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SKIN TISSUE INTEGRITY UNDER SHEAR

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Welcome to the first STINTS Newsletter

The STINTS European Training Network currently involves a cohort of 12 early stage researchers hosted at six universities and two multi-national companies across Europe and the Middle East. The network is focused on the interaction of skin with support surfaces and medical/personal care devices to prevent skin damage resulting from sustained mechanical loading and adverse microclimates (ranging from skin irritation to Pressure Ulcers and Diabetic Foot Ulcers).

In our first newsletter, the ESRs introduce themselves and their individual projects.

Funded by the Horizon 2020 Framework Programme of the European Union

Ana Évora, BSc MSc

I am a young Portuguese biochemist whose academic life was lived in the "Antiga, mui nobre, sempre leal e invicta cidade do Porto" ("Old, very noble, always loyal and undefeated city of Porto"). During the third year of my Bachelor Degree in Biochemistry, I completed an internship of five months as an ERASMUS student in Szeged, Hungary, at the Biological Research Centre (BRC) - studying the role of a Heat Shock Protein on Alzheimer's disease. Hungary was the European experience I needed to understand how much an international environment can enrich a young mind and how it is a necessity in the world of Research – where the difference of culture and education usually means diversity of thought and vision. I returned to Portugal with a certainty that I would have to go abroad again, even if not right away.

As a biochemist, I tend to look at the chemical processes occurring on a cellular level and that was exactly what my work during my Master's Thesis at the Faculty of Sciences of the University of Porto was about. There I studied the possible biochemical effects of anthocyanins, natural pigments, applied to the skin as cosmetic compounds. Even though that was a food related project, my passion for studying the skin started to grow and I got motivated to learn more about the immense world of cosmetics. From a Master's in Biochemistry, I went through an online course in Organic Formulation and for a year, I developed my own homemade natural lotions and body butters. This was when STINTS came along.

As an ESR on the STINTS project, working in the Department of Chemical Engineering at the University of Birmingham, I look at the core problem – Pressure Ulcers – with the mind of a biochemist: what is changing when skin is under pressure, what mechanistic processes are happening inside the cells that may be changing their morphology or biochemistry. However, pressure is, in fact, a mechanical problem, which is directing me to study the effect of pressure on the mechanical properties of skin cells, particularly of corneocytes (see Figure 1). This is what my project will focus on – understanding the role of pressure on the morphological, chemical and mechanical properties of corneocytes on a first instance, and then building to a tribological view of the effects of pressure on the skin, always taking particular interest on the role of moisture on the processes leading to pressure ulcer formation.

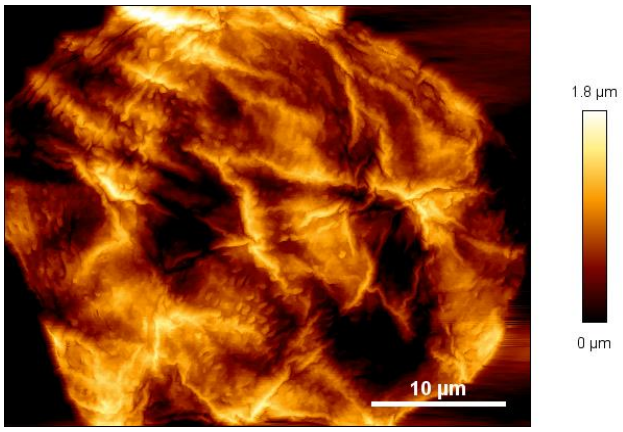


Figure 1 - Topographical image of a corneocyte obtained by AFM contact mode technique.

This project will contribute to build fundamental knowledge about pressure ulcers formation at a cellular and tissue level and to formulate strategies to prevent it.

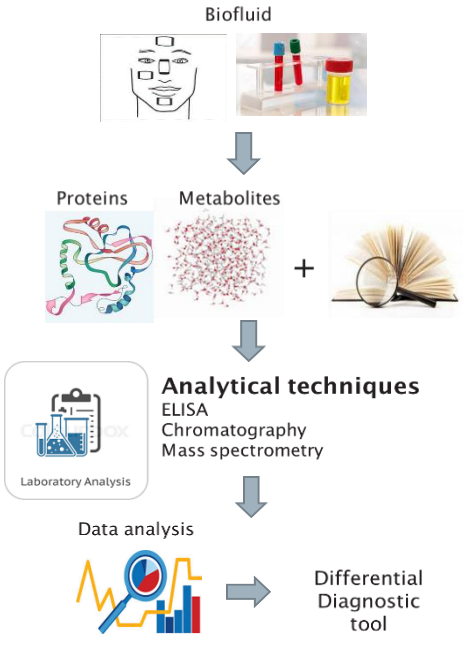
Hemalatha Jayabal, BTech MTech

I started my research career with the aim of using engineering tools to provide better quality of life for the community. I strongly believe in the famous quote '**There's plenty of room at the bottom'** by Dr. Richard Feynman**.** The application of engineering principles and understanding of physical phenomena at lower scales brings about a whole new array of applications that are relevant to improved health care and effective diagnostics.

I began my career as a technical engineer in a fertilizer industry understanding fluid transport at the industrial scale, following my bachelor's degree in chemical engineering from Anna University, India (2013). I then pursued my master's degree in chemical engineering from Indian Institute of Technology, Bombay, India (2017). During this postgraduate course, I worked on "Developing a biomarker-based point of care device for detecting tobacco usage". This enabled me to master a number of analytical measurement techniques for measuring biomarkers. These included approaches to address challenges such as poor sensitivity and lack of sophisticated measurement tools at point-of-care by applying principles of chemistry and microfluidics.

Subsequently, I joined a leading consultancy firm (Tata Consultancy Services) in India as a researcher to study the efficacy of cosmetics and drug delivery through the skin layers. During this period, I developed multiscale models to understand the mechanical properties of skin and experimentally validated a nanoparticle-protein based transdermal drug delivery model. The augmentation of computational knowledge to my experimental skills enabled me to appreciate the combination to solve engineering problems.

At University of Southampton, as a Marie-Curie Early Stage Researcher under the guidance of Prof. Dan Bader and Dr. Peter Worsley, I am working on developing a diagnostic method using biomarkers and physical sensors to detect early changes in skin integrity. This project will focus on providing a robust non-invasive, objective measurement that would aid clinicians to prevent the occurrence of skin damage, thereby saving treatment costs and eliminating health risks. The hands-on experimental knowledge gained from my previous project and the understanding of structure and function of skin will prove helpful in achieving the goal of a diagnostic tool. The project workflow has been summarised in the figure (right).



Project workflow

Nkemjika Abiakam, BSc MRes MSc

“They say that the most selfish thing someone can do in this world is helping someone else. Why is it selfish? Because nothing is better than the gratification and good feelings that comes with it”.

I have always been interested in both acute and chronic wounds, particularly in the understanding of the mechanisms that lead to their manifestation and the development of scientific tools that could improve wound prevention and management, enabling an enhanced quality of life to vulnerable individuals.

I was awarded a BSc in Medical Biotechnologies in 2013 at the University of Parma, Italy followed by a MRes in Biotechnologies applied to Regenerative Medicine, Pharmaceutical and Veterinary at the University of Parma (2015). In 2018 I also gained a MSc in Regenerative Medicine and Nanotechnology from a part-time course at the University College London (UCL), UK.

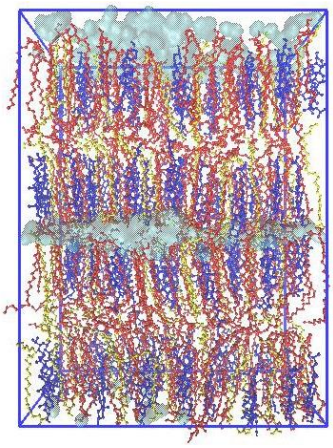
I started my research experience in a multidisciplinary team at the Interdepartmental Centre Biopharmanet-Tec in Italy. The Centre is active in the development of manufacturing processes of new compounds, drug delivery platforms and in nano pharmaceutical technologies. During this period, I faced many issues about the optimum strategy for drug delivery using non-invasive routes, the use of nanotechnologies as an adjuvant to promote immune response in vaccination systems and the use of 3D scaffolds for wound regeneration. Working in this Centre accelerated my academic development and provided me the possibility to broader my research skills, ranging from cell culture to working with animal models. I also worked as a senior Clinical Trials Assistant, an experience that enabled me to gain an insight of the end user’s perspective, with particular interest in the use of new cutting-edge- strategies for disease prevention and management. It also provided an opportunity to learn the challenges and rewards with working in a multidisciplinary team to conduct clinical trials research with various patient cohorts.

My project as a Marie Curie Fellow is focused on the use of different non-invasive physical sensors and biomarkers to detect early changes of the skin status, prior to the full development of soft tissue damage in the form of Pressure ulcers (PUs), Diabetic Foot ulcers (DFUs) or Incontinence Associated Dermatitis (IAD). The knowledge acquired from this research will aid clinicians to optimise and adopt improved prevention strategies thereby minimising the risk of these disabling conditions. This will benefit both patients as well as healthcare services, including the UK National Health Service (NHS).

Nicola Piasentin, BSc MSc

I am Nicola Piasentin, an Italian student that has recently joined the STINTS project.

I graduated in Physics at Università degli Studi di Trieste in Italy, where I got both my bachelor's and master's degree. As a kid I was always fascinated by science and by the study of living things. That's why I tried to join my interests in physics and biology and chose to focus on the branch of biophysics, where we use theoretical/computational models to describe and hopefully understand better some complex properties of living matter. As a university student I worked mainly on tumours and their properties, both from a chemical and structural point of view. In particular, for my master's thesis I collaborated with a biologist and a physicist in order to write a mathematical model to describe the regulation of pH in tumour cells.



My thesis helped me to understand what I liked and what I was looking for in my future. Firstly, I really enjoyed working in a strongly interdisciplinary environment; having the opportunity to collaborate and share knowledge with scientists from other fields is exciting and, at the end of the day, you always learn something new. Secondly, I found that working on hot topics for public and private health systems, such as tumours, was motivating. Being able to give a contribution, even a small one, is really rewarding and is one of the main reasons why I am interested in research. Lastly, developing and implementing computationally a model to describe a living thing was interesting and incredibly challenging, characteristics that I would be glad to find in my every-day job.

I believe that this brief introduction well explains why I joined STINTS and, specifically, my project within it. I like the idea of working on pressure ulcers, a burden for both patients and national health systems, using a computational approach. The core idea of my research here at Unilever is to develop an in-silico model to gain a biophysical insight on the effects of skin hydration on friction and damage. To this end, I use molecular dynamics packages to run simulations of small systems that are described from an atomistic perspective; in my case, I build lipid bilayer configurations that mimic the composition and the structure of human skin cell walls.

Moisture is an important parameter of skin local microclimate and is linked to skin breakdown due to changes in its elastic properties. Therefore, through these simulations we aim to shed light on how the presence of water changes the lipidic structure of skin and we try to understand how microscopic properties, like hydration, affect macroscopic ones, like elasticity.

Jessica Ralvoni, BSc MSc

I am an Italian PhD student at Eindhoven University of Technology (TU/e). I am a Bioengineer, graduated from University Federico II of Naples, where I obtained both my BSc and MSc Degrees. In 2016, I got my BSc Degree in Biomedical Engineering. During my studies I discovered my interest in Biomechanics and Tissue Engineering and I got my MSc Degree in Industrial Bioengineering in May 2019.

In September 2018, I started my MSc project at TU/e department of Mechanical Engineering (research group Polymer Technology), where I investigated the mechanical and rheological behaviour of adipose tissue under shear stress by building up a tool in Toolkit Finite Element Method.

This experience abroad helped me with the choice of my future career, because I discovered a strong interest for modeling and biomechanics. Moreover, I found the multicultural environment a fascinating reason for which I decided to move abroad to start my PhD in the Skin Tissue Integrity under Shear (STINTS) project at TU/e department of Biomedical Engineering (research group Soft Tissue Engineering and Mechanobiology).

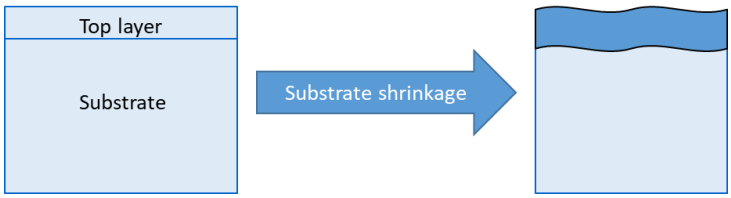


Figure 1 - Scheme of a bilayer induced instability with top layer representing the skin (stratum corneum, epidermis and dermis) and substrate representing the adipose tissue.

I am carrying out a research about the skin abdomen folding due to large weight loss after undergoing to bariatric surgery. The aim of this study is to develop a predictive Finite Element model to understand the main material and structural parameters influencing the folding process. This is a common problem of obese people with Body Mass Index (BMI) in the range of 35 – 40 $\frac{kg}{m^2}$. These people experience skin folding after undergoing bariatric surgery, which is a procedure used to induce large weight loss. It consists of stomach reduction, therefore the food absorption decreases causing fast and massive weight loss. Skin excess is due to irreversible remodelling of the tissue structure caused by obesity. Slimming leads to instability of the skin top layers, epidermis and dermis, the stability is reached again when the material folds. The Finite Element method is used to simulate the folding process of a bilayer structure representing skin (stratum corneum, epidermis and dermis) and adipose tissue (Fig. 1).

Moreover, the knowledge about the causes of this issue and the prediction of the skin folding risk will improve the life quality of patients in the hospital. Customized therapies could be developed to avoid undesirable infections.

Zülal Kizilaslan, BSc MSc

I am a Turkish mechanical engineer who aims to work on human body. Although during my bachelor degree I studied on materials such as steel, plastic and polymers, with master project I stepped to biomedical world at the Mersin University. After completed all master courses in the first year at this university, I had a chance to be in UTP University of Science and Technology, Poland as an Erasmus exchange student for 10 months. During this time period I not only started my thesis which is about developing reconstruction algorithm of micro computed tomography images of trabecular bone sample, but also gained experience of living far away from my accustomed environment and adopted another culture. I returned to Turkey with the data all I need for my master thesis and a broadened horizon.

As a mechanical engineer and would-be biomedical engineer, I am interested in analysing the system which needs to be improved or fixed. For human body, imaging is one of the most favourable way to understand the problem. So, the project I worked on during my master thesis at my both host and Erasmus universities was related with my interest. During this project I also had an opportunity to writing codes and creating algorithm which I started with baby steps. Since I have mechanical engineering background working in a biomechanics laboratory - which I describe it the point where mechanical and biomedical engineering meets - while keeping my mechanics knowledge fresh, upskilled me on bio materials.

As an ESR on the STINTS project, working in the Biomedical Engineering Department at the Eindhoven University of Technology, I focus to develop and validate methods to perform high resolution functional imaging of large areas of skin and build patient-specific mechanical models to estimate the mechanical properties of the different tissue layers. Several applications (prevention of Pressure Ulcer, excess skin after weight loss, interaction of skin with medical and cosmetic devices, etc.) require patient-specific in-vivo mechanical properties.

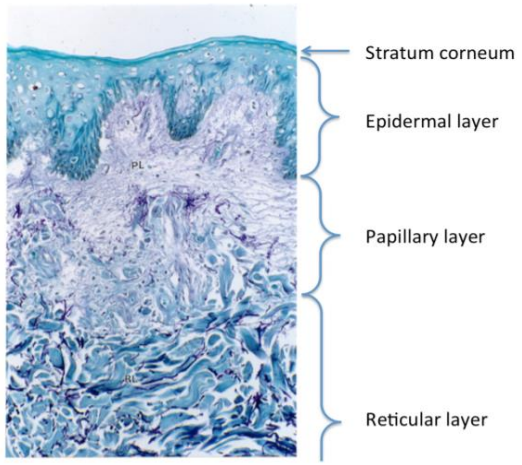


Figure 2 - D L Bader, C V C Bouten, D Colin, and C W J Oomens, editors. Pressure Ulcer Research. Springer Verlag, October 2005.

Pakhi Chaturvedi, BTech MS

I am a young professional, brought up in Mumbai, India, who is passionate about improving people's lives through innovation in healthcare. I received my B.Tech. in Biomedical Engineering from Manipal Institute of Engineering, Manipal, India. Curious about career prospects, I completed summer internships at Ambani Hospital, Siemens, and Roche Diagnostics, learning about the working principles of commercial medical devices. I conducted my bachelor's thesis at Bhabha Atomic Research Centre in Mumbai, helping the Nuclear Medicine Department validate the design for their in-house built Thyroid Uptake Probe. Eager to learn more about medical device development, I proceeded to earn a M.S. in Bioengineering from University of Illinois, Chicago, USA. My master's thesis focused on developing a product to prevent hypothermia in neonates in low resources countries. Simultaneously, I participated in multidisciplinary co-curricular activities with University groups, and qualified to State and National level entrepreneurship competitions, pragmatically learning about the creative biodesign process. Following graduation and emphasizing my interests in healthcare innovation, I worked at MATTER, an incubator for healthcare startups in Chicago, for 1.5 years. In my role on the Partner and Venture Programs team, I interacted with corporate professionals and entrepreneurs daily, forming a strong understanding of consumer needs and stakeholder requirements in product development. I decided to continue my education to make a global contribution in the field of consumer care when I applied for the Marie Curie PhD position with Philips, Drachten, Netherlands.

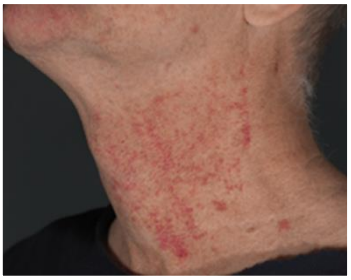


Figure 1: Image of irritated skin following device

My project within the STINTS group focuses on quantifying the variability in interpersonal skin tissue responses due to stimulus at the skin/device interface (refer Figure 1). With supervision from the Male Grooming team at Philips and the Skin Health Group at University of Southampton, I am working on a holistic approach to define and quantify characteristics of skin sensitivity, studying the biophysical and biochemical processes in the tissue following skin irritation. After evaluating current methodologies to measure structural and functional properties of skin, I have started experiments with multi-modal Optical Coherence Tomography of skin, including structure, elasticity and perfusion (refer Figure 2). My research will help to unravel interaction between skin responses, to identify people potentially at-risk of device-induced loss of skin integrity.

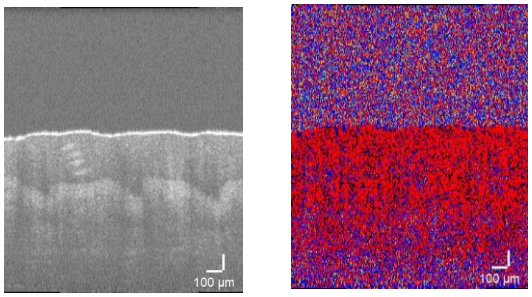


Figure 2: OCT Intensity and Phase images of skin structure (fingertip).

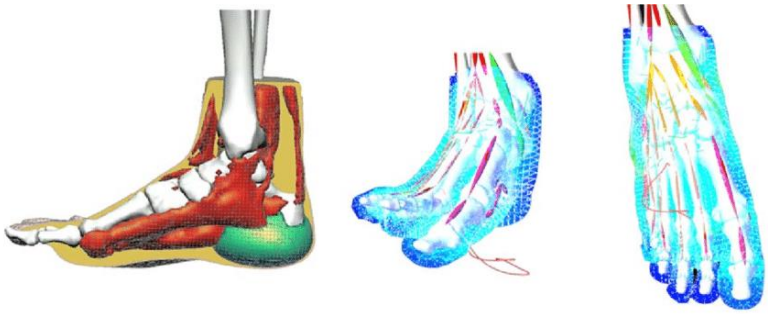
Alessio Trebbi, BSc MSc

Cheers! My name is Alessio Trebbi and I am a PhD student of the Marie Skłodowska-Curie Actions program. My thesis is developed at the University Grenoble Alpes in France and is part of the Skin Tissue INTegrity under Shear project. The goal is to develop and evaluate a subject-specific biomechanical model of the foot in the context of pressure ulcer prevention. This model is composed by rigid bone structures in contact with each other and soft tissues modeled by the finite element method. These soft tissues represent the skin tissues, fat, muscles and different ligaments of the foot. The development of the subject-specific model and its evaluation, by comparison with data from medical imaging, will be at the heart of my research work. Coupling the foot model with external devices such as orthotics or shoes, will address the investigation towards the development of plantar pressure ulcers.

Before the start of my PhD I worked as an intern in the laboratory of biorobotics in the University of Sao Paulo in Brazil. My work focused on the design of a 3D printed impedance controlled haptic paddle to investigate the adaptation of the human controller to different virtual haptic environments.

I have obtained my Master degree from the University of Twente in the Netherlands in the subject of biomechanical engineering. In this part of my education I focused my studies to learn about the mechanical interactions between humans and machines. My master thesis focused on the design and evaluation of an admittance controlled robot to estimate the stiffness of the knee during gait.

Since I have started my higher education I have been fascinated by the mechanics of the human body. I have the feeling that one of the challenges of this new decade is to widen the horizons in the field of biomechanics in order to fully understand the dynamics of pressure injuries and be able to create solutions for their prevention.



Ekaterina Mukhina, BSc MSc

Originally, I come from Saint Petersburg, beautiful Russian city. And in September 2019 I have started my PhD as a part of the STINTS project in Université Grenoble Alpes.

I've acquired my first Master in Applied Mechanics from the Peter the Great St. Petersburg Polytechnic University and it provided me with the strong theoretical basics. After that, I worked for almost 4 years as a structural analysis engineer in the petroleum industry, where I learned to apply my skills on practice. Later, in pursuit of finding the area of work where I could improve someone's life, I've obtained second Master degree in BioMedical Engineering with joined diploma of Université Paris-Descartes and Arts et Métiers ParisTech. There I've got a chance to learn about the human body mechanics. This program gave me a clearer understanding of many engineering opportunities in relation with the medical field. Particularly, it was interesting for me to learn the distinctions in the mechanical behaviour of the different biological tissues and to get a better understanding of how they interact with each other. Therefore, I decided to pursue a doctoral degree in the field of the soft tissue biomechanics.

Pressure ulcers (PU) are localized skin or soft tissue injuries that could significantly affect the quality of life. Previous research has shown that there are at least two damage mechanisms responsible for the onset of PU: ischemia / reperfusion damage and direct cell damage by direct (shear) deformation. The numerical modeling could provide insights into the mechanisms of the soft tissue injury. And inflammatory biomarkers were proven to show correlation with the tissue deformation, as rupture of cell membranes attracts immune system cells and triggers the inflammatory response. The project I work on as a part of the STINTS is related to the subject-specific modeling of the buttock's region under shear loading. Each patient has his unique mechanical (individual geometry, tissue stiffness) and biological (susceptibility to the loading) characteristics. To be able to provide personalized care algorithms, it is essential to consider these differences. Therefore, it was decided to investigate the interplay between the mechanical response and the individual biological inflammatory response in the numerical model.

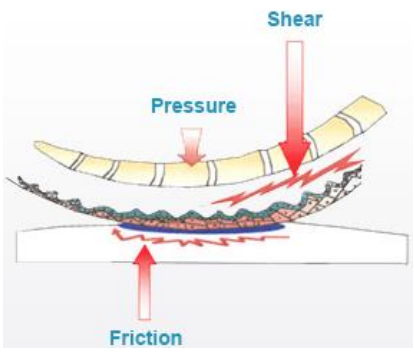


Figure 1. Adopted from http://www.urgomedical.com/wounds/pressure-ulcers/

To achieve the main purpose, coupling between mechanical and biological responses in the soft tissues under the loading, some conditions need to be taken into account. Low thickness of the soft tissues layer would improve the accuracy of the material properties estimation needed for numerical modeling; moreover, the flat surface would allow to get relevant information from the inflammatory biomarkers.

We decided to focus on the sacrum area (Figure 1) because it is one of the most common areas subjected to pressure ulcers; furthermore, it has a low thickness of soft tissues and the previous work on measuring inflammatory response on that site showed encouraging results.

Aleksei Orlov, BSc MSc

I have finished my BSc and MSc at Baltic State Technical University "Voenmeh" (Saint Petersburg, Russia) in Applied Mechanics. To date, I am a PhD student at the Department of Biomedical Engineering in the Faculty of Engineering at Tel Aviv University (TAU) under the supervision of Prof. Amit Gefen. As well as, I am a part of STINTS project.

Let me tell you a little bit about my current research. Regulated negative pressure wound therapy (NPWT) is a commonly used approach for healing wounds that are difficult to treat.

In this approach, negative pressure is applied to a foam material which is placed inside the wound and therefore creates dynamic stimulations to the wound bed and surrounding tissues.

In our present study, we attempt to detect the influence of dynamic stretches on cell migration rate into a wound. For this purpose, we developed a miniature incubation system and a dynamic stretching device. In order to evaluate cell migration rates we created wound assays and calculated wound sizes over time during different stretching protocols.

Using our live cell imaging, we attempt to get a better understanding of the kinematics of cell cultures during the wound healing process under dynamic stretching. It is known that cyclic loading positively affects the healing process of the wound however the exact protocols remain unknown.

Ultimately, this may be useful in the clinical application of NPWT in the healing process of wounds.

Controlling the stretch levels at the wound bed and surrounding tissues can be achieved by using specific 'smart materials' that induce specific stretching levels and stretching time characteristics as 'stand-alone' in the wound bed or in interaction with support surfaces.

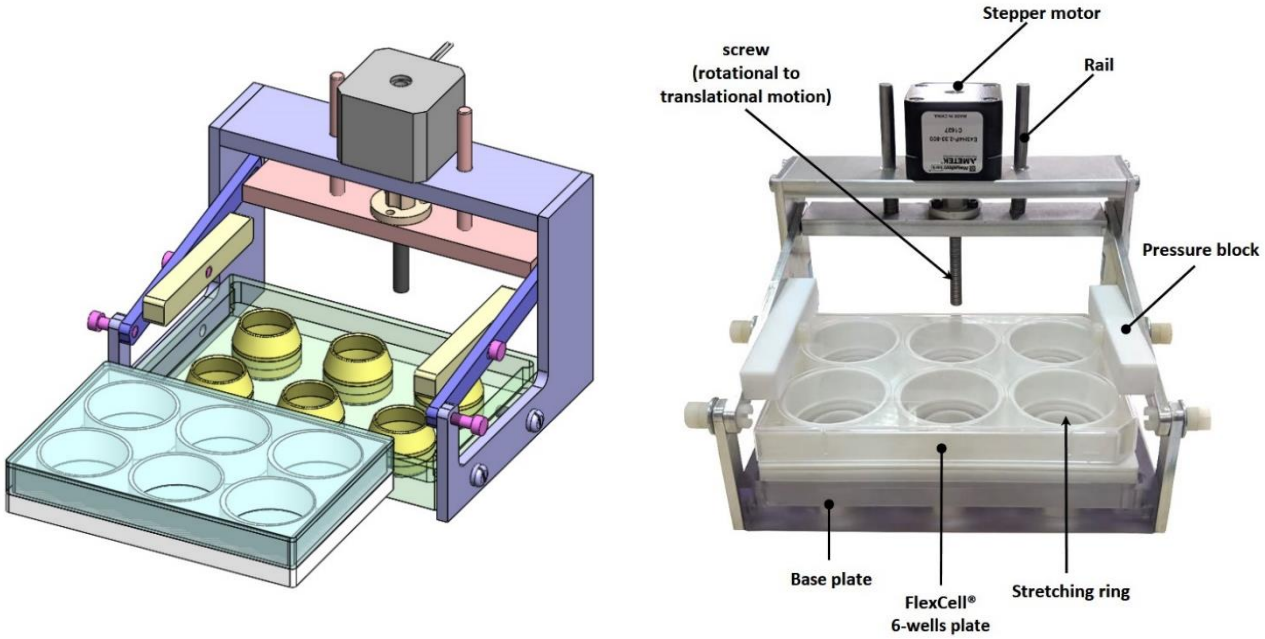


Figure 1. (A) SolidWorks design of cell stretching device. (B) Illustration of all parts of cell stretching device.

Elis de Castro, BSc MSc

Born in Teresina, the warmest state capital of Brazil, I have an Electrical Engineer's degree in the fields of Electrical Power Systems from the Federal University of Piauí. During my Bachelor's Degree, I had an exchange program that brought me to France, in 2014, where I studied for one year at the University of Perpignan Via Domitia.

In 2019, I got a master's degree. During the master's studies, I really started my passion for research. At the Federal University of Paraná, I worked on a project of a Photovoltaic Power Station on a microgrid implemented at the University. At this time, I started working on Power Systems Control, which was new for me. In 2018, I had a new opportunity to go to France, for a Summer School promoted by a partnership between CRIStAL & L2EP labs and the International Academy of Lille. One year later I found myself back, working at L2EP and doing research, with a new and exciting field: healthcare.

For me, the best thing about research is that we can help positively the people and the world we live in. We have the responsibility to build and use the knowledge for the wellness and sustainable progress of society. In STINTS project, I hope to contribute with the design of a portable early diagnostic tool for Pressure Ulcers by intelligent fusing of data about sensory function decline and mechanical property evolution.

I expect to establish a link between tactile sensitivity decline and local mechanical properties for early stage Pressure Ulcer risk using a vibrating plate, such as the one shown on Figure 1 [1]. The frequency of the vibration we will test will be Low Frequency Ultrasound, which may be between 20 and 40 kHz.

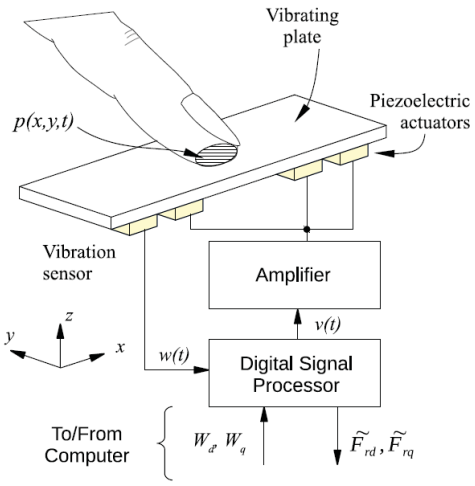


Fig. 1. Principle of the acoustical force measurement.

[1] Kaci, A., Torres, A., Giraud, F., Giraud-Audine, C., Amberg, M., & Lemaire-Semail, B. (2019, July). Fundamental Acoustical Finger Force Calculation for Out-of-Plane Ultrasonic Vibration and its Correlation with Friction Reduction. In 2019 IEEE World Haptics Conference (WHC) (pp. 413-418). IEEE.

Yisha Chen, BSc MSc

I am a Chinese, born in Hunan province and spent my early research years in Xiamen University, Fujian province. My academic background lies in Electrical Engineering, and received bachelor and master degree in 2016 and 2019, respectively. It was my misdiagnosis experience with lumbar vertebra problems in 2015 that inspired my interests in biomedical engineering. Through my bachelor thesis project (*Morphological Analysis of Meibomian Glands*) and master degree thesis (*Non-invasive Screening of Oesophageal Disease Based on Swallowing Vibration*), I got to deeply understand the fascination of combining electrical engineering with biomedical field. Appreciating the significance of human health and precision medical equipment, I determined to devote myself to the development of advanced medical devices so that patients could receive treatment properly and timely.

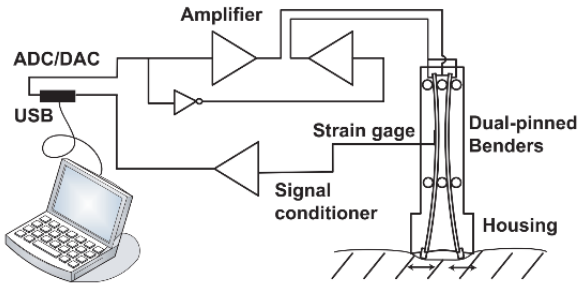


Fig.1 First version device [1]

It's an honour to be part of STINTS project in 2019, since it enables me to continue contributing in healthcare field. As a PhD student in the laboratory L2EP, University of Lille, I am going to discover changes in skin mechanical properties during the formation of pressure ulcer (PU) with a portable probe. Fig.1 shows the preliminary design of the probe. We are looking forward to using the probe to realize *in vivo* detection of early stage PU risk economically and effectively. The developed device is expected to relief social cost in pressure ulcers from a long term.

[1] Q. Wang, L. Kong, S. Sprigle, and V. Hayward, "Portable Gage for Pressure Ulcer Detection," in *2006 International Conference of the IEEE Engineering in Medicine and Biology Society*, 2006, pp. 5997–6000, doi: 10.1109/IEMBS.2006.260070.