Dottorato/PhD in
Bioingegneria e Scienze Medico-Chirurgiche / Bioengineering and Medical-Surgical Sciences

(in convenzione con Università degli Studi di Torino e il Politecnico di Torino / jointly activated by Università degli Studi di Torino and Politecnico di Torino)

XXXIV ciclo

Elenco delle tematiche per specifiche borse di Dottorato, posti in apprendistato, assegni di ricerca / List of research topics bound to PhD scholarships, positions with apprenticeship contract, positions with research fellowships

(Aggiornato al 21 giugno 2018)
(Last updated on: 21st June 2018)

1) 3D augmented reality in robot-assisted urological surgery: implementation and automatization of the 3D virtual models of organs in the robotic surgical field. (borsa Università di Torino), (supervisor: Francesco Porpiglia)

2) Inflammatory Bowel Diseases: New biological drugs' indication and surgical indication / Malattie infiammatorie croniche intestinali: Indicazione alla terapia con i nuovi farmaci biologici e indicazione alla chirurgia. (borsa Università di Torino), (supervisors: Mario Morino, Alberto Arezzo)

3) La diagnostica salivare nelle patologie paradontali/ Salivary diagnostics in periodontal diseases. (borsa Università di Torino), (supervisor: Stefano Carossa)

4) Preclinical and translational research for new technologies in vascular surgery: evaluation of the angiogenic effects of extracellular vesicles. (borsa Università di Torino), (supervisors: Mario Morino, Alberto Arezzo)

5) Soft tissue: culture in dynamic bioreactors and mechanical characterization. (borsa Politecnico di Torino), (supervisors: Alberto Audenino, Diana Massai)
6) Biomaterials and Nanotechnologies for advanced therapies. *(borsa Politecnico di Torino)*, *(supervisors: Gianluca Ciardelli, Valeria Chiono, Gianni Ciofani)*

7) Biomaterials-mediated direct cell reprogramming for myocardial regeneration. *(Politecnico di Torino, ERC Consolidator Grant BIORECAR)*, *(supervisors: Valeria Chiono, Carla Divieto)*

8) Advanced technologies for the assessment of the neuromuscular system. *(borsa Politecnico di Torino)*, *(supervisors: Marco Gazzoni, Alberto Botter)*

9) Wearable devices for the assessment of human activities. *(borsa Politecnico di Torino)*, *(supervisors: Marco Gazzoni, Marco Knaflitz)*

10) Biofluid Mechanics Clinical Applications. *(borsa Politecnico di Torino)*, *(supervisors: Umberto Morbiducci, Diego Gallo)*

11) Growth factor release upon acidic environment in bone resorption-GRACE. *(borsa Politecnico di Torino)*, *(supervisor: Chiara Vitale Brovarone)*

12) Computational Drug Discovery. *(borsa Politecnico di Torino)*, *(supervisor: Jack Tuszynski)*

13) “Sviluppo di tecniche innovative per la diagnosi autonoma del ritmo cardiaco da implementare in defibrillatori semiautomatici” *(posto in apprendistato Politecnico di Torino – Elpro srl)*, *(supervisors: Eros Pasero, Cesare Mangone)*
PhD in Bioengineering and Medical-Surgical Sciences

cycle XXXIV

(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research Title:
“3D augmented reality in robot-assisted urological surgery: implementation and automatization of the 3D virtual models of organs in the robotic surgical field”

Funded by
UniTO

Supervisor
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Context of the research activity
The concept of “precision surgery” is nowadays intrinsic in the management of the genitourinary cancers. A detailed case-specific understanding of the surgical anatomy represents the key point for a tailored treatment planning. In this setting, the 3D reconstruction of the standard two-dimension cross-sectional imaging has known increasing diffusion. Such technology is perceived as a useful tool in the surgical planning, the surgeon’s training and the patient’s counselling, because avoids the “building in mind” process of the two-dimension cross-sectional imaging. It allows a better comprehension of anatomy, vascularization and position of the organs, key steps in the surgical management of prostate and kidney cancers. But the real step forward in this setting is undoubtedly represented by the possibility to be guided by such reconstructions during the surgery. Nowadays the experiences of 3D virtual model guidance are still anecdotal and based on the availability of 3D models (virtual or printed) consultable during the surgery, in order to perform “cognitive” procedures. By now, a real 3D virtual navigation guidance during the surgery is still lacking.

Objectives
The general objective and aim of the research is to develop a software that can integrate the 3D virtual model of the urological organs and tumours inside the Da Vinci (Intuitive, Sunnyvale, CA, USA) robotic console during robotic procedures. With the virtual model superimposed on the real anatomy, the surgeon can increase his perception of organs and tumours’ location, can have a better understanding of the vascular
The process starts with the 3D reconstruction of urological organs and tumours from high resolution (1 mm sliced) multi-parametric Magnetic Resonance Imaging (mp-MRI) or Computed Tomography scan Imaging (CT).

- The 3D models have to be integrated in the robotic console by a dedicated software that allows the model to be moved and superimposed to the surgical field.
- Once the superimposition of the virtual model is obtained and the 3D virtual organ can be moved manually in the surgical field, to adapt its shape and orientation to the real one on the basis of the specific phase of the surgery, the project proceeds with the development of a second dedicated software, that allows to synchronize the movements of the 3D virtual model with the in-vivo anatomy, in order to perform an automatized augmented reality uro-oncological surgery.

### Skills and competencies for the development of the activity

The characteristics of the successful candidate are:

- Expertise in the anatomy of the urogenital system
- Expertise in urologic surgery with special competence in prostate and kidney cancer
- Expertise in robotic surgical technology and 3D virtual rendering of the organs from traditional imaging
- Documented participation to research projects with acquired knowledge in the context addressed
- Proactive approach to join a three-years research program and carry out interdisciplinary research
PhD in Bioengineering an Medical-Surgical Sciences

cycle XXXIV

(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research Title: “Inflammatory Bowel Diseases: New biological drugs' indication and surgical indication” (Malattie infiammatorie croniche intestinali: Indicazione alla terapia con i nuovi farmaci biologici e indicazione alla chirurgia)

Funded by

Università di Torino

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Inflammatory bowel diseases, mainly Crohn’s disease and Ulcerative colitis, are chronic, disabling disease the affect patients with a peak of incidence between 20 and 30 years. The incidence is rising and at least 200,000 Italians are affected.

The cause is unknown, but it is thought to derive from an interaction between the genetic predisposition, the immune system and the intestinal microbiome.

The inflammation in these patients could affect not only the bowel, but also the joints, skin, eyes and other organs.

About 70% of Crohn’s disease patients will undergo to surgical resection one time in the life and almost 20% of these will undergo to at least another bowel resection. The presence of granulomas in resection specimen and the myenteric plexitis are predictor of early post-operative recurrence, making the role of the pathologist also fundamental. Furthermore, about 30% of Crohn’s disease patients suffer from perianal disease, field in which a collaboration between the gastroenterologist who prescribe biological drugs and the surgeon is mandatory. The surgical resection for ulcerative colitis
consist of colectomy with ileo-anal pouch anastomosis, but also after the surgery the disease could return with an inflammation of the pouch.

New biologic (anti-integrin, anti-IL12-23) and small molecules (anti-Janus Kinase) are more and more entering in the market, but it is not clear if these drugs are able to reduce the number of surgical resections and to change the natural history of the disease.

It must be emphasized that surgery is not always a failure of medical therapy, but could be the first choice in some circumstances (i.e. a short, not inflamed, tract of the terminal ileum).

The early assessment of the therapeutic response and the tight control of the disease seems to obtain better long-term outcome compared to classic management based on the clinical symptoms. Till now the gold standard of the therapeutic assessment is the ileocolonoscopy, a demanding procedure often not well tolerated by the patients. Alternative techniques to evaluated the mucosal healing are strictly necessary (i.e. capsule devices capable of control of movement).

From all this, it emerges that optimal patient’ management derives from the collaboration of more specialists, among which the gastroenterologist, the surgeon, the rheumatologist, the radiologist, the dietician, the pathologist and others.

**Objectives**

The primary objectives of the research are the optimization of the management of these patients that is becoming increasingly complex.

In particular, since the therapeutic choices are always wider, the main focus of the research will be to find the predictors of the therapeutic response (pattern of interleukins, markers of bowel permeability) to help the clinicians to choose between the drugs with different mechanism of action and to know when there is no place for the drugs and the surgery should be the way.

In addition to the research of the predictors of response, another objective will be the early evaluation of the response using new non-invasive technological devices as new endoscopic capsules that, with an interface application, allow the clinician to stop and direct the device into points of interest for detailed inspection/diagnosis (evaluation of mucosal healing). For example, using miniature legs carrying a wheel, capable of traverse through the small bowel, and to stabilize itself without obstructing its locomotion and thus
offering smooth video capture without missing any pathologies.

Furthermore, the shared management of the patient among more specialists (gastroenterologist, surgeon, dermatologist, rheumatologist) should tailored the cure to the single patient, reducing the need to be visited on different days from different specialists, with less loss of work days and an increase in productivity, as well as a better management of limited resources for high-cost drugs that will result from the sharing of the choices among different specialists.

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<th>Skills and competencies for the development of the activity</th>
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<tr>
<td>Gastroenterology or general surgery specialization.</td>
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<td>Long-term experience in the shared management between gastroenterologist, general surgeon, dermatologist, rheumatologist of complex patients suffering from inflammatory bowel disease.</td>
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<td>Extensive publications over the past 5 years on PubMed - ISI Web of Science in the field of inflammatory bowel diseases.</td>
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<td>Curriculum between medicine and engineering (degree in Medicine and Surgery and degree in Engineering).</td>
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PhD in Bioengineering an Medical-Surgical Sciences

**cycle XXXIV**

*(jointly activated by Università degli Studi di Torino and Politecnico di Torino)*

**Research Title:** LA DIAGNOSTICA SALIVARE NELLE PATOLOGIE PARODONTALI/ SALIVARY DIAGNOSTICS IN PERIODONTAL DISEASES

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<th>Università di Torino – Borsa di Studio finanziata dal CIR Dental School su fondi (COD. AIMPRICTRG)</th>
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**Context of the research activity**

Le malattie parodontali (MP), che includono gengiviti e parodontiti, sono patologie infiammatorie croniche che coinvolgono la gengiva, il legamento parodontale, il cemento radicolare e l’osso alveolare. Dall’analisi dei dati sulla diffusione a livello mondiale delle patologie non trasmissibili emerge che la parodontite severa rappresenterebbe la sesta condizione infiammatoria a maggiore prevalenza nell’uomo con circa 743 milioni di persone affette. La spesa stimata nel 2010 per le patologie orali è stata di 442 bilioni di dollari.

Attualmente, la diagnosi delle MP si basa sulla rilevazione di parametri clinici e radiografici. Tuttavia, i criteri clinici risultano spesso insufficienti per individuare i siti in cui la malattia è in fase attiva, per monitorare in termini quantitativi la risposta alla terapia o per misurare il livello di suscettibilità individuale alla progressione della patologia. Per questi motivi, c’è un grande interesse nella individuazione di nuovi biomarkers all’interno dei tessuti gengivali, nella saliva e nel fluido crevicolare.

La saliva contiene molecole di derivazione locale e sistemica e può essere campionata in modo non invasivo. La ricerca in ambito salivare potrebbe, pertanto, rappresentare la base per lo sviluppo di test diagnostici da utilizzare in ambito parodontale. La possibilità di eseguire prelievi salivari multipli e successivi nel tempo è un ulteriore vantaggio di cui tenere conto per monitorare l’andamento della patologia parodontale.

Negli ultimi anni, diversi studi hanno fornito un contributo significativo alla comprensione dei network biochimici coinvolti nelle MP e nell’identificazione di potenziali biomarkers diagnostici: enzimi rilasciati da batteri o dall’ospite, peptidi, mediatori dell’infiammazione, DNA di derivazione batterica o dell’ospite.
L’applicazione di questi biomarkers nella diagnostica parodontale necessita di essere ulteriormente validata in termini di sensibilità e specificità. I recenti progressi in ambito tecnologico hanno reso possibile un miglioramento nella comprensione dei sistemi biologici e un avanzamento nella ricerca sul fluido salivaore grazie alle scienze omiche. Queste ultime forniscono strumenti promettenti per arrivare ad una definizione globale dei cambiamenti metabolicci nei sistemi biologici. In considerazione della complessità dei dati prodotti, richiedono analisi statistiche multivariate a partire dalla selezione del marker biologico fino alla costruzione del modello ed alla sua validazione. Pertanto, questo filone di ricerca si pone in un contesto di multidisciplinarietà in cui nuovi sistemi diagnostici sono testati e integrati con altri allo scopo di approfondire le conoscenze sulle MP.

Periodontal diseases (PD) including gingivitis and periodontitis are chronic inflammatory conditions involving gingivae, periodontal ligament, root cementum and alveolar bone. According to recent data on the global burden of oral non-communicable diseases, severe periodontitis is the six most prevalent human inflammatory disorders, affecting around 743 million of the worldwide population. The global economic impact of oral diseases has been estimated in 2010 at US$ 442 billion.

At the present time, the diagnosis of the PDs is primarily based on clinical examination and radiographic parameters. Traditional clinical criteria are often insufficient for determining sites of active disease, for monitoring quantitatively the response to therapy or for measuring the degree of susceptibility to future disease progression. Therefore, there is a strong effort to discover new biomarkers in the gingival tissues, saliva, and gingival crevicular fluid. Whole saliva contains local and systemic derived biomarkers and can be easily collected through non-invasive means. Thus, it may offer the basis for a patient-specific diagnostic test for PDs. Feasibility of multiple subsequent sampling is an added advantage for disease monitoring.

In recent years, several studies have provided a significant contribution to the detailed understanding of the biochemical network in the PDs pointing to several putative diagnostic biomarkers: enzymes of host or bacterial origin, peptides, inflammatory mediators, DNA of host or bacteria origin. Anyway the application of these markers for PD diagnosis needs to be further validated in terms of sensitivity and specificity. The recent technological advances enabled the progress in systems biology and saliva research is moving into the omics world. Omics methods are promising techniques allowing a global evaluation of the metabolic changes in a biologic milieu. Due to data complexity, they require multivariate statistical techniques ranging from biomarker selection to model building and validation.

Therefore, the context of this research is a multi-disciplinary field in which new diagnostic systems are tested, and coupled to other systems in order to widen the knowledge about PDs.
**Objectives**

L’obiettivo principale è esplorare nuovi approcci nella diagnostica salivare applicata alle malattie parodontali e, in particolare, analizzare i profili biomolecolari delle parodontiti, croniche ed aggressive, e confrontarli con quelli propri di una condizione di salute parodontale. Obiettivi specifici sono:

- Sviluppo di protocolli per la raccolta e la preparazione di campioni salivari per una robusta analisi dei dati e interpretazione dei biomarkers in termini biologici.
- Applicazione di strategie innovative per identificare il profilo metabolico distintivo della parodontite.
- Applicazione di strategie innovative per monitorare l’attività della malattia parodontale e valutare l’efficacia delle terapie eseguite.

La comprensione e lo studio delle più promettenti tecnologie e della loro applicazione clinica costituiranno la base per l’implementazione di metodi diagnostici innovativi.

The main objective is to explore new approaches in salivary diagnostics of periodontal diseases and particularly in the assessment of the distinctive biomolecular pathways of chronic and aggressive periodontitis compared with periodontally healthy status. Specific objectives of the research will be:

- Development of protocols for salivary sample collection and preparation for robust data analysis and ultimately biological interpretation of biomarkers discovery.
- Applying innovative strategies to profile the metabolic signature of periodontitis.
- Applying innovative strategies for monitoring periodontal disease activity, and examining the effectiveness of oral care treatment.

The understanding and the study of some of the most promising technologies and their clinical significance will be the basis for the implementation of innovative diagnostics methods.

**Skills and competencies for the development of the activity**

Il candidato deve dimostrare solide basi in ambito di ricerca parodontale, capacità di lavorare in squadra, una documentata esperienza nell’analisi statistica dei dati e dovrebbe avere già seguito ricerche su mediatori biologici di interesse parodontale.

The successful candidate has a strong background in periodontal research, skills on working in a team, a documented expertise in statistical data analysis and should have followed studies on biomarkers in periodontal diseases.
PhD in Bioengineering and Medical-Surgical Sciences

cycle XXXIV

(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

**Research Title:** PRECLINICAL AND TRANSLATIONAL RESEARCH FOR NEW TECHNOLOGIES IN VASCULAR SURGERY: EVALUATION OF THE ANGIgenic EFFECTS OF EXTRACELLULAR VESCICLES

**Funded by**
UNIVERSITY OF TURIN

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**Context of the research activity**
Peripheral artery disease is a progressive atherosclerotic disorder that leads to poor quality of life, an increased risk of mortality, major amputations, hospitalization and high cost of care. Critical limb ischemia (CLI), the most severe form of peripheral artery disease, includes patients with ischemic rest pain, non-healing ulcers and gangrene. Within 6 months from the diagnosis of CLI, 30% of patients undergo to major amputation, 20% live with unresolved pain, 25% die. Approximately up to 20-40% of patients with CLI are unsuitable for surgical or endovascular treatment. In the last decades novel and more effective strategies including stem cell therapy have been proposed as a therapeutic option. Currently several randomized studies concerning the efficacy and safety of autologous bone marrow derived cells in CLI are underway. The interim results are promising but it seems that not all the patients are responders to this kind of therapy. The
pathogenesis of CLI includes both microvascular and macrovascular abnormalities. Stem cell therapy, which improves microvascular density seems to be not sufficient to heal the loss of tissue. Therefore, an alternative strategy has been proposed by Ranghino et al (Int. J. Immunopathology and Pharmacology, 2012). It consists of the use of endothelial progenitor cells (EPC) derived extracellular vesicles (EVs), which are able to activate angiogenic program in quiescent endothelial cells by a horizontal transfer of RNA. It has been shown that EPC- EVs can improve neovascularization in severe hind limb ischemia-induced (HLI)mice.

Objectives

We intend to develop a model of chronic limb ischemia by using ameroxid constrictors (Yang et al. J VasculSurg, 2008). The progression of damage will be monitored by laser Doppler for 21 days. The following parameters will be used to define the grade of the damage: laser Doppler analysis, counts of CD31 vessels and damaged muscular fibers. To evaluate the revascularization effect of EVs in chronic HLI, mice will be treated with different doses of EVs when the reperfusion reaches the lowest value, measured by Laser Doppler. Route of injection will be selected based on the data obtained in on the acute model. Mice will be sacrificed after 21 days and the same analysis described below will be performed. To test the angiogenic pathways activated by EVs, we will perform tubulogenesis assay with primary human endothelial cells. RNA and proteins will be isolated from EV treated and untreated human endothelial cells (HUVEC). Angiogenic pathways responsible for the EV activity will be evaluated and compared with the VEGF stimulation. Moreover, screening of the angiogenic pathways activated by EV treatment will be studied also in vivo. Muscles of mice subjected to HLI and treated with EVs will be isolated and RNA will be extracted for further evaluations.

Skills and competencies for the development of the activity

- Knowledge of physiopathology of critical limb ischemia
- Knowledge of medical and surgical clinics and instrumental tools in the diagnostic process of critical limb ischemia
- Knowledge of regenerative medicine basic principles
- Knowledge in data analysis and database design
# PhD in Bioengineering and Medical-Surgical Sciences

*(jointly activated by Università degli Studi di Torino and Politecnico di Torino)*

**Soft tissue: culture in dynamic bioreactors and mechanical characterization**

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[http://www.dimeas.polito.it/en/research/research_groups/solid_and_fluid_biomembranes/bioreactors_transport_phenomena_unit](http://www.dimeas.polito.it/en/research/research_groups/solid_and_fluid_biomembranes/bioreactors_transport_phenomena_unit) |

**Context of the research activity**

Bioengineering is a multidisciplinary research field that brings together engineering, medicine, biology, physics, chemistry, mathematics, with the key aims to advance knowledge and to support the development of ground-breaking diagnostic and therapeutic strategies.

In the regenerative medicine approach, where the final aim is to replace or restore damaged or diseased organs, the integration of biotechnological and bioengineering competences is crucial for understanding tissue behaviour and for developing efficient regenerative strategies. In particular, given the critical role of tissue mechanics in regulating cell response, promoting tissue regeneration, and directing development of tissues and pathologies, the understanding of soft tissue mechanics becomes essential for the development of advanced engineered tissues.

Moreover, to create tissue constructs in vitro that have native-like morphological, biological, mechanical and functional properties, the micro and macro culture environment should mimic the in vivo conditions.

In this context, the research activity will be focused on two main objectives: 1) Multiscale mechanical characterization of soft tissues; 2) Development of bioreactors for biological tissue culture and investigation.

| Objectives | The research objectives of the PhD program will be:  
1) Multiscale mechanical characterization of soft tissues |
Accurately characterising the tissue mechanical behaviour is of relevance for diagnostic purposes, regenerative medicine applications and for the development of in-vitro models, but it is highly challenging due to the intrinsic complex nature of biological tissues. Indeed, the macroscopic behaviour of a tissue is governed by its intrinsic material behaviour, but also by its overall geometry and the boundary conditions acting upon it. Therefore, a multiscale and multidisciplinary approach will be adopted. Experimental characterization will be based on different mechanical test set-ups at the macro (e.g., uniaxial/biaxial tensile testing) and microscale (e.g., nanoindentation), in order to capture the typical features of biological tissues under investigation. In parallel, constitutive models for biological soft tissues, which describe the relation between physical quantities, will be implemented and developed. By combining constitutive models with experimental data, parameter fitting will be performed by using nonlinear optimization schemes, taking care to account as much as possible for the irregularities and inhomogeneities of the investigated tissue. Moreover, finite element simulations will be considered for modelling the complex geometries of biological tissues. The final aim will be to provide guidelines for several issues related to the mechanical testing of soft tissues and to identify standardized testing methods.

2) Development of bioreactors for biological tissue culture and investigation
In the body, tissue is embedded into a complex physico-chemical micro and macro environment, which determines its development and specific functions. Like in vivo development, in vitro tissue development inherently relies on the principles of spatial and temporal organization. During the PhD, bioreactor solutions to provide in vitro biomimetic culture environments and for tissue investigation will be designed and developed. In particular, technological solutions for guaranteeing 3D culture, native-like physico-chemical stimuli, continuous perfusion, and monitored and automated procedures, will be developed with the final aim to improve the overall process efficiency and to decrease costs by fulfilling labor-intensive manual tasks.

Skills and competencies for the development of the activity
- Soft Tissue Experimental and Computational Biomechanics; Image and Data Processing; Computer Programming; Bioreactor Design and Development; Technical Drawing; Electronics and Sensors; Teamwork skills and ability to work with multidisciplinary teams.
**PhD in Bioengineering and Medical-Surgical sciences**

*(jointly activated by Università degli Studi di Torino and Politecnico di Torino)*

**Research Title:** BIOMATERIALS and NANOTECHNOLOGIES for ADVANCED THERAPIES

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<td>Prof. Gianluca Ciardelli, Prof.ssa Valeria Chiono, Prof. Gianni Ciofani</td>
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<td>Contact</td>
<td><a href="https://www.polito.it/">https://www.polito.it/</a>, <a href="http://www.dimeas.polito.it/la_ricerca/gruppi/materiali_per_le_bionanotecnologie_e_laboratorio_biomedico">http://www.dimeas.polito.it/la_ricerca/gruppi/materiali_per_le_bionanotecnologie_e_laboratorio_biomedico</a></td>
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**Context of the research activity**

Advanced therapy refers to new medical products that use gene therapy, cell therapy, and tissue engineering. They represent the next generation of medicines for complex diseases and pose particular challenges to medicine regulation. In this contest Regenerative Medicine is a broad field that includes tissue engineering but also incorporates research on self-healing – where the body uses its own systems, sometimes with help of foreign biological material to recreate cells and rebuild tissues and organs. The terms “tissue engineering” and “regenerative medicine” have become largely interchangeable, as the field hopes to focus on cures instead of treatments for complex, often chronic, diseases. These fields, consequently, are highly multidisciplinary and draws on experts from clinical medicine, mechanical engineering, materials science, genetics, and related disciplines from both engineering and the life sciences.

The Industrial Bioengineering Group has a large history at the POLITO from 1978 in education and research. The unit coordinated by prof. Ciardelli is active in areas such as engineering in surgery, biomolecular, cellular and tissue engineering; controlled drug delivery; bioartificial systems and materials. In the last years, the research group has gained relevant experience in the field of bioactive polyurethanes and hydrogels for drug and cell delivery, in the field of biomimetic coatings for biomedical implants, aimed at guiding tissue/cell response at the implant interface and in the model design of healthy and pathologic organs/tissues.

**Objectives**

The aim of the PhD will be focused on the development of new strategies for the treatment for complex diseases. In particular the
research activities should combine the advanced technologies at the macro and nanoscale with the biological ones needed in order to obtain an innovation platform for advanced therapy. Typical objectives of the research activities will be:

- Development of a platform of polymeric materials and design of 3D-hierarchical structures, mimicking healthy and pathologic tissues.
- Design of smart nanomaterials able to provide appropriate instructive cues to cells and tissues.
- In vitro test to evaluate developed technologies.

Skills and competencies for the development of the activity

We are looking for talented candidates, preferably with a Master Degree in Biomedical Engineering, Biology, Nanotechnology, Physics and Chemistry of Matter, Material Science are considered with previous expertise in the field of biomaterials, nanotechnology and tissue engineering.
PhD in Bioengineering and Medical Surgical Sciences

(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research Title: Biomaterials-mediated direct cell reprogramming for myocardial regeneration

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<tr>
<td>Supervisor</td>
<td>Valeria Chiono (Politecnico di Torino) Carla Divieto (INRIM, Torino)</td>
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Context of the research activity

Myocardial infarction (MI) is caused by the obstruction of coronary arteries, resulting in the death of approximately 1 billion cardiomyocytes in the left ventricle within a few hours, acute inflammation and degradation of the cardiac extracellular matrix (ECM), with the formation of a fibrotic scar. Cardiac scar is mechanically stiffer than the original tissue, it is mainly populated by cardiac fibroblasts (CFs), and lacks beating cardiomyocytes. Cardiac scar may undergo continuous remodeling, leading to left ventricle dilation and progressive congestive heart failure, which is the current leading cause of mortality and morbidity in industrialized world. The only standard therapy addressing the irreversible loss of functional cardiomyocytes is heart transplantation. An ideal cardiac regenerative medicine strategy should replace lost cardiomyocytes and recover myocardial functional contractility. Up to now, cell-based regenerative therapies, and tissue engineered scaffolds/patches have failed in such aim because of: (i) the poor grafting, survival and integration of implanted cells in the infarcted area and (ii) the limited endogenous regenerative potential of adult heart. Hence, the regeneration of a damaged heart still remains a major clinical challenge with a deep social and economic impact. Direct reprogramming approaches, able to directly convert CFs into induced cardiomyocytes (iCMs) have emerged since 2010 as a new intriguing possibility for myocardial regeneration. Proof of
concepts results of in vitro and in vivo conversion of mouse CFs into iCMs have been published and direct in vitro reprogramming of human CFs has also been reported. However, the approach is still rather immature and inefficient to prospect a short-term clinical translation. In early studies, reprogramming efficiency was generally very low (1-20%) and highly dependent on the experimental protocol for its evaluation, employed untargeted and unsafe delivery methods such as viral vectors, and fostered the generation of predominantly immature, partially reprogrammed and non-beating cardiomyocytes. Additionally, reprogramming experiments in simple 2D in vitro models underestimating reprogramming efficiency.

The Ph.D student will work in the BIORECAR ERC Consolidator project to address the current limitations of direct cell reprogramming, developing a novel combined multidisciplinary and multifunctional cell direct reprogramming approach, integrating tools from nanomedicine, biomaterials science and tissue engineering.

The final aim will be to achieve a significant advancement in the knowledge of direct cell reprogramming of human CFs into cardiomyocytes in the perspective of a future clinical application of the therapy.

The candidate should perform the preparation procedures and physicochemical characterizations in the labs of Politecnico di Torino located in Turin and in Alessandria.

The activity foresees the collaboration with INRIM (Turin), Humanitas Research and Clinical Hospital (Milano) as well as University of Naples “Federico II” for what concerns the biological trials. The candidate should be available to perform part of the experiments in the collaborators’ headquarters, when required.

**Main references**


**Objectives**

The objective of the Ph.D activity within BIORECAR will be:

- To set a combination of microRNAs and drugs for the direct
reprogramming of human cardiac fibroblasts starting from “miRNA combo” (T.M. Jayawardena et al. 2012; T.M. Jayawardena et al. 2015; Y. Li et al. Scientific Reports 2016) by in vitro cell tests using human cardiac fibroblasts and human dermal fibroblasts. Reprogramming will be evaluated mainly by immunocytochemistry and PCR analysis.

- To develop an injectable and biomimetic 3D hydrogel able to reinforce direct cell reprogramming
- To develop polymer nanoparticles encapsulating the reprogramming agent as efficient systems for direct cell reprogramming. The nanoparticles will be characterized for their physicochemical characteristics (e.g. SEM, dynamic light scattering, zeta potential), drug encapsulation ability and in vitro drug release, their ability to be internalized by the cells (fibroblasts), cytotoxicity towards myocardial cells (e.g. fibroblasts, cardiomyocytes, endothelial cells), their efficiency in direct reprogramming of fibroblasts in the absence and presence of the 3D hydrogel matrix releasing them.

- To prepare periodic reports on the scientific activity
- To participate to periodic project meetings
- To disseminate results in conferences (oral or poster presentation)
- To prepare and submit scientific papers (at least 3 during the PhD activity)

Skills and competencies for the development of the activity

The candidate should have these skills and competences:

- Direct previous experience in in vitro cell culture tests, such as cell adhesion, proliferation and differentiation trials.
- Knowledge and previous experience in cell transfection using microRNAs, which are the reprogramming oligonucleotide agents used in the project.
- Knowledge and previous experience in the main molecular characterization techniques: PCR, RT-PCR, qRT-PCR, extraction of DNA, RNA and proteins, Western Blot, immunohistochemistry, immunofluorescence
- Knowledge of the following techniques for analysis: UV-Vis spectroscopy, x-ray diffraction, HPLC, LC, NMR, mass spectroscopy, fluorescence microscopy
- Knowledge on the main natural and synthetic polymers used in tissue engineering, as well as on the main techniques for polymer nanoparticle and hydrogel preparation and physicochemical characterization.
- Basic knowledge on direct cell reprogramming principles, methods and main achievements up to now.

One preferred requirement will be represented by a previous research experience in the field of cell transfection using microRNAs.
# PhD in Bioengineering and Medical-Surgical Sciences

*(jointly activated by Università degli Studi di Torino and Politecnico di Torino)*

**Research Title:** Advanced technologies for the assessment of the neuromuscular system

<table>
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<tr>
<th>Funded by</th>
<th>Politecnico di Torino</th>
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| **Supervisor**     | Prof. Marco Gazzoni ([marco.gazzoni@polito.it](mailto:marco.gazzoni@polito.it))  
                     | Prof. Alberto Botter ([alberto.botter@polito.it](mailto:alberto.botter@polito.it)) |
| **Contact**        | Dept. Electronics and Telecommunications, Politecnico di Torino  
                     | (http://www.det.polito.it) / Research group website: [lisin.polito.it](http://www.det.polito.it) |

## Context of the research activity

People of industrialized countries are living longer and, consequently, the burden of severe chronic disabilities is increasing with high social costs. Wearable sensors for biomechanical and electrophysiological signal acquisition are gaining high attention for the monitoring of subjects during real life activities or during rehabilitative treatments in clinics and at home.

In recent years, systems for the detection and analysis of neuromuscular activity undergone to relevant advancements. The use of multi-channel detection systems opened new frontiers in the non-invasive investigation of the neuromuscular system, from the study of peripheral muscle properties to the extraction of neural strategies underlying muscle activation.

Even though multi-channel sEMG opened new perspectives in neuromuscular assessment, several challenges related to signal acquisition and interpretation are still open especially in dynamic conditions. From the hardware point of view, the current state of the art consists in grids of electrodes individually wired to a multi-channel acquisition device. This results in cumbersome systems which hampers the use of multi-channel sEMG in dynamic conditions and clinical applications. Improving the electrode technology and reducing the size and weight of the devices seems
to be a necessary condition for the use of multi-channel sEMG in applied settings or in real life scenarios.

The context of the research activity is the development of innovative techniques for neuromuscular assessment. The overall goal will be to overcome the current limitations of the existing systems and to improve the clinical applicability of innovative research results.

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<tr>
<th>Objectives</th>
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<td>The main topics will be the development of: 1) methods for the investigation of motor behaviour in healthy and pathological subjects, 2) advanced systems for human machine interface.</td>
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The specific objectives will be:

- The development of configurable electrode systems for sEMG detection.
- The development of miniaturized wearable acquisition devices.
- The development of signal processing techniques for real time extraction of relevant features from single channel/multi-channel sEMG.
- The application of the developed tools in applied scenarios such as rehabilitation and sport.

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<tr>
<th>Skills and competencies for the development of the activity</th>
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<tr>
<td>The successful candidate has experience in biomedical signal acquisition, processing, and interpretation. The candidate should have expertise in the design and management of experimental protocols. Since the research activity includes the design and development of innovative electronic solutions for sEMG detection, the candidate should have a good knowledge in analog and digital hardware design and experience in the use of electronic laboratory instrumentation.</td>
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PhD in Bioengineering and Medical-Surgical Sciences

(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research Title: Wearable devices for the assessment of human activities

Funded by
Politecnico di Torino

Supervisor
Prof. Marco Gazzoni (marco.gazzoni@polito.it)
Prof. Marco Knaflitz (marco.knaflitz@polito.it)

Contact
Dept. Electronics and Telecommunications, Politecnico di Torino
(http://www.det.polito.it)

Context of the research activity
Human Activity Recognition and Quantification (HARQ) is an emerging field in the healthcare context, involving applications such as wellbeing and personal fitness tracking, monitoring of elderly and frail people, assessment of rehabilitation treatments and, in general, all those activities in which a personalized feedback is required. Moreover, HARQ is of increasing interest also in sports training and ergonomics.

In general, a HARQ system is made of two sub-systems: one that continuously acquires several signals that describe the subject movement during his daily life and the second that properly processes the acquired signals and returns the type of activity performed in a specific moment and its intensity.

A first challenge is to carry out signal acquisition, processing, activity recognition and quantification within each sensor, thus unifying the two sub-systems in a single device. This device is to be worn by the subject and hence it must be lightweight, small, and have long battery life. Current technology allow for facing this challenge with a fair probability of success.

A second challenge is to develop methods and algorithms for HARQ suitable to be implemented on embedded systems based on low power microcontrollers.

The ultimate goal of this research activity is the development of innovative intelligent sensors and algorithms for HARQ that do not require to be connected to a host system.
### Objectives

The main phases of the research activity will be the development of novel intelligent sensors for HARQ and the necessary signal processing algorithms. Sensors will be designed, implemented, and then tested on healthy volunteers as well as in patients suffering from different motion disabilities.

The main research activities will be:

- The design and implementation of innovative embedded sensors for HARQ.
- The development of specific algorithms for signal processing, data interpretation, and classification.
- The development of systems based on sets of intelligent sensors for specific applications.
- The application of the developed systems in applied scenarios such as rehabilitation and sport.

### Skills and competencies for the development of the activity

The successful candidate has experience in biomedical signal acquisition, processing, and interpretation. The candidate should also have interest in the electronics design of high-performance, low-power, microcontrolled systems. Interest in the development of algorithms to be implemented on embedded systems is also fundamental, as well as interest in experimental, on-the-field, activities.
PhD in Bioengineering an Medical-Surgical Sciences

(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research Title: Biofluid Mechanics Clinical Applications

Funded by

Politecnico di Torino

Supervisor

Umberto Morbiducci (umberto.morbiducci@polito.it)
Diego Gallo (diego.gallo@polito.it)

Contact

http://www.dimeas.polito.it/la_ricerca/gruppi/biomeccanica_dei_solidi_e_dei_fluidi

Umberto Morbiducci’s profile on ResearchGate -
https://www.researchgate.net/profile/Umberto_Morbiducci

Context of the research activity

The research of novel hybrid “in vivo & in-silico” approaches for quantitative hemodynamics, coupled to a better understanding of physiological systems, could lead to the development of new and affordable diagnostic tools for cardiovascular diseases, thus allowing for (1) a deeper comprehension of the biophysical phenomena involved in cardiovascular disease, and (2) a more effective clinical diagnostics and decision support. A deeper knowledge of the complexity of the arterial hemodynamics and of its biological variability could improve not only the diagnostic processes, but also the development of drugs/therapies, and the design of blood recirculating devices, which are all key points for more sustainable health systems in the international research programs.

Objectives

The aims of the research activity within the Doctoral program are manifold and interlaced: (1) tight integration of cardiovascular imaging and in silico hemodynamics; (2) identification of hemodynamic patterns involved in the onset/progression of cardiovascular disease; (3) application of numerical schemes typical of computational fluid dynamics to in vivo measured hemodynamic
The integration of medical imaging and numerical methods is a powerful approach to elucidate the role of hemodynamics in the development, diagnosis and treatment of cardiovascular diseases. This program can be further broken down along three lines: (i) image-based hemodynamics modeling, which exploits medical imaging data to construct patient-specific computational fluid dynamics (CFD) models; (ii) virtual imaging, which uses computational models to simulate the impact of complex anatomy, flow and motion on medical images supporting clinical decision making; (iii) building up of an integrated clinical imaging-computer modelling framework for subject-specific cardiovascular simulations, compatible with clinical times.

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<th>Skills and competencies for the development of the activity</th>
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<tr>
<td>Cardiovascular fluid mechanics; Solid mechanics; Transport phenomena; Image processing; Computational fluid dynamics; Computer programming</td>
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PhD in Bioengineering and Medical-Surgical Sciences
(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research Title: Growth factor release upon acidic environment in bone resorption-GRACE

Funded by
Politecnico di Torino

Supervisor
Prof. Chiara Vitale Brovarone

Contact
chiara.vitale@polito.it

Bone is a living tissue that continuously undergoes a dynamic process between bone resorption by means of osteoclasts and new bone deposition by osteoblasts. This process is called bone remodeling and is driven by a precise exchange of biochemical signals between osteoclasts and osteoblasts (coupling). With age, bone resorption can progressively overcome bone deposition, thus leading to a reduction in bone mass and quality and to an overall picture of bone fragility (osteoporosis). Throughout the world, an osteoporotic fracture occurs every 3 seconds, with huge social and economic burdens. During bone remodeling, the resorption of bone portions by active osteoclasts involves the excretion of enzymes that are able to digest the collagenous fibers and locally alter the pH, thus leading to the dissolution of the mineral phase (HA). When this occurs, the GFs stored in the bone matrix are released and they stimulate osteoblast migration and activity, which lead to new bone deposition in the reabsorbed area. Our aim is to address this clinical and social need through the support of cutting-edge materials and technologies, in order to produce the first biomimetic smart scaffold able to mimic the chemistry (collagen and nano-HA), topography and biology of healthy human bone. As the human bone encases, in its trabecular structure, several biomolecules (growth factors-GFs) able to stimulate a proper Oc activity, the developed smart scaffold should also be able to mimic this feature. This can be achieved by favoring a chemical bond between the collagen fibers, the HA crystals and the GFs and/or by engineering dedicated
Objectives

This research project aims to develop and validate several strategies to encase bone growth factors in a 3D-fabricated structure. The 3D fabricated scaffold will be developed in the frame of the ERC BOOST whereas the growth factor encasement will be mainly framed in the project GRACE. The different strategies for printing/encasing that will be investigated include:

- Ink-jet technology
- Porous materials with ultra-large pores (up to 100nm)
- Biodegradable nanocapsules

Protective smart coating (single and double layers) or ad hoc bioresorbable matrix will be developed and investigated in order to trigger the release of the growth factors with the aim of simulating the physiological bone resorption process. Chemical synthesis and material characterisation will be carried out on all the produced systems in order to define the most promising solutions. In parallel, Western Blotting and cellular tests with both osteoblasts and osteoclasts will be used to assess the maintenance of the structural integrity and activity of the encased growth factors.

Skills and competencies for the development of the activity

The characteristics of the successful candidate are:

- Expertise in biomimetic materials
- Expertise in cell culture tests
- Skills on working in a team
- Proactive approach to join a multidisciplinary research program and to spend time in different Laboratories.
- Research time spent abroad will be considered a plus.
### PhD in Bioengineering an Medical-Surgical Sciences

*(jointly activated by Università degli Studi di Torino and Politecnico di Torino)*

**Research Title: Computational Drug Discovery**

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<th><strong>Funded by</strong></th>
<th>Politecnico di Torino</th>
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<tr>
<td><strong>Supervisor</strong></td>
<td>Jack Tuszyński <em>(<a href="mailto:jacek.tuszynski@polito.it">jacek.tuszynski@polito.it</a>)</em></td>
</tr>
<tr>
<td><strong>Contact</strong></td>
<td>Jack Tuszyński’s profile on ResearchGate - <a href="https://www.researchgate.net/profile/Jack_Tuszynski">https://www.researchgate.net/profile/Jack_Tuszynski</a></td>
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#### Context of the research activity

The overarching aim of our research activities is to develop and extend existing computational techniques for the rational design of novel drug entities to treat cancer. While there already exist a number of successful drugs to treat many different types of cancer, such as the highly effective paclitaxel, Vinca alkaloids and epothilones, most of these drugs also unfortunately target healthy cells. This often results in therapeutic concentrations of chemotherapy drugs that are only slightly lower than their toxic concentration. Successful chemotherapeutic drugs must therefore take advantage of the differences in the relative vulnerabilities of some target protein or pathway in cancer cells versus normal cells. This has been the premise for research into cancer treatment for several decades, yet a specific, appropriate target has yet to be discovered. To overcome this barrier, numerous molecular targets will be examined for differences at the atomic scale, a process that ultimately involves the rigorous computational analysis of the protein-drug interaction. This generally involves molecular dynamic (MD) computations, based on information about both proteins and drug molecules.

#### Objectives

Our main objective is to use fast computational techniques to filter libraries of compounds that will then be experimentally validated. This database screening, coupled with secondary and tertiary protein structure analysis and prediction will reduce the overall search space required. Our computational research effort comprises an iterative process involving several different modeling techniques proceeds in the following stages: 1) selection of competent drug targets; 2) molecular refinement of structurally
based or homology models; 3) screening and design of suitable drugs; 4) refined modeling of drug-target interactions; and 5) classification of candidate drugs into unique pharmacophores specific for each target protein. Initially, we will create meta-models of the drug binding sites for key cell cycle regulatory proteins. Using either literature or own homology modeling algorithms will provide us with precise molecular characteristics of each binding site. Next, high throughput molecular docking simulations are typically performed between each compound in the database (e.g. ZINC) and each binding site in a given protein. In the docking procedure, the binding orientation of each compound and its binding affinity for the target protein are calculated. Algorithms, such as AUTODOCK, are able to identify small molecules that can fit into the ligand binding sites on proteins of known structure and have been used successfully to identify novel protein-ligand interactions. The docking procedure reduces the number of compound to hundreds or less. These compounds are further filtered with post-screening methods such as detailed MD calculations. Finally, usually about 10~50 compounds are selected for experimental testing. These techniques will allow us to probe new or pre-existing drug-binding sites with novel drugs to identify new important interactions. Promising candidates from these screens can then be used as scaffolds to create novel compounds, which can be fed back into the first approach, enhancing binding affinities, hopefully leading to the development of novel drugs for the targeting of cancer cells. The models and simulations described above will be invaluable for rational drug design and study of protein-protein and protein-drug interactions hopefully resulting in pre-clinical development and ultimately clinical trials.

Skills and competencies for the development of the activity

Familiarity with bioinformatic and chemi-informatic databases such as PDB, GeneBank, DrugBank, GEO, ZINC, etc. Coding skills in C++, Java, Matlab, or equivalent. Basic competence using molecular dynamics, sequence alignment and homology algorithms and docking software. Ability to use density functional methods of quantum chemistry would be an extra asset.
In consideration of the determination of the Regione Piemonte – Direzione Coesione sociale No. 504 of June 12, 2018, which approved the following apprenticeship position for the PhD project proposal submitted by the Politecnico di Torino in the framework of a specific regional call for proposals (Apprendistato di Alta Formazione e Ricerca 2016-2018 - Avviso Pubblico per la realizzazione dei percorsi formativi di: Laurea triennale e magistrale, Diploma Accademico di primo e secondo livello, Master di primo e secondo livello Universitario, Dottorato di ricerca e Diploma accademico di formazione alla ricerca, Attività di ricerca approvato con Determinazione 537 del 3/8/2016):

**PhD in Bioengineering and Medical-Surgical Sciences**

*(jointly activated by Università degli Studi di Torino and Politecnico di Torino)*

**Research project “Sviluppo di tecniche innovative per la diagnosi autonoma del ritmo cardiaco da implementare in defibrillatori semiautomatici”**

**Politecnico di Torino – Elpro srl**

| Supervisor | Prof. Eros Pasero – Politecnico di Torino  
|            | eros.pasero@polito.it  
|            | Cesare Mangone – Elpro S.r.l. - Strada del Rondello 5, 10028 Trofarello (TO)  
|            | cesaremangone@gmail.com |

| Contact | www.neuronica.polito.it  
|         | http://www.elpromedical.com/ |

**Context of the research activity**

Both the private company (ELPRO) and the research institute (NEURONICA LAB) work with cardiological devices. The research project is therefore focused on this common subject matter. Wearable devices are considered today the new frontier for future telemedicine. The electrocardiogram is a well known typical
Medical exam to verify cardiological problems. Traditional ECG systems require long times to make a reservation for a medical examination, undress and apply the electrodes. A wearable device with no wires for electrodes and the possibility to communicate by a wireless connection with a smartphone and a cardiologist can improve this kind of analysis. Today wearable devices available on the market are not ECG but only heart rate monitors. This project research will investigate technological issues related to reliable, low cost, user friendly devices which can be used for fast analysis and help the new generation of defibrillators which are under developments by ELPRO.

The company has planned for the winner of this position a collaboration within a contract of high apprenticeship according to the Italian Legislative Decree 81/2015, art. 45.

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<th>Objectives</th>
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<tr>
<td>The goals of the project are to improve the company skill in the development of new devices and new techniques to diagnose heart diseases. New defibrillators, innovative algorithms to analyse vital parameters in a more efficient way. The PhD student will be involved in the study of the human impedance to remove the movements artifacts during the intensive care to allow the heart rhythm analysis during the defibrillation. The goal is therefore to apply sophisticated theoretical studies to real life cases to improve the safety of the existing devices.</td>
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<th>Skills and competencies for the development of the activity</th>
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<tr>
<td>The candidate for this project is supposed to have good bioengineering skills with a specific experience in heart topics. Also electronic circuits skills are well considered to allow the development of ecg and defibrillator circuits. A knowledge of the CE procedures to apply to certificate the medical devices is also required. The candidate must also be less than 30 years old at the moment of the hiring from the company.</td>
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