Vibratory Neurostimulator for Patients with Essential Tremor

Delgado G., Gavilanes J., Mena L., Encalada P.

***Abstract*— The present research shows a prototype that seeks the suppression of essential tremor in a neuroprosthesis that emits vibrations to saturate the channels of communication of this pathology, initially presents a general concept of the disease, and the treatments that seek to correct this symptom known as tremor. It was essential to follow the general outlines of the design and development of the device, and subsequently the results obtained and conclusions that validate the hypotheses raised, the authors propose a series of works that validate the system and the hypotheses itself.**

***Index Terms*—Essential tremor, neuroprosthesis, Pacini corpuscles, , upper extremities, vibratory actuators.**

I. Introduction

A tremor is an abnormal and involuntary type of movement characterized by excess movement that may interfere with the individual's ability to perform everyday tasks such as eating, writing, and so on. It can affect various parts of the human body such as the hands, head, torso and legs, [3]. Within the numerous disorders of the body movement, tremors are the most common form, they are a frequent occurrence in elderly people, sometimes being part of a helpless and incapacitated image of old age, a tremor must be assumed as a situation of a disease and not as part of aging. Among tremors, essential tremor is the most frequent, and is produced by specific alterations of the cerebellum, which is where the disorder is generated,[1]. Essential tremor should not be confused with Parkinson's disease, although there may be progression. To date there is no scientific evidence to prove its complete cure, either with pharmacological treatment, surgical or brain stimulation, [13]. The primary goal of all treatments is to maintain the patient's basic functions so that he or she can have as normal and independent a life as possible while reducing the disorder.

If we consider that drugs used are not useful in 50% of patients and that the patient's tolerance to drugs decreases with age, along with the impossibility of applying invasive therapies in elderly patients, demonstrates that research and new more effective therapeutic options are needed to stop the tremor, [18]. That is why this research proposes the development of a system capable of supplying vibratory waves to the sensory system of the human body, which connects with the cerebellum, and with this it aims to reduce the Essential Tremor (E.T.) in the upper extremities of the patient. It should be noted that the system is based on a novel hypothesis and the goal of this work is to develop a platform that allows us to validate and evaluate the most adequate values of amplitude and frequency of mechanical vibration, so that the signal transmitted from the mechanoreceptors to the central nervous system is as effective as possible in suppressing the tremor.

G. Delgado is a professor at Universidad del Azuay, Ecuador (e-mail: gabrieldelgado@uazuay.edu.ec)
J. Gavilanes is a professor at Escuela Superior Politécnica de Chimborazo, Ecuador (e-mail: javier.gavilanes@espoch.edu.ec)
L. Mena is a professor at Escuela Superior Politécnica del Litoral, Ecuador (e-mail: lismena@espol.edu.ec)
P. Encalada is a professor at Universidad Técnica de Ambato, Ecuador (e-mail: pg.encalada@uta.edu.ec)

A. Hypothesis

The description of the pathophysiology of Essential Tremor, which is more accepted by the medical community, shows that the essential tremor could be caused by the anomalous and maintained activation of the Inferior Olivary Nucleus (ION), which can be translated into pathological oscillations in the olive- cerebellum-thalamo-cortical during movement, being able to be responsible for the postural and kinetic tremor observed in the extremities in patients with E.T., [19].

Taking into account that ION can be inhibited by stimulation of the cuneiform nucleus, the first data station of the tactile information, the possibility of continuous Paccini receptor stimulation at high frequencies (vibratory sensitivity using a wide range of frequencies)) could to produce a stimulation of the cuneiform nucleus capable of suppressing ION activity, [20] thereby changing the pathological oscillations of ION and thereby producing a decrease or abolition of postural and kinetic tremor observed in patients with E.T.

This finding is in agreement with a recent work on the restoration of locomotion in rodent models through spinal cord stimulation. Therefore, current evidence supports the idea that stimulation of afferent pathways may alleviate the symptoms of tremors, [21].

II. The essential tremor

Essential tremor (E.T.) is a neurodegenerative disease [1], that affects mainly adults older than 65, [2]; this disease manifests itself with a postural tremor, which most of the time is symmetrical and involves the hands and forearms [3]

Around 90% of patients present tremor in the upper limbs from the beginning, although it may affect other parts of the anatomy such as the head, voice, lower limbs, jaw and, less frequently, the trunk or tongue, [5]. Koller, [6] emphasizes in his studies that patients suffering from essential tremor may be considered handicapped either by physical limitations or by the social disorder that the tremor can cause. Essential tremor is usually less severe when compared to parkinsonian tremor, however, it often causes more social dysfunction, [12].

A. Pathophysiology of tremors

The pathophysiological processes involved in the origin of the tremor are mostly speculative; however, neurophysiological studies based on electromyography have been performed on the affected muscles and by means of accelerometry and the application of computer technology have contributed in a relevant way to our knowledge about the physical characteristics of the tremor.

There is a central generator whose neurons discharge spontaneously in a rhythmic way and consequently produce tremor. This has been seen in neurophysiological studies with an intraneuronal record in the lower olive, the ventral thalamus, the subthalamic nucleus and in the inner pallid globe [7].

The mechanical component of the tremor depends on the physical properties of the oscillating limb because its mass and inertia provide a resonance frequency. The frequency range of essential tremor is characterized differently among researchers. Jain, [8] states that the range of the essential tremor is between 5 and 8 Hz while Cooper from 4 to 12 Hz, [9], and Elble from 3 to 11 Hz, [10].

B. Treatments

There is no drug capable of solving the problem of each patient, [12]. On the contrary, some drugs may work well in some patients and not be effective in others, also we should point out that many scientific research institutes are trying to find a solution that does not require surgery or medication.

C. Technological assistance to the superior members of the body.

Some studies show that, in the long term, medical treatment fails in 85% of cases. g, has influenced the growth of biomechanical load application research as a treatment method for the reduction of pathological tremor, a series of research shows that the increase in inertia or damping of the system could reduce an involuntary shaking movement, [13].

Among the recently investigated tremor reduction systems is the WOTAS (Wearable Orthosis for Tremor Assessment and Suppression) exoskeleton Fig. 1. The WOTAS platform was designed for the elbow and wrist joints, to allow the application of different control strategies on the patient.

III. NEUROPROSTHESIS CONCEPTUAL DESIGN

For this study, it is necessary to know the corpuscles found in the skin, since it is innervated by different types of independent nerve endings and receptors that recognize stimuli, facilitating skin as a sensorial organ.

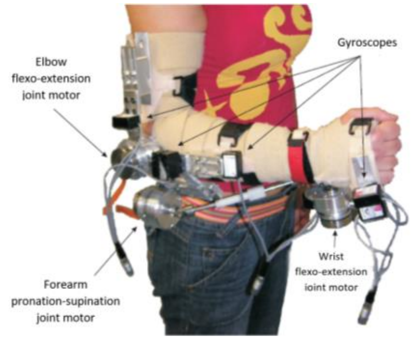

Fig. 1 WOTAS Exoskeleton.

Pacini corpuscles and Meissner corpuscles located in the subcutis are sensitive to mechanical vibrations and deformations, and detect different frequency ranges. Once stimulated, they transmit sensory information through the posterior cord to the cuneiform nucleus, where relay neurons transmit this information to the sensory thalamus and from there to the somatosensory cortex, [14]. The cuneiform nucleus contains GABAergic neurons projecting towards the inferior olivary nucleus [17], which hypothetically reduces the amplitude of the tremor. Paccini's corpuscles detect a range of frequencies from 80Hz to 450Hz, while Meissner's detect low frequencies between 10Hz and 80Hz.

A. System Architecture

The vibration system proposed for the upper limb of a patient consists of four fundamental stages: 1) Stage of Action in charge of generating the oscillatory movement at frequencies perceptible by the corpuscles; 2) Control stage, capable of producing different waves and amplitudes by the user; 3) Monitoring Stage, which will be the agent that registers the trembling movement of the patient and finally: 4) Software Stage, which joins all the stages through a graphic interface (HCI) that facilitates the handling by the operator.

1) Actuation stage

The actuation is the main stage for the operation of the system, since it is responsible for generating the vibrations as close to the dermis as possible so they can be captured by the corpuscles of Pacini. It is also responsible for the selection of the type of control and software for its handling. The devices responsible for transforming energy to vibration are called piezoelectric type actuators, which give a variation of position or movement, proportional to the voltage when a potential difference is applied to them. [15] (Fig. 3), but in fine variations, making this device very sensitive and precise, useful for the system requirements, being able to work in open loop by its linearity.

2) Control architecture

Considering the piezoelectric actuator, it is possible to use a driver for these actuators, which raises the input voltage according to its set gain configuration. In turn, Texas Instruments has a modifiable evaluation module for the driver called DRV8662EVM. These characteristics and their reduced size make it suitable for this work, so that the DRV8662 chip will allow designing and building a new card to control the vibratory actuators in a right way.

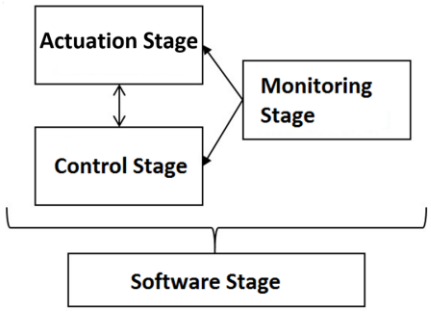

Fig. 2 System Architecture

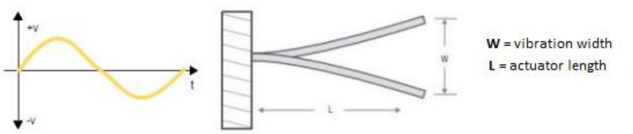

Fig. 3 Voltage Vs. Piezoelectric Actuator Displacement

3) *Monitoring stage*

The monitoring stage is covered by IMU inertial sensors of the company TECHNAID, which facilitates monitoring both the patient's tremor and the effect of the piezoelectric actuators on the patient, from which only two will be used in the monitoring of the patient's activity with E.T.

Essential tremor typically affects both upper extremities, particularly hands and forearms. It is always accompanied by a rhythmic tune of discharge from the motor units that forces the body to go into oscillation.

According to studies and experiments of some experts (Koller, Jainda, Cooper, Elble, Deuschl) it is concluded that the frequency of essential tremor differs in each patient, however, the range varies from 3 to 15Hz. Therefore, using software a band pass filter has been designed for the reading of only the values where the E.T is present. In such a way that it is possible to evaluate the usability of the prototype in patients.

The stages analyzed synthesize the conceptual design of the system, as shown in Fig. 4.

IV. Definition of Validation Protocol

In Table I some experimental protocols of system validation are proposed, as well as the description of the process.

A clinical validation of the concept should also be carried out where typical neurological examinations are considered as:

- Resting arm in the lap
- Keeping both arms extended
- Movement of the finger towards the nose.

Each one of these tasks has 60 seconds monitoring time, while the patient is sitting comfortably.

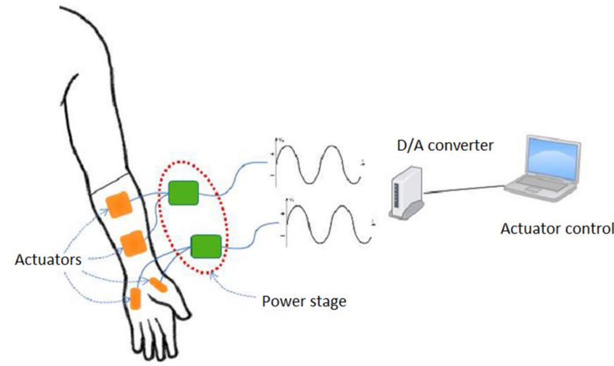

Fig. 4 Detailed conceptual design.

The garment will work in two ways to validate the process:

- Simulated Mode. - Frequencies generation for therapeutic purposes lower than 60Hz
- Verum Mode. - Therapeutic frequencies generation between 60-400 Hz, where the exact frequency is given by the experimental procedures named in Table 1.

In each session, 3 people will be present:

- Patient
- System operator
- Medical specialist

During the trial neither the patient nor the physician will know when the system is in simulated or Verum mode, with the purpose of avoiding the placebo effect of the system on the patient [16].

The complete development of the neuroprosthesis was performed, with each one of its stages. It is important to point out that this is a prototype capable of analyzing the effects produced by the vibration on the mechanoreceptors of the patient. Fig. 5 shows a photograph of the attachment of the vibratory actuators on the surface of the patient's arm, a garment was used for holding the entire palm of the hand as shown in the figure.

During the placing of the neuroprosthesis on a patient with E.T, protocols were carried out to validate the hypothesis, a measurement was established with inertial sensors placed strategically on the wrist and the patient's hand; Fig. 6 shows the patient's tremor signal in the time domain.

TABLE I
EXPERIMENTAL PROTOCOLS

Number	Experiment	Description
1	Operation of actuators in the hand	The frequency and amplitude are chosen, which can be varied to evaluate the patient's reaction.
2	Operation of actuators in the forearm.	Like method 1, frequency, amplitude and time of operation are varied, also applying frequency sweep.
3	Operation of actuators in the hand and forearm at the same frequency.	The actuators operate at the same frequency in two different parts of the arm.
4	Operation of actuators in the hand and in the forearm at a different frequency	The actuators operate at different frequencies in two different parts of the arm.

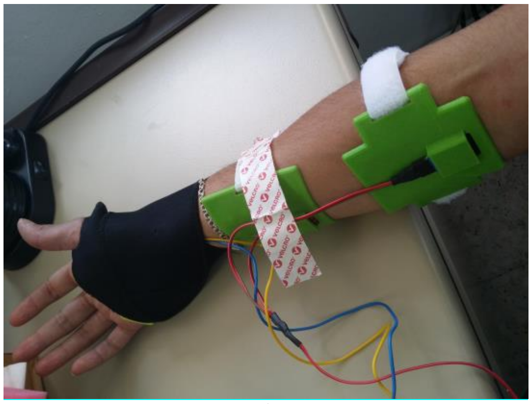

Fig. 5 Attachment of vibratory actuators.

V. Presentation of Results

After receiving and validating the E.T, a vibration frequency signal is sent in Crescendum mode (Ramp Up), from 70 to 350 Hz in 60 seconds; Fig. 7 takes the E.T. data while the patient receives that vibration. At the end, the patient enters a rest period of 30 seconds without monitoring the activity of Essential Tremor (E.T) and after this time the patient's data is taken again in 60 seconds to perform an overlap between E.T Preprocess and E.T Postprocess (Fig. 8).

As in the case analyzed, multiple vibration frequencies were sent to the patient, the next figures (Fig. 7 to Fig. 12) show the most significant frequency graphs for the final analysis on the patient.

In order to show a correct final analysis of the process, the patient's essential tremor graphs are superimposed, before and after the process, obtaining a reduction of the tremor in the patient of 61.43%.

In Fig. 13 the analysis is better appreciated, where the Preprocess is in blue and the Postprocess is in orange.

VI. Conclusions

During the development of this work, a prototype of a neuroprosthesis was built, which was capable of supplying vibrations on the skin of a patient with Essential Tremor, for this purpose the best components were selected in the corresponding stages:

Actuation Stage: The piezoelectric vibration actuators have a very wide range of operation, which was suitable to obtain frequencies necessary to be detected by the Pacini corpuscles, which have a direct connection with the inferior olivary nucleus that controls the motor functions and generates the tremor.

Control Stage: Printable materials with 3D technology allowed to design and make subjections with better transfer of the vibration towards the skin of the patient, without being a nuisance.

Monitoring Stage: From inertial sensors, it was possible to obtain a quantitative feedback of the effect that the vibration produces on the patient.

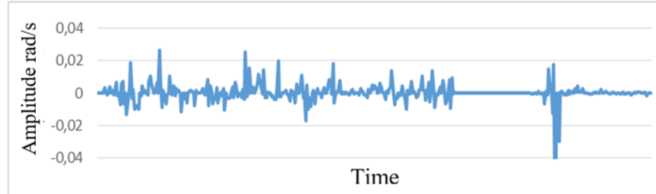

Fig. 6 Initial Tremor Preprocess of the patient in 60 seconds

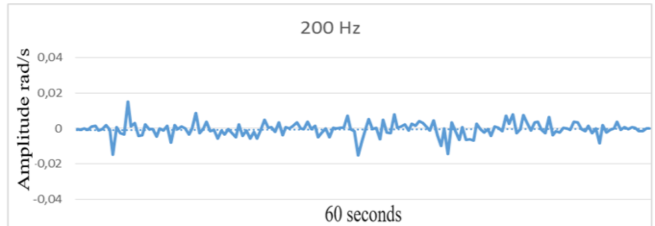

Fig. 7 Patient trembling in 60 seconds at 200Hz.

Fig. 8 Patient trembling in 60 seconds at rest.

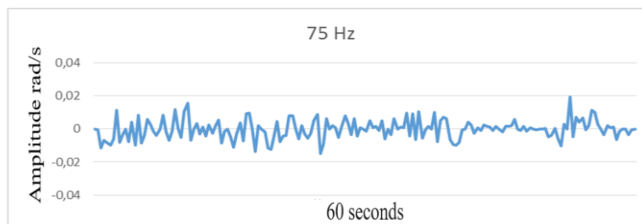

Fig. 9 Patient trembling in 60 seconds at 75Hz.

Fig. 10 Patient trembling in 60 seconds at rest.

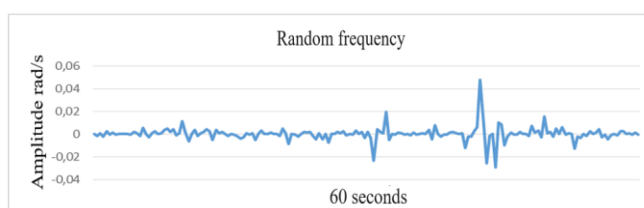

Fig. 11 Patient trembling in 60 seconds at random frequency

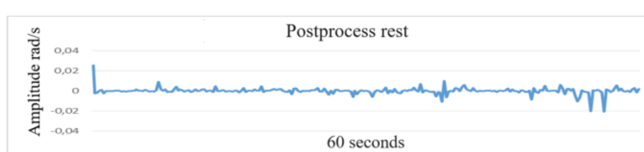

Fig. 12 Patient trembling in 60 seconds during postprocess

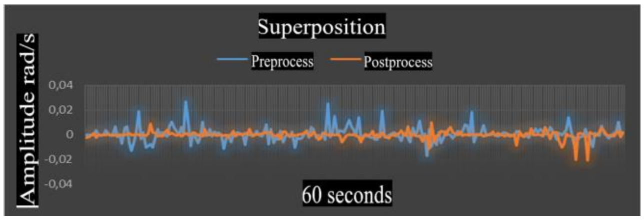

Fig. 13. Patient's tremor in 60 seconds during Pre-processing and Post-processing

Software Stage: An experimental protocol was presented for the validation of the neuroprosthesis capable of varying its frequency in an automatic way to observe the effects that said frequency exerts on the patient.

Validation stage: The experimental protocol gave us a small sample of what the presented hypothesis of suppression of tremor in a patient with E.T can validate, reducing 61.43% of the tremor.

VII. Future Work

Conduct research on different vibration frequencies on patients with E.T and obtain which are the best for each person.

Design and build flexible piezoelectric actuators capable of being placed in clothes to improve the patient's comfort.

Carry out an analysis of the neuroprosthesis for a larger group of patients in order to obtain an accurate validation of the hypothesis, since it is still premature to validate it with a single patient.

References

[1] U. Bonuccelli, "Essential tremor is a neurodegenerative disease," J. Neural Transm., vol. 119, no. 11, pp. 1383-7; discussion 1373, Nov. 2012.
[2] E. D. Louis, "Essential tremor.," Lancet Neurol., vol. 4, no. 2, pp. 100-10, Feb. 2005.
[3] G. Deuschl, P. Bain, and M. Brin, "Consensus statement of the Movement Disorder Society on Tremor. Ad Hoc Scientific Committee." Mov. Disord., vol. 13 Suppl 3, pp. 2-23, Jan. 1998.
[4] E. D. Louis and M. S. Okun, "It is time to remove the 'benign' from the essential tremor label.," Parkinsonism Relat. Disord., vol. 17, no. 7, pp. 516-20, Aug. 2011.
[5] K. L. Busenbark, J. Nash, S. Nash, J. P. Hubble, and W. C. Koller, "Is essential tremor benign?", Neurology, vol. 41, no. 12, pp. 1982-3, Dec. 1991.
[6] Elble, Rodger J., and William C. Koller. Tremor. Johns Hopkins University Press, 1990.
[7] S. E. Hua, F. a Lenz, T. a Zirh, S. G. Reich, and P. M. Dougherty, "Thalamic neuronal activity correlated with essential tremor." J. Neurol. Neurosurg. Psychiatry, vol. 64, no. 2, pp. 273-6, Feb. 1998.
[8] S.S. Jain y S.C. Kirshblum. Movement disorders, including tremors. In A. Joel y J.B. DeLisa, editors, Rehabilitation Medicine: Principles and practice, volume 2. Lippincott Company: Philadelphis, 1993.
[9] G. Cooper y R. Rodnitzky. The many forms of tremor. Precise classification guides selection of therapy. Postgraduate Medicine online, July 2000.
[10] R.J. Elble. Essential tremor frequency decreases with time. Neurology, 2000.
[11] Marsden CD, Origins of normal and pathologic tremor. En: Findley LJ, Capildeo R (Eds). (1984). Movement Disorders: Tremor. New York: Oxford University Press, pp 37-84. En: Fahn S, Jankovic J (Eds). (2007).
[12] J. Benito-León and E. D. Louis, "Essential tremor: emerging views of a common disorder.," Nat. Clin. Pract. Neurol., vol. 2, no. 12, Dec. 2006.
[13] Kotovsky J and Rosen MJ. A wearable tremor suppression orthosis, J Rehab Res Develop, 1998.
[14] E. Kandel, J. Schwartz, and T. Jessell, Principles of Neural Science. 2000.
[15] CURIE, Jacques; CURIE, Pierre. Développement, par pression, de 'électricité polaire dans les cristaux hémièdres à faces inclinées. Comptes Rendus, 1880, vol. 91, p. 294-295.
[16] E. Rocon, J. M. Belda-Lois, A. F. Ruiz, M. Manto, J. C. Moreno, and J. L. Pons, _Design and validation of a rehabilitation robotic exoskeleton for tremor assessment and suppression, _ IEEE Trans. Neural Syst. Rehabil. Eng., vol. 15, no. 3, pp. 367_378, Sep. 2007.
[17] A. R. Gibson, K. M. Horn, and M. Pong, _Inhibitory control of olivary discharge. Ann. N. Y. Acad. Sci., vol. 978, pp. 219_31, Dec. 2002.
[18] J. Benito-León, "Essential tremor: one of the most common neurodegenerative diseases?," Neuroepidemiology, vol. 36, no. 2, pp. 77–8, Jan. 2011.
[19] K. E. Zeuner and G. Deuschl, An update on tremors., Curr. Opin. Neurol., vol.25, no. 4, pp. 47582, Aug. 2012.
[20] P. Geborek, H. Jörntell, and F. Bengtsson, Stimulation within the cuneate nucleus suppresses synaptic activation of climbing bers.,Front. Neural Circuits, vol. 6, no. January, p. 120, Jan. 2012.
[21] R. Fuentes, P. Petersson, and M. A. L. Nicolelis, Restoration of locomotive function in Parkinson's disease by spinal cord stimulation: mechanistic approach., Eur. J. Neurosci., vol. 32, no. 7, pp. 11008, Oct. 2010.

Delgado G. was born in Ecuador, Cuenca City, in 1990. He received the B.S. in Electronics Engineering from Universidad del Azuay, Cuenca - Ecuador in 2014 and the MSc. degree in Automation and Robotics from University Polytechnic of Madrid, Spain in 2015.
In 2014 -2015 He was a Research Assistant in Group of Neural and Cognitive Engineering from Centre for Automation and Robotics (CSIC-UPM) in Spanish National Research Council.
Since 2016, He has been professor in Universidad del Azuay, Cuenca - Ecuador and he has been Research. His research interests include, artificial intelligence, artificial vision, manipulators robot, mobile robots, machine learning and control systems.

Gavilanes J. was born in Ecuador, Santo Domingo City, in 1987. He received the B.S. in electronics engineering from Escuela Superior Politécnica del Chimborazo, Riobamba Ecuador in 2012 and the MSc. degree in automation and robotics from University Polytechnic of Madrid, Spain in 2015.
In 2014 -2015 He was a Research Assistant in Field & Service Robotics Group from Centre for Automation and Robotics (CSIC-UPM) in Spanish National Research Council. He collaborated in the Tiramisu European project.
Since 2016, He has been professor in Escuela Superior Politécnica del Chimborazo, Riobamba Ecuador and he has been Research Assistant with Biomechanics Studies Research Group. His research interests include artificial vision, biomechanics, mobile robots and additive manufacturing.

Mena L. was born in Ecuador, Ambato City, in 1987. She received the B.S. in electronics engineering from Salesian Polytechnic University, Quito Ecuador in 2012 and the MSc. degree in automation and robotics from University Polytechnic of Madrid, Spain in 2015.

In 2014 -2015 she was a Research Assistant in Field & Service Robotics Group from Centre for Automation and Robotics (CSIC-UPM) in Spanish National Research Council. She collaborated in the Tiramisu European project.

Since 2016, she has been professor with the Electrical and Computer Engineering Department, Escuela Superior Politécnica del Litoral, Guayaquil Ecuador and she has been Research Assistant with Vision and Robotics Center. Her research interests include locomotion systems, mobile robots and additive manufacturing.

Encalada P. was born in Ecuador, Ambato City, in 1986. He received the M.S.c degrees in Automatic and Robotic from the University Politehnica of Madrid, España, in 2016 and the degree in engineering of Electronic and Instrumentation from ESPE, Ecuador, in 2012.

From 2015 to 2016, he was a Research Assistant with the CAR of the University Politehnica of Madrid.

Since 2013, he has been an Professor with the Electrical and Comunication and Industrial Engineering Department of the Universidad Técnica de Ambato.

He is the author of one chapter of a Robocity 2016 and his research interests include robotic systems, machine learning and control systems.