mold then cooled outside the oven for at least 20 minutes. It is noteworthy that the dipping and heating steps were repeated until the healing insole was approximately 1.5 mm thick. After the vulcanization period, the insole was kept at room temperature for 24 hours to complete the preparation process. At the end of the process, the mold was removed under running water. The function of the insole is to redistribute pressure uniformly across the plantar surface of the foot by reducing excess pressure in regions that are at risk of injury and transferring this excess pressure to no-risk areas. This is recommended to prevent the onset of foot injuries and also to help in the treatment of wounds in the final stages of healing. Other features are related to the support surface elevation up to the sole of the feet and the ability of the insole to provide custom comfort, as it is formed according to the anatomical shape of the foot to provide a sensation of softness and well-being. Taking into consideration the correct distribution of plantar support between the feet, the insole is designed to improve the support base and improve stability between the feet. The fully individualized and customized preparation of this insole based on the anatomy and characteristics of the patient's feet permits the shock absorbers to be positioned at the exact and ideal points, which is necessary for deep absorption of shock impacts while walking and an exact plantar pressure distribution. In addition, this customized preparation process perfectly accommodates any foot deformities present (feet cavus or flat foot, bunions, claw toes, and hammer toes, among others). In contrast, in the fabrication of insoles with cushioning systems that are not made in a personalized and individualized manner with respect to size, shape, and proportions, with only the standard model of the shoe-size system considered, it is impossible to accommodate any foot deformities that may be present. In this preliminary study, in addition to the above specifications, the degree of plantar pressure and its distribution, which consequently influences its amount, location, and size, were considered in the customization and individualization of the shock absorbers. For other insoles described in the technical and market literature, only one standard model is considered in the preparation of the shock absorbers and in their positioning. The dimensions of this standard model are practically the same, regardless of the location on the insole. This is an important fact: if shock absorbers must be made according to the size, shape, and proportions of the wearer's foot, mainly in relation to the pressure exerted on that position, the required dimensions of the shock absorbers determined during the preparation process may vary widely from one wearer to another. When you have a custom-designed and individualized insole, the control over the degree of pressure and specifically the position and size of the shock absorbers are highly controllable, which was among the aims of this preliminary study. Lack of customization and individualization in insole and shock absorber development does not allow for such control in quantity, position, and size. Other insoles with cushioning systems that do not present such differentiation as a way to compensate for such control are made with numerous shock absorbers (which increases the cost) or have shock absorbers only in the calcaneus and forefoot regions. In the first case, the shock absorbers cover all or nearly all of the top surface of the insole, which may bring have disadvantages for wearers, such as pain and discomfort, until they become accustomed to the insole, which might take a long time. In the second case, the cushioning of impact typically occurs in the heel and sometimes also in the forefoot, first and foremost, leaving other regions exposed to impact. Doctors and specialists claim that the area's most prone to plantar pressure peaks and future plantar ulcers are the hallux, toes, metatarsal heads, middle of the foot, and heel. With a simple examination using adequate equipment, plantar pressure peaks, which occur at locations that are highly susceptible to the formation of plantar ulcers, can be identified on the foot. Each of these peaks should then receive treatment with shock absorbers. The shock-absorbing insole proposed in this preliminary study may be an essential addition to therapies to fight diabetes if applied in a preventative manner before the appearance of wounds or if applied after resolution of the case with the objective of assisting in specific treatment and avoiding the recurrence of the wound. Figure 6 shows the prototype of this shock-absorbing insole.

Figure 6. Photo of the shock-absorbing insole prototype with the shock-absorbers highlighted.

Figure 7 shows the pressure capture results, including the locations of pressure peaks, for patient 1 while wearing the insole shown in the previous figure. This new pressure distribution was captured under the same capturing conditions described previously.

Based on the results of previous studies, the authors adopted the strategy in this study of seeking to provide support through qualitative and quantitative changes in the forces applied to the foot by the ground, by means of an interaction passively controlled by the insole in the

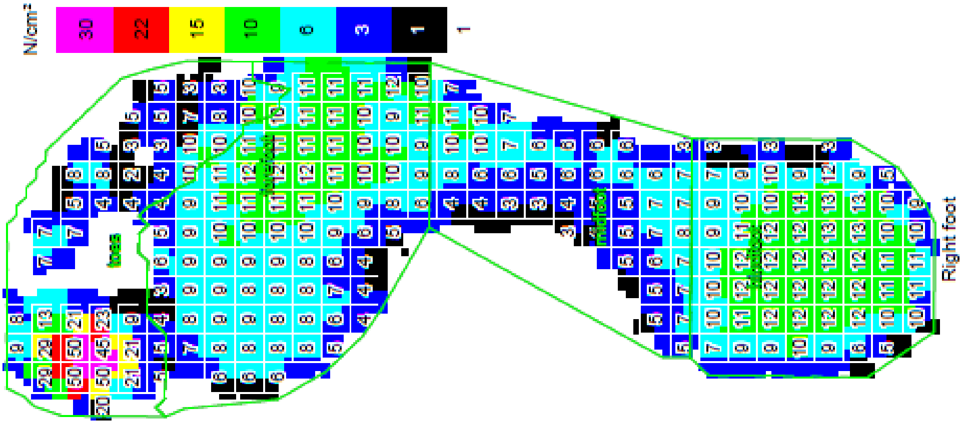

Figure 7. Results of using the insole to reduce plantar pressure.

foot-to-floor interface. This strategy has two main aspects: "control" which in essence is simply the regulation of a given element, and "organic," which pertains fundamentally to the organism controlled. The insole is intended to support the patient's walking and have the potential to change plantar pressure by controlling the parameters that affect it, as shown in this study. The regions with greater force concentrations can thereby be enhanced, leaving those with lesser force concentrations with greater loads than they usually bear. Removing the load or its redistribution is an attempt at a method that directly interacts with the system response to minimize overload and turn it into offload. Body balance was evaluated using stabilometry, which is a method of analyzing balance through the quantification of body oscillations. For this purpose, we used the AccuSway Plus® force platform, connected to a computer that recorded the movements of the pressure center (PC) on the platform plane (X, Y) in the anteroposterior (Y) and lateral (X) directions, by means of the force exerted on the platform by the soles of the feet, captured by the software. Assessing how the shock-absorbing insole can interfere with the control of a diabetic patient's semi-static posture can open up possibilities for developing a passive insole system with biofeedback, to compensate for neuromuscular deficits in DM patients. These muscular responses delimit an area within a base to indicate body stability. Associated with this support base concept is a stability limit that has been shown in many studies to be considerably reduced in cases of some diseases, such as Parkinson's disease and diabetes. In this context, based on the stability evaluation results, one question was asked: is it possible to maintain stability limits with the introduction of the shock-absorbing insole? That is, can performance indexes be changed to demonstrate a response that promotes better balance than without the insole? The results of qualitative assessments by observation show that the introduction of the insole helps to reduce passive stiffness of the muscle-to-tendon structure. This fact was verified in tests of time remaining in balance showing that the tendency of the body to fall forward was reduced, i.e., the momentum magnitude of the gravitational force was reduced. With the introduction of two shock absorbers and a mass, the conservation principle of mechanical equilibrium, as presented in equations [1] and [2], is verified, focusing only on external forces more common while maintaining an upright posture. In future studies, we intend to include the analysis and direct assessment of internal forces, such as disturbances generated by the delayed activation of the muscles, which can be evaluated as hysteresis or looseness, by analogy to translational/rotational mechanics. In addition, the insole can be classified as an anticipatory postural adjustment element that causes an underestimation of the magnitude of the ground reaction force in maintaining a postural orientation. The data collected from the force platform tests with and without the insole were captured 5 times for 30 seconds apiece. The following stabilometric parameters, suggested by [51] were also analyzed: i) average displacement and standard deviation (SD) of the pressure center in the anteroposterior (YAvg) and latero-lateral (XAvg) directions, with XAvg (cm) and YAvg (cm); ii) displacement average velocity (VAvg, cm/s); iii) the circular area (Area) that corresponds to the area that best fits the trajectory of the pressure center. As an initial hypothesis, for a single-foot analysis, it was believed that without the insole, a DM patient would present greater imbalance than with the insole, because of the motor deficit developed. It is known that there is a relationship between the static balance deficit and the number of falls. Thus, the lower the patient's ability is to maintain his balance, the greater the probability is of the patient having a fall. In a state of dynamic equilibrium, both the center of mass and the support base move, and the center of mass will never align with the support base during the movement's single-foot stance phase. Ankle mobility influences balance in that the more the ankle moves, the greater the capacity of the individual to maintain balance. In Figure 8, the change in amplitude as defined by item i) above is plotted to illustrate the amplitude variation attributable to the introduction of the insole.

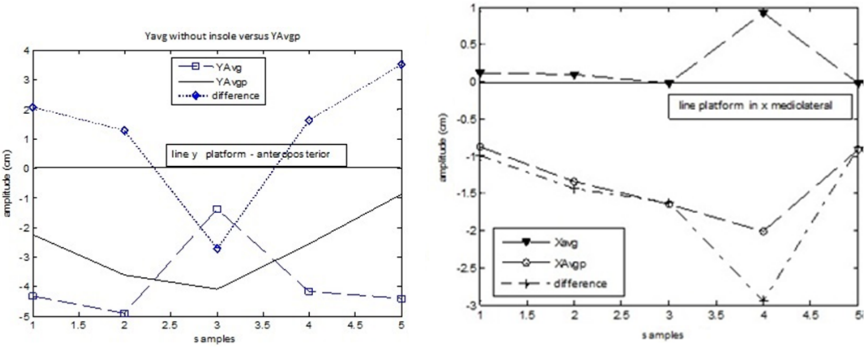

Figure 8. Comparisons between the displacement variations in X and Y with and without the insole.

In related studies, the authors confirmed that the introduction of the insole to the feet of DM patients using appropriately made (customized) shock-absorbers has shown that the effectiveness of the postural control insole is directly related to the pressure center displacement amplitude. Large amplitude variations in movement indicate poor-quality balance control, whereas acceptable control is indicated by small amplitudes of displacement in the Y and X directions. Increases in oscillation in the single-foot static upright posture were also verified.

These oscillation increases can occur because of a decrease in the corrective torque generated by the insole to control the oscillations and body velocity and because of an increase in the time required to feel the presence of the insole, transmit and process a response, and activate the muscles. Figure 9 illustrates the velocity amplitude changes caused.

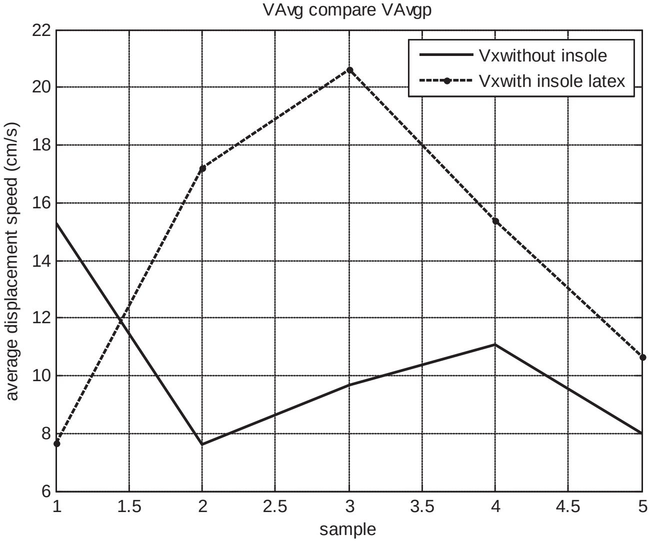

Figure 9. Comparison of average single-foot velocity with and without the insole.

A correlation exists between the displacement average velocity values VAvg (cm/s): an increased displacement velocity—that is, a higher speed in perceiving imbalance and attempting to stabilize the pressure center—decreases the imbalance. This may be because wearing the insole: i) reduces the ground reaction force; ii) reduces the resulting vector amplitude, and iii) generates greater body stability through greater velocity to control these oscillations. Figure 10 shows the velocity variation for each collection captured.

The circular area that corresponds to the area that best fits the trajectory of the pressure center is shown in Figure 11.

When we analyze the response variation data in the time domain, we obtain useful information, but to supplement the analysis. For a system without shock absorbers, the antiresonance corresponds to the absence of movement in all coordinates where the response is considered. Peaks in this frequency response occur in the time part of the diagram where the maximum response was observed because of entry excitation represented by the ground reaction force on the foot. We note that the vibration amplitude changes when we modify the oscillation frequency of the applied force. This result also shows that by varying the oscillation frequency of the force, both increases and decreases in vibration amplitude occur at different points on

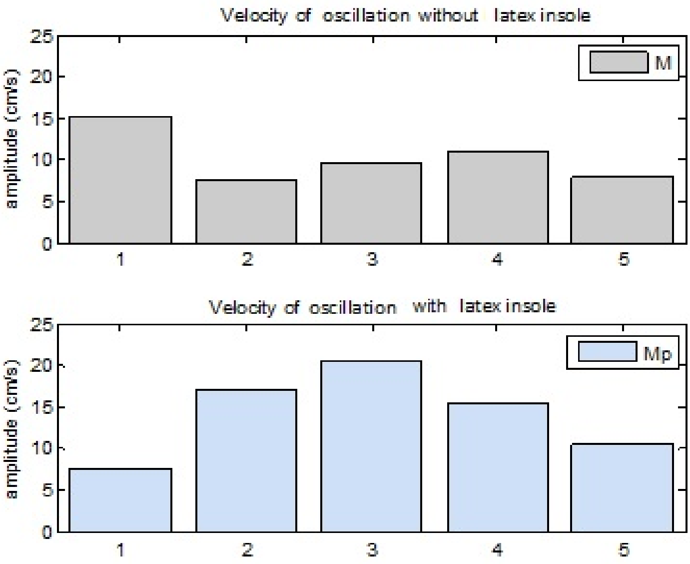

Figure 10. Comparison of the variation in velocity with and without the insole.

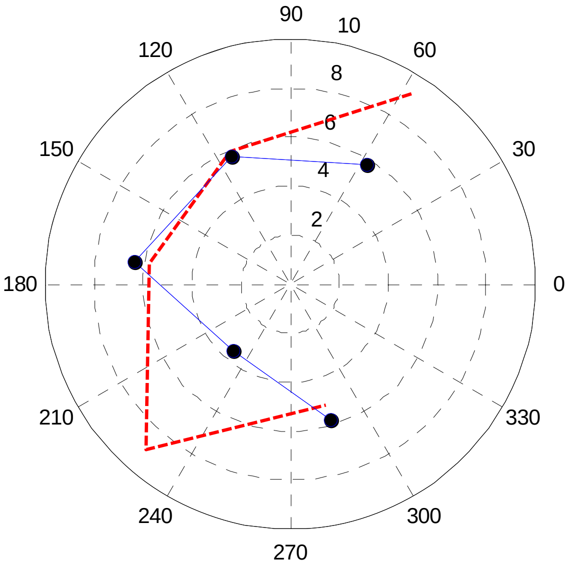

Figure 11. A graph generated in radar format to show that the stability region with the insole was increased by increasing the limits. The red line indicates the area with the insole, and the blue line indicates the area without the insole.

the time scale. In the time domain, there are natural frequencies and respective modal forms associated with these frequencies, which are inherent in each insole structure designed. These are basically characteristics that depend on inertia and rigidity. The introduction of shock absorbers with viscosity and mass characteristics and softness and flexibility features affect the response of the foot structure when it is excited by a force of some type.

5. Healing insole

The healing insole is disposable and sterile. The same preparation process used for the latex biomaterial centrifuged to 60% was used for the insole. In the process of preparing the insole, latex was placed in acrylic molds that were previously cleaned and dried. The latex biomaterial was spread out until it formed a thin layer covering the surface. Rather than resting the latex in the oven horizontally, it was rested completely upright so that all excess latex drained. This contributed to the insole becoming clearer. An oven was not used for the insole polymerization; it was polymerized at room temperature, which also promoted transparency. This process was repeated 6 times to reach a final insole thickness of 0.5 mm. The latex insoles were sterilized in ethylene oxide. Some small holes, approximately 2 mm in diameter, were made in the insoles so that during use, exudation (secretion) could be eliminated from the wound. This research examined an innovative method of tissue regeneration for diabetic ulcers consisting of the combined and simultaneous action of the latex biomaterial and low-intensity red LED light. The tissue regeneration electronic circuit is formed by a signal-emitting cell that is based on the tissue neoformation principle involving the use of LEDs. The LED cells are placed only on ulcerated regions of the foot. The cells are placed outside the insole and are covered with a sheet of latex. They emit radiation with a fluency of 25 J/cm^2. Figures 12 and 13 refer to patient 6. This patient is 62 years old and 8 years of diagnosis of DM, her profession is housework. The ulcer 1 (Figure 12) is situated in the region 7 (instep) the existence of time to approximately 7 months already told before amputation. The ulcer appeared through a bruised evolving dramatically with infection coming to osteomyelitis, not to provide answers to antibiotic treatment was necessary amputation of the second to the fifth toe. Then his picture of infection and osteomyelitis have not healed completely and reached the 1st toe (hallux), which was necessary to perform a further amputation. Thus, the present research, to heal these surgeries amputations, applied the treatment with silver foam during the patient's stay in the GC and then the inductor system tissue formation while in the GE.

The ulcer 2 (Figure 13) due to complications arose from the first, and also by mechanical trauma, caused by lack of rest. The wound is situated in area 3, the existence of time to approximately 5 months. As already mentioned, ulcers 1 and 2 (Figures 12 and 13) were followed for 1 month in the GC. Then, in an attempt to accelerate the healing process, the wounds were also accompanied in GE using the inductor system tissue formation. Figures 14 and 15 show the results. This patient already had three ulcers from diagnosis of DM and two amputations.

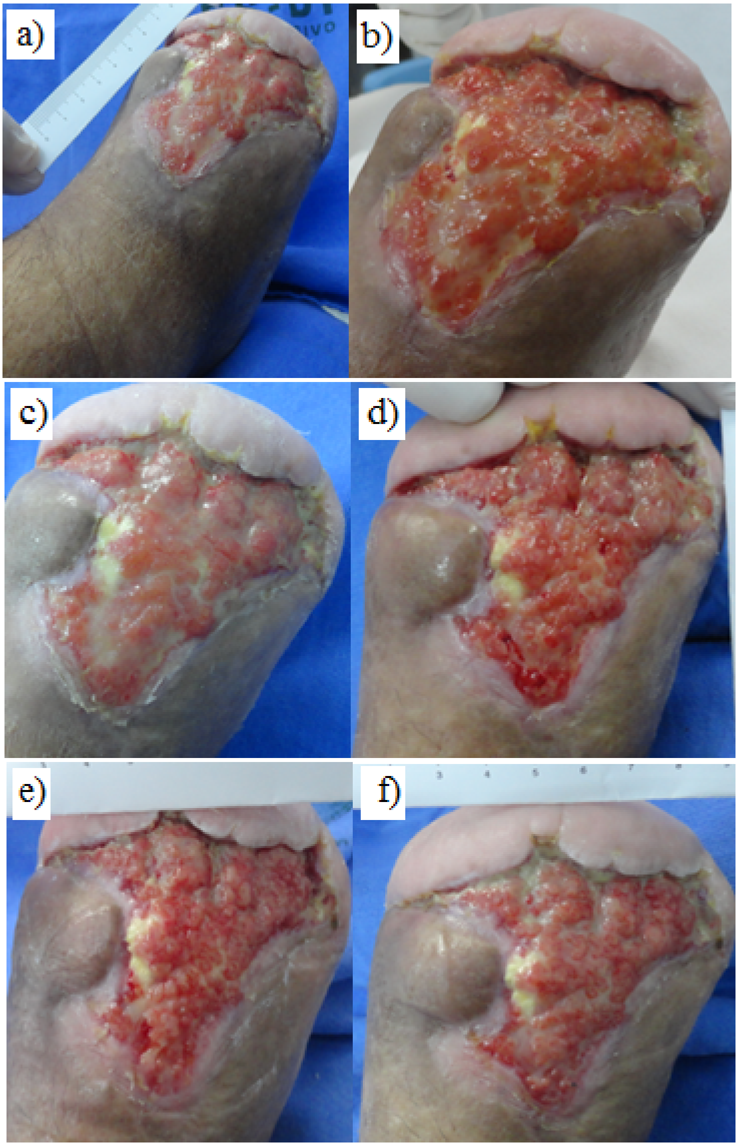

Figure 12. Clinical photo follow-up Patient 6 (1 ulcer)-GC: a) the ulcerated foot region; b) pre-treatment (initial); c) post-treatment (1 week); d) two weeks; and) 3 weeks; f) 4 weeks.

The two figures (Figure 14 and Figure 15) pertain to the patient 6, pictured in the preceding Figure 12 and Figure 13. In each ulcer in this patient, it was evaluated the behavior of two different methods of healing: foam with silver (GC) and system inducing tissue formation (GE). Because of the location of the ulcer 1 this patient, ulcers on both 1 and 2 were applied only to

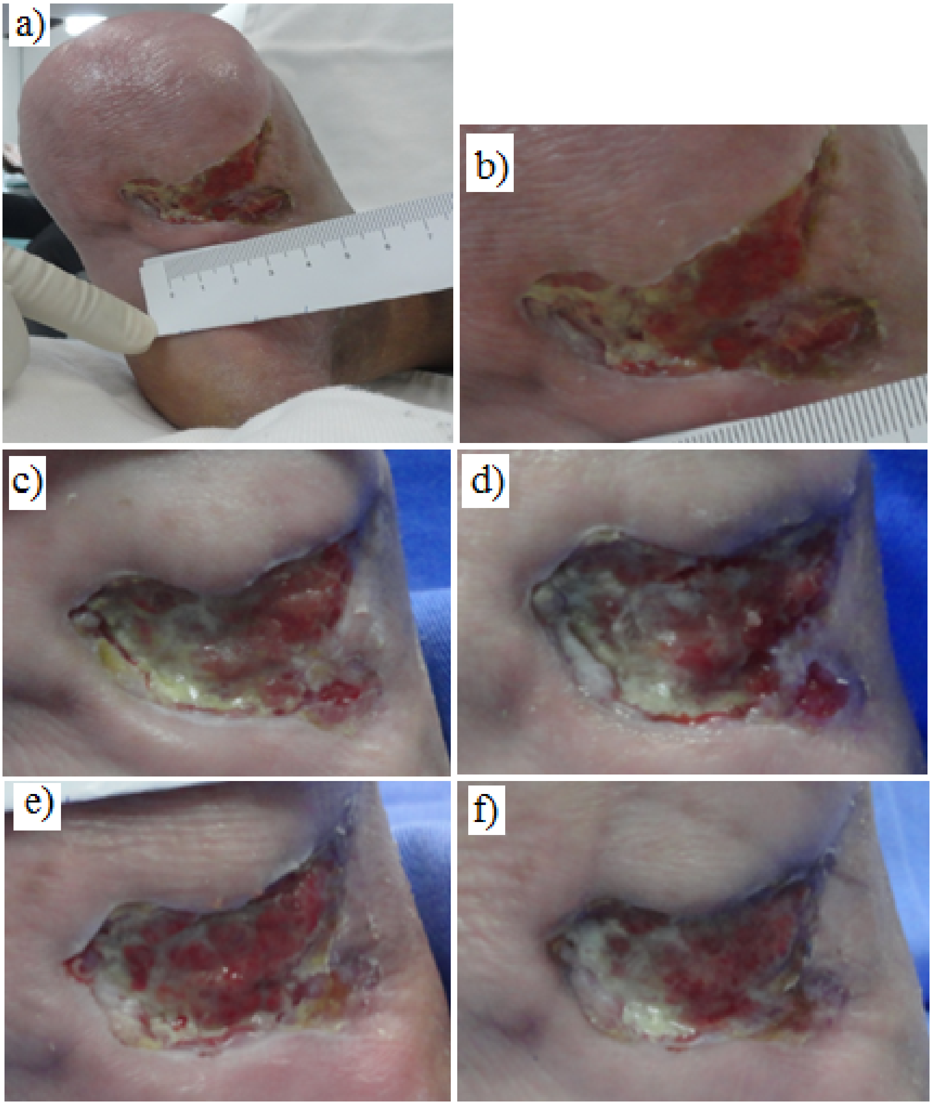

Figure 13. Clinical photo follow-up. Patient 6 (2 ulcer)-GC: a) region of the ulcerated foot; b) pre-treatment (initial); c) post-treatment (1 week); d) two weeks; and) 3 weeks; f) 4 weeks.

slide latex and electronic circuitry for tissue regeneration. Again being demonstrated that within the inductor tissue formation system can be used only blade latex and LED light to induce healing. Comparing the images in Figure 12 (GC) and Figure 14 (GE), one observes a faster ulcer healing 1 while in the GE. It is also noticed that the GE ulcer 1 showed better color, higher and more debridement of granulation tissue and reepithelialization. The same assess-

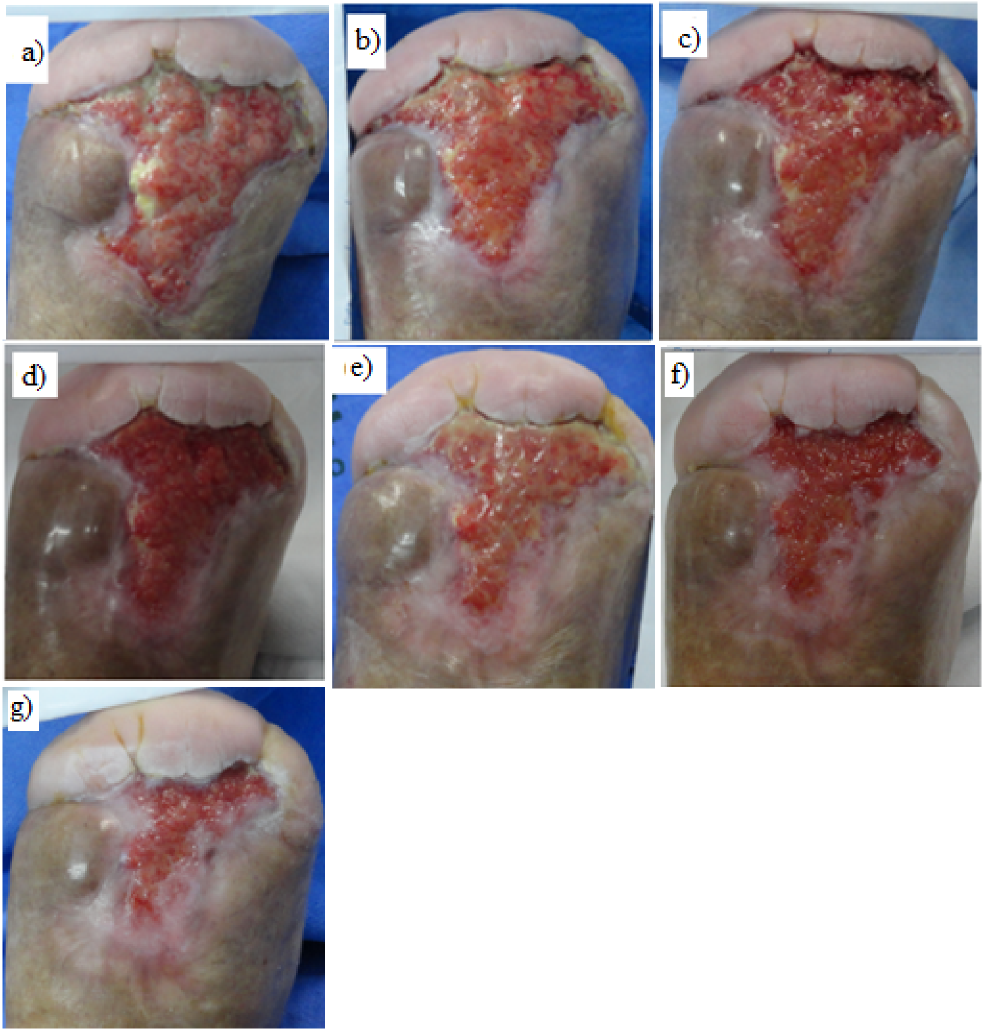

Figure 14. Clinical photo follow-up. Patient 6 (1 ulcer)-Experimental Group: a) early (before the inductor system tissue formation); b) post-treatment (after using the inductor system tissue formation)-1 week; c) two weeks; d) 3 weeks; e) 4 weeks f) 6 weeks g) 8 weeks.

ment can be made between Figures 13 and 14, which displays the ulcer healing was also second fastest while in the GE. Both this patient's ulcers were followed up at 6 GE for 8 weeks. Figures 14 and 15, it was observed that after 8 weeks of treatment with the inducer system for tissue formation, both ulcer decreased significantly in size.

An analysis of the progression of healing of ulcers, conducted by the patient's medical staff, showed full reepithelialization in eight weeks, as illustrated in Figure 16.

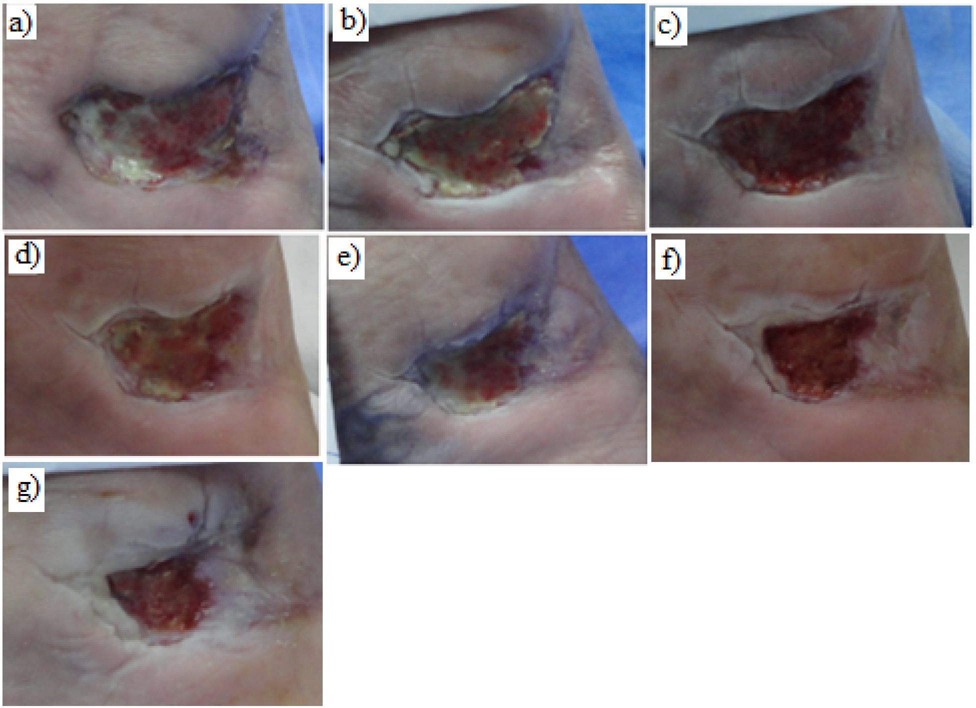

Figure 15. Clinical photo follow-up. Patient 6 (2 ulcer)-Experimental Group: a) early (before the inductor system tissue formation); b) post-treatment (after using the inductor system tissue formation)-1 week; c) two weeks; d) 3 weeks; e) 4 weeks f) 6 weeks g) 8 weeks.

The wounds were photographed on a weekly basis using a digital Sony DSC-H70 camera with 16.1-megapixel resolution. The images were taken with the patient positioned lying down in a chair, with the camera mounted on a tripod parallel to the wounds, and with a focal length of 15 centimeters. A metric ruler was placed alongside the wound for subsequent computational analysis. The digital images obtained were analyzed using the ImageJ® software to quantify the total area of the ulcers. The latex and LED light action gradually favored contraction around the edge of the wound. The coloring of the wound also improved considerably over the course of the 9 weeks. After a week of treatment, the wound appeared more reddish in color. Furthermore, there was a significant increase in granulation tissue. At the beginning of treatment, the wound had a slight depth, and over the course of the 9 weeks of treatment, new tissue gradually formed, making the lesion appear to be filling and healing. In order for low-intensity LED therapy to have positive effects, a protocol of application is essential. The biological effects of this type of therapy depend on the irradiation parameters, such as the wavelength, fluence, irradiation time, and emission mode. A rating of this study was to compare the behavior of two different methods of healing in the same patient. This fact refers to the patient 1, in which the silver foam

(GC) of the right foot ulcer (metatarsal area) and tissue formation-inducing system (GE) to the ulcer of the left foot (the heel area) was applied. Comparing the ICU in both cases in the 2nd, 4th, 6th and 8th week, patient 1 showed better results in GE. This means that the system inducing tissue formation favoring the evolution of healing better than the foam with silver.

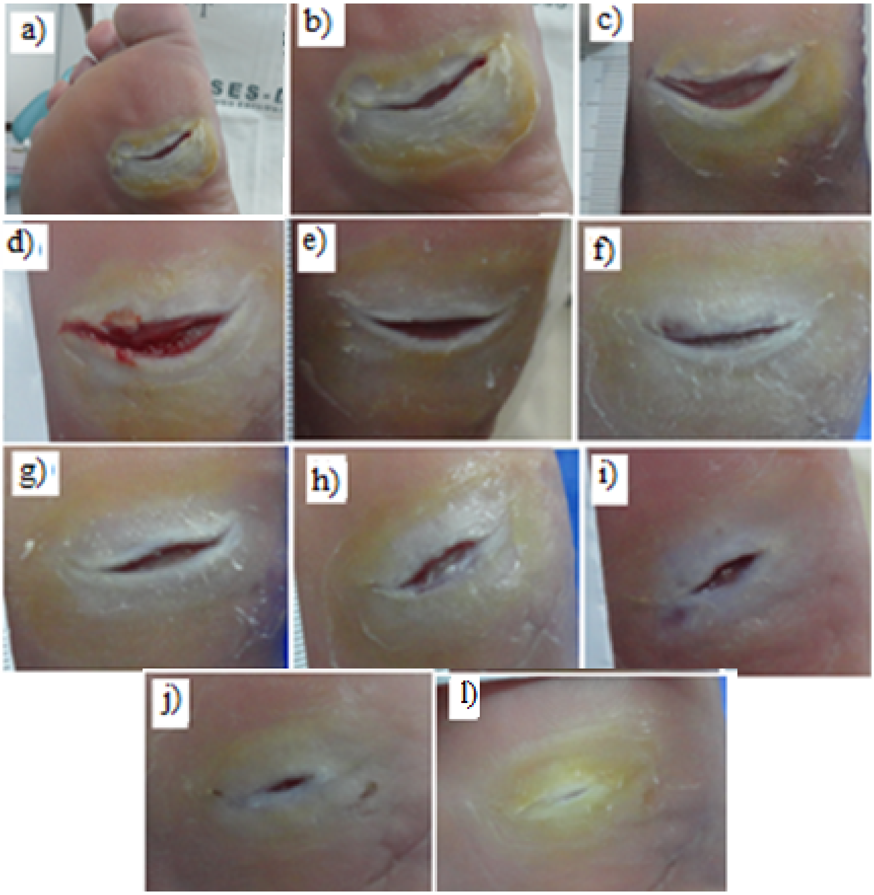

Figure 16. Clinical photo follow-up. Patient 1 – a) ulcerated foot region, b) pre-treatment (initial treatment), c) post-treatment (1 week), d) 2 weeks, e) 3 weeks, f) 4 weeks, g) 5 weeks, h) 6 weeks, i) 7 weeks, j) 8 weeks, l) 9 weeks.

6. Conclusions and contributions

Diabetes mellitus is a chronic disease and is characterized by a variety of complications, including diabetic foot stands, considered a serious and often devastating consequences on the results of ulcerations problem. The formation of sores that become infected and poorly healing can lead to gangrene and even amputation of toes, feet or legs. The essence of this study is intended, under the etiological-mechanical approach, to the intersection of an external element (latex-derived insole – the passive control) with diabetic passive stride. There is impact on the variation of some key variables such as change in mass and contact with soil. Then, we also analyze the parameter sensibility/robustness of the dynamical model obtained, and the effect of the addition of the insole controller in this sensibility. This study showed that the modeling of the diabetic gait is a challenging task, having previous researches already presented contributions which must be added to those brought up by this study. This parametric study's results provide the first steps towards the discovery of tendencies, aiming to obtain new perspectives with regard to this complex disease. Thus this research considers the disease's main etiology and parameters related to the patient's gait, anthropometry and social reality, for he/she might perform certain roles that require their feet to bear different loads – for instance, hairdressers and teachers. This must influence the design process of future insoles, which will function as controllers derived biomaterials acting directly on the dynamics of the gait. The center of pressure of the human foot is displaced in carriers of diabetes, which attests the necessity of a study of the patient's gait prior to the manufacturing of the insole. Second, presented in this study will be an intellectual preparation for the emergence of a new concept, proposed with the idea of controllers derived biomaterials. This methodology will be critical to the creation of a "bioinspired" theory in the field of Biomedical Engineering, which will further assist in the construction of the concept (which says what the thing is) called controlling derived biomaterial (this study insole latex). Based on the literature, it was observed that the introduction of assistive devices is common for changing the stride. But this study presented, that element was characterized and analyzed as a controller that, through qualitative and quantitative changes in the charges applied to the foot, proved possible to correct the diabetic stride. Finally, a search for a new possibility for the treatment of diabetic foot. Accordingly, an inductor system for new tissue formation novel diabetic foot with light emitting circuit LEDs and use of natural latex has been developed. This system consists of a healing insole and an electronic circuit for tissue regeneration. Cicatrizing insole is derived from the rubber tree latex brasiliensis and made a personalized and individualized. This innovative method of healing diabetic foot ulcers consists of the joint and simultaneous action of biomaterial latex and light irradiation of low intensity LEDs. The clinical findings were analyzed qualitatively and quantitatively, which showed that the results obtained by the experimental test suggests that the inducing tissue neoformation system is characterizing.

Author details

Suélia de Siqueira Rodrigues Fleury Rosa[1*], Maria do Carmo Reis[1], Mário Fabricio Fleury Rosa[2], Diego Cólon[3], Célia Aparecida dos Reis[4] and José Manoel Balthazar[5]

*Address all correspondence to: suelia@unb.br

1 Engineering and Biomaterials Laboratory – BioEngLab®, Biomedical Engineering, University of Brasilia, Brasil

2 University of Brasilia-Post-Graduate Program of Sciences and Technology in Health, Brasil

3 University of São Paulo-Polytechnic School, Automation and Control Laboratory, Brasil

4 Estadual Paulista Júlio de Mesquita Filho, School of Sciences, Mathematics Department of Bauru, Brasil

5 Paulista State University Júlio de Mesquita Filho, Institute of Geosciences and Exact Sciences of Rio Claro, Brasil

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