Press release
December 2013

EU funds 6 million Euro for new tech solutions to combat phantom limb pain

Phantom limb pain (PLP) is a frequent consequence of amputation, and it is notoriously difficult to treat. A new research project just begun aims to challenge the status-quo of PLP treatment. The project group will develop dedicated technological solutions that provide sensory feedback to patients which will restore the neuroplastic changes in the cortex and thereby control and alleviate pain. EPIONE is a consortium of 12 partners from Europe and the US involving clinical, industrial and academic institutions.

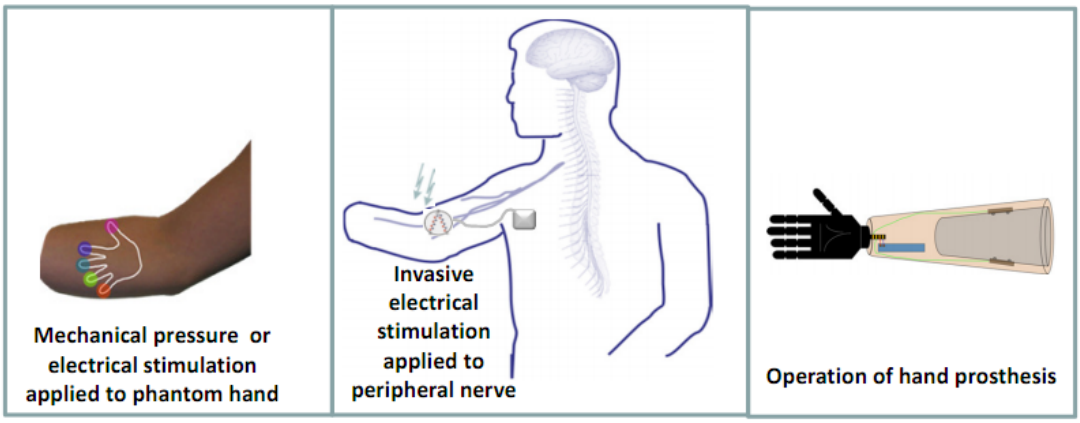
Phantom limb pain affects many amputees and current treatment is inadequate
Amputation usually follows traumatic injuries or surgery as a result of e.g. vascular diseases, diabetes or tumors in cases where the loss of the limb is required for the survival of the patient. The amputation is usually followed by the sensation that the lost body part is still present. In 50-80% of amputees neuropathic pain develops in the lost limb, which is also referred to as phantom limb pain (PLP). Throbbing, piercing and needles sensations are among the most commonly used descriptors of pain in amputees. Today, it is not completely understood why the pain occurs. Different factors may influence the occurrence and extent of phantom pain. Several studies have shown that most currently available treatments for PLP (pharmacological, surgical, anaesthetic, psychological and other) are ineffective and fail to consider the mechanisms that underlie PLP.

EPIONE will address the bottlenecks to understanding PLP
The mechanisms underlying the painful perception of a missing body part are still unclear. The EPIONE project will investigate whether PLP can be explained by changes in the cortical map that follows amputation, and whether PLP can be quenched by restoring the cortical map.

EPIONE will deliver innovative solutions that will help translate research into solutions for patients.
There are no dedicated medical technologies available on the market with the aim of providing sensory feedback to control and alleviate pain. EPIONE aims to build new technological systems for delivering invasive/non-invasive sensory feedback based on existing solutions emerging from previous EU-funded research.

''No effective, long-term treatments are currently available for treatment of PLP. And, there is no consistent knowledge on which type of sensations may be effective in affecting the cortical plasticity, and the strategy for applying sensory feedback. We aim to directly compare two routes for providing a more long-term or permanent solution for amputees,'' says project coordinator and main project responsible Dr. Winnie Jensen from the Dept. Health Science and Technology at

Aalborg University. She adds that ''We hope to better understand why phantom limb occurs, what affects the pain, and how we can help patients overcome the pain.''



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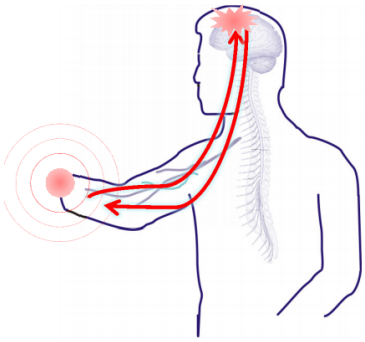
''We will develop and assess a non-invasive sensory feedback solution and an invasive sensory feedback solution that in the future will offer the ultimate, permanent, invisible and cosmetically acceptable interface.'' says Winnie Jensen.

Further information

Combating phantom limb pain by reversing neuroplastic changes



Cortical reorganization is related to pain. Amputation of a hand is immediately followed by significant reorganization in the somatosensory pathway and cortex, i.e. the hand area in the brain is invaded by neighbouring areas, such that the normal homunculus is shifted. Painful sensations appear to be related to reorganization of the primary somatosensory cortex (S1) in the brain.

Sensory feedback may reverse the cortical reorganization following amputation. Previous research has demonstrated the favourable effect of enhancing the sensory feedback related to the missing limb to alleviate PLP. For example, patients with PLP, who intensively used a myoelectric prosthesis or used daily surface electrical stimuli applied to the stump experienced significant reduction of PLP. Direct electrical stimulation of severed nerves proved to be capable of eliciting tactile or proprioceptive sensations by implanted 'LIFE' electrodes in human subjects; also, control of a robotic hand reduced PLP.

Partners in EPIONE

The EPIONE consortium consists of 12 partners from Europe and the US who together possess the state-of-the-art expertise necessary to reach the ambitious objectives of the project. Below you will find descriptions of their roles and expectations for the work.

Aalborg University, Denmark – Dr. Winnie Jensen
One of the main technological challenges will be to deliver the sensory feedback and assess the effect of the sensory feedback in a fast, reliable and repetitive manner in the clinic. The main technological contribution from Aalborg University will be to design a psychophysical testing platform, i.e. a computer platform that can perform these tasks. From a clinical point of view Aalborg University will also be responsible for investigating the effect of surface electrical stimulation.
By participation in the EPIONE consortium we expect to gain knowledge from a larger group of patients that will otherwise difficult to obtain that ultimately should drive us towards understanding and combating phantom limb pain.

Aalborg University Hospital, Denmark – Dr. Preben Sørensen
At Aalborg University Hospital we hope to gain sophisticated experience and knowledge with the function and effect of invasive feedback systems for treatment of phantom limb pain. The goal is to contribute to the development of efficient and patient-safe treatments for phantom limb pain. Aalborg University Hospital will contribute with participation in the clinical trial implanting and testing intraneural electrodes.

Universita' Cattolica del Sacro Cuore , Italy – Dr. Paolo Maria Rossini
Above all, being a team mainly composed by medical doctors, our hope is to find a way to help patients with phantom limb pain syndrome, a frustrating condition both for amputee and physicians. Based on our previous experience and work we think to be on the right way and we hope to obtain useful information to standardize a new therapeutic approach available for all patients with this kind of pathology for drug-resistant patients. Finally, being scientists, we hope to gain useful information to enrich our knowledge on phantom limb pain syndrome pathophysiological mechanisms and direct interface with peripheral nerves.
Our main role will be to surgically implant and consequently to test the prototype system composed by intraneural electrodes, stimulator and hand prosthesis properly designed to treat the phantom limb pain and to restore the somatosensory feedback from the missing hand.
The biggest scientific challenges from our side will be to find out the most efficacious stimulation pattern for a durable effect and to obtain a good integration between the restored somatosensory feedback and the hand prosthesis.

Centre hospitalier universitaire vaudois, Schwitzerland – Dr. Raffoul Wassim and Mrs Lee Ann Laurent-Applegate
Our participation in this FP7 project will unite fundamental science with clinical experience for a pathology that is not treated to satisfaction. We will have access to state-of-the-art materials for implant and of bi-directional control of hand prosthetic devices that may revolutionize patient care in the future.
We will be able to help establish clinical protocol for implantable devices so that this may become routine procedure with new implants available for the patient.

Our largest challenge will be to define the best clinical protocol for implantation to allow better acceptation of the implant in local soft tissue surroundings and to permit a more effective bi-directional control of hand prosthetics that together will increase the long-term usability of the EPIONE approach for the patient.

Albert Ludwigs Universität Freibug, Germany – Dr. Thomas Stieglitz

We hope to transfer developments of nerve interface from preclinical research into a useful application and work towards a medical device within the framework of EPIONE. The more experience is gained in clinical trials in this project with implantable nerve interfaces the higher is the probability to transfer results into a product on the long term run.
Our group will manufacture the implantable electrodes to invasively interface the nerves in the stump. Spatially selective electrical stimulation of the nerves in the stump shall deliver electrical signals that the brain interprets as "physiological" and starts reorganizing the cortex to reduce the cortical part of phantom limb pain.
The biggest technical challenge is to deliver tiny little microsystems as electrodes that are stable in the body and last for the lifetime of the patient. From the scientific side we still have to find out what the best stimulation pattern of the nerves might be to obtain strong and long-lasting reduction of phantom limb pain. The "right" spots to stimulate will vary from patient to patient due to different etiologies of the patients.

Laboratoire d'Informatique de Robotique et de Microelectronique de Montpellier, France – Dr. David Guiraud

We hope to contribute, though advanced software and hardware technologies, to answer the big challenges raised by the EPIONE project. Working in a high level consortium group entails us to develop a complex technology with high clinical requirements in very close relation with all partners.
The DEMAR team, hosted by university of Montpellier, is focused on the development of neuroprosthesis together with their control to restore lost functions.
Our main contribution will be to propose miniaturized stimulators with embedded software that will be able to drive the multicontact intrafascicular electrodes with a wide range of stimulation's parameters settings possibilities.
The main challenges will be to set the clinical requirements taking into account electrodes' range of functioning within reasonable complex user interface and hardware complexity.
On a scientific point of view, accurate electrophysiological effects induced by the complex stimulation that we could provide will be investigated in this new paradigm (implantable electrodes).
Ensuring technical and scientific support to the clinical team in a multicentric evaluation will be a challenge with the collection of data linked to hardware / software uses and electrophysiological consequences.

École Polytechnique Fédérale de Lausanne, Switzerland – Dr. Silvestro Micera

Several studies have shown that sensory stimulation can be extremely useful in the treatment of many neurological disorders such as phantom limb pain. Moreover, the delivery of sensory feelings to the subjects while using an artificial limb can significantly increase its effectiveness opening up interesting scenarios for the replacement of missing limbs. However, the potentials and limits of different invasive and non-invasive approaches for sensory feedback are to be clarified.
Development of hand prostheses voluntary controlled by the users using muscular activities and able to provide sensory information by exploiting different techniques including electrodes implanted into the peripheral nerves.
From a clinical point of view the main challenge will be the achievement of an effective chronic

model usable in a clinical trial with several patients. From a technological point of view, the main challenges are the development of chronically usable electrodes and of a final system, which could be used outside the laboratory environment in the "real world". Scientifically, it will be interesting to investigate the limits that current technologies have in delivering sensory feedback in terms of richness and usability of the information provided.

Lund University, Sweden - Dr. Fredrik Sebelius
At Lund University we are responsible for investigating functional components for the non-invasive sensory feedback systems. Lund University will also integrate, deliver and support the technologies for the non-invasive sensory feedback system.
Furthermore, we will be responsible for testing the efficacy of non-invasive sensory feedback to assess the efficacy of non-invasive feedback to reduce/suppress phantom limb pain with or without the simultaneous operation of a hand prosthesis device.

Indiana University - Purdue University Indianapolis USA – Dr. Ken Yoshida
At Indiana University Purdue I hope to contribute to the development of a prescribed and effective treatment for a currently untreatable condition. Further, I hope to obtain a glimpse at how and why such a condition comes to be in the first place. A treatment to the condition would constitute a major impact to those afflicted by PLP.
The idea that the precise application of minute electrical impulses directed at the nervous system in the arms and legs may be a useful means to elicit sensations was hatched some 20 years ago. In the intervening years, this vision has been shared, influenced, and modified through the work with those with similar visions, bringing together a community of researchers from various disciplines to address, understand and develop a treatment for phantom limb pain.
My main contribution has been the development of the electrode system used to deliver those minute electrical impulses, and to determine how intensive the electrical application must be to result in a change in the PLP sensation. In EPIONE, I will continue to contribute by lending my knowledge of the implanted electrode system to those involved with the implantable system and will conduct investigations with less invasive surface application of electrical stimulation to ascertain its efficacy on reducing PLP.
IUPUI will also be responsible for developing a common method of assessing and delivering the various interventions to be tested in this project such that the information and volunteer experiences gathered from the various partners can be compared, combined and analyzed.

Universitat Autònoma de Barcelona , Spain – Dr. Xavier Navarro
The UAB group will contribute in three main tasks for the project. First, we will provide a standardized set of validated questionnaires and tools for the assessment of PLP in the patients, which will make the comparison of the results obtained in the different clinical centres feasible. Second, we will provide support, clinical and statistical analysis of the set of data collected in the intervention trials. Third, the group will contribute with the needed experimental studies conducting to the refinement of the technical elements for the invasive intervention, based on nerve selective stimulation.

Novosense AB, Sweden, Mr. Jonas Tilly
Novosense, NS, will be leading the work package responsible for exploitation. The company has expertise in development of medical devices and accordingly is certificated to EN ISO 13485. The exploitation of the noninvasive technologies will be of main interest for NS.

Useful links

Project website: www.project-epione.dk
FP7: http://cordis.europa.eu/fp7
Aalborg University, Dept. Health Science and Technology: http://www.hst.aau.dk/
Aalborg University, Center for Sensory-Motor Interaction: http://www.smi.hst.aau.dk/home/
Aalborg University Hospital: www.aalborguh.rn.dk
Universita' Cattolica del Sacro Cuore: www.unicatt.it
Centre Hospitalier Universitaire Vaudois: www.chuv.ch
Albert Ludwigs Universität Freibug: www.imtek.de/en?set_language=en
Laboratoire d'Informatique de Robotique et de Microelectronique de Montpellier: www.lirmm.fr
École Polytechnique Fédérale de Lausanne: www.epfl.ch
Lund University: www.elmat.lth.se/english
Indiana University - Purdue University Indianapolis: www.iupui.edu
Universitat Autònoma de Barcelona: www.uab.es
Novosense AB: www.novosense.se
Obelia: www.obelia.eu

Contact information on project partners

Aalborg University **Department of Health Science and Technology** **Center for Sensory-Motor Interaction** **Denmark** **Dr. Winnie Jensen** wj@hst.aau.dk Tel: +45 9940 9825	**Expertise**: Theoretical and experimental expertise on design and test of implantable devices in animal models to interface the nervous system and development of neural rehabilitation systems. **Role in project:** Project coordinator. Deliver a 'psychophysical testing platform' (interactive computer system) for all clinical trials to deliver sensory feedback and measure the subject's response. **Academic partner - University**
Aalborg University Hospital **Dept. of Neurosurgery** **Denmark** **Dr. Preben Sørensen** prebsoe@rn.dk Tel: +45 9932 2750	**Expertise:** Neurosurgeon with expertise in implantable neural interfaces for the peripheral nervous system in humans (cuff electrodes, Actigait system) **Role in project:** One of three hospitals to function as clinical implant and test site for the invasive sensory feedback system **Clinical partner – University Hospital**
Universita' Cattolica del Sacro Cuore, **Institute of Neurology** **Department of Geriatrics, Neurosciences and Orthopedics** **Italy** Dr. Paolo Maria Rossini paolomaria.rossini@afar.it Tel: +39 0630 154459	**Expertise:** Expertise in implantable neural interfaces for the peripheral nervous system in humans (earlier generations of the intrafascicular electrode). Research in biomedicine, bioengineering, neuroscience, clinical neurophysiology in relation to the sensorimotor system. **Role in project:** Main responsibility for the three hospitals engaged as clinical implant and test sites **Clinical partner – University Hospital**
Centre ospitalier universitaire vaudois, **Schwitzerland** Dr. Raffoul Wassim Wassim.Raffoul@chuv.ch Mrs Lee Ann Laurent-Applegate Lee.Laurent-Applegate@chuv.ch Tel: +41 21 314 22 22	**Expertise:** Neurosurgeon. Specialist in plastic and reconstructive surgery, burns, hand surgery and peripheral nerves. **Role in project:** One of three hospitals to function as clinical implant and test site for the invasive sensory feedback system **Clinical partner – Hospital**
Albert Ludwigs Universität Freiburg **Germany** **Laboratory for Biomedical Microtechnology** **Department of Microsystems Engineering - IMTEK and Bernstein Center Freiburg** Prof. Dr.-Ing. Thomas Stieglitz stieglitz@imtek.uni-freiburg.de Tel: +49 176 24 33 00 38	**Expertise:** Theoretical and experimental research on neural interfaces and implants for the peripheral and central nervous system. Prototype development and manufacturing of microelectrodes and implants for animal and human use. EN ISO 13485 certified laboratory for electrode manufacturing **Role in project:** Deliver implantable electrodes for human use to be integrated in the invasive sensory feedback system. Academic partner - University
University of Montpellier - LIRMM **Laboratoire d'Informatique de Robotique et de Microelectronique de Montpellier, France** Dr. David Guiraud david.guiraud@inria.fr Tel: +33 467 418 621	**Expertise:** R&D on design and control of machines and robots and HMI. Design and test of microelectronic devices. Sensory motor modeling and control through neuroprostheses. **Role in project:** Deliver the software part for the electrical stimulation unit to be integrated in the invasive sensory feedback system. **Academic partner - University**

École polytechnique fédérale de Lausanne **Translational Neural Engineering Laboratory** **Center for Neuroprosthetics and Institute of Bioengineering** **Switzerland** Dr. Silvestro Micera silvestro.micera@epfl.ch Tel: +41 21 693 1048	**Expertise:** Theoretical and experimental research on biomechanical and electrophysiological modeling and signal-processing as well as applied research and technology transfer activities mainly in the biomedical domain. **Role in project:** Integrate hand prosthesis control with invasive sensory feedback system. **Academic partner - University**
Lund University **Dept. of Measurement Technology and Industrial Electrical Engineering** **Sweden** Dr Fredrik Sebelius Fredrik.sebelius@elmat.lth.se Tel: +46 73 650 22 95	**Expertise:** The group has extensive experience in research in the areas of nerve related hand problems, sensory feedback and hand prosthesis systems. The ULUND group is a collaboration between Dept. of Clinical Sciences and Dept. of Measurement Technology and Industrial Electrical Engineering **Role in project**: Adapt, test and characterize a non-invasive tactile feedback system **Academic partner – University**
Indiana University - Purdue University Indianapolis **Biomedical Engineering Dept** **USA** Dr. Ken Yoshida yoshidak@iupui.edu Tel: +1 317 274 9714	**Expertise:** Inventor of the tfLIFE and TIME intrafascicular electrodes. Theoretical and experimental expertise on non-invasive/invasive devices to activate nerves and stimulation strategies. **Role in project:** Responsible for clinical trial governance. Assist in testing and characterizing non-invasive electrical stimulation feedback system **Academic partner – University**
Universitat Autònoma de Barcelona **Institut Neurociències** **Spain** Dr. Xavier Navarro xavier.navarro@uab.cat Tel: +34 93 5811966	**Expertise:** Experimental and applied research on peripheral nerve injuries and repair and neuropathic pain. Extensive experience on evaluation of interfaces with the nervous system for the development of neuroprostheses. **Role in project:** Assist in all matters related to clinical trials governance. Small animal testing facility. **Academic partner – University**
Novosense AB **Sweden** Mr. Jonas Tilly jonas.tilly@novosense.se Tel: +46 709 90 57 25	**Expertise:** Development of Medical devices, EN ISO 13485 certificated, wireless self-contained sensors, sensory feedback system. **Role in project:** Responsible for exploitation activities. Specific exploitation of non-invasive technologies. **Industrial partner**
Obelia **France** Mr. Jean-Louis Divoux jldivoux@neuromedics.biz Tel: +33 4 97 21 30 40	**Expertise:** Design, development and manufacturing of AIMD (i.e. cochlear implant systems). EO sterilization for clinical use. Full EN ISO 13485 + NF EN ISO 11135-1certifications, CE marking of medical devices **Role in project:** Manufacture neurostimulator hardware. Exploitation of implanted technologies. **Industrial partner**