PROJECT FINAL REPORT

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Project Coordinator:	**Prof. Winnie Jensen**
	Aalborg University, DK
	Email: wj@hst.aau.dk,
	Phone: +45 99409825
Project website address:	**www.project-epione.eu**

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Dissemination Level

PU	Public	**X**
PP	Restricted to other programme participants (including the Commission Services)	
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (including the Commission Services)	

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1. Final publishable summary report

1.1. Executive Summary

Background. Amputation of a limb may result from trauma or surgical intervention. The amputation traumatically alters the body image, but often leaves sensations that refer to the missing body part. In 50-80% amputees, neuropathic pain develops, also called phantom limb pain (PLP). Both peripheral and central nervous system factors have been implicated as determinants of PLP. Also, PLP may be triggered by physical (changes in the weather) and psychological factors (emotional stress). Recent evidence suggests that PLP may be intricately related to neuroplastic changes in the cortex, and that these changes may be modulated by providing sensory input to the stump or amputation zone. However, the understanding of why PLP occurs is still poor, the basic research results have not been tested on a large scale in the clinic, and there are no fully effective, long-term treatments readily available on the market. We therefore aimed to challenge the status-quo of PLP therapy by offering technological solutions that will invasively or non-invasively induce natural, meaningful sensations to the amputee to restore the neuroplastic changes in the cortex and thereby control and alleviate PLP.

Objectives. *O1:* Through coordinated multi-centre clinical trials, we aimed to assess the effectiveness of providing invasive/non-invasive sensory feedback (direct peripheral nerve stimulation/mechanical pressure or electrical stimulation) with or without simultaneous operation of hand prosthesis device for controlling phantom limb pain. *O2:* We aimed to assess the associated cortical neuroplastic, psychological and cognitive components of pain. *O3:* We aimed to provide clinical guidelines. *O4:* We aimed to build novel innovative technological pre-industrial systems for delivering invasive/non-invasive sensory feedback based on existing solutions emerging from previous funded EU research.

Technical developments. *Route 1: Direct peripheral nerve sensory feedback.* The invasive technology was planned to be tested at three hospitals in Europe. Multiple transverse, intrafascicular electrodes (TIME-4H) were implanted in the median and or ulnar nerves of volunteer amputee subjects. Electrical stimulation was delivered through the active sites by the multi-channel, miniaturized electrical stimulator placed outside the body. The TIME-4H electrodes were surgically removed after completion of the study. *Route 2: Non-invasive sensory feedback.* The non-invasive technology was tested at five universities in Europe and the USA. We applied mechanical sensory feedback (i.e. air pressure) through silicone pads, or electrical stimulation through of-the-shelf electrodes with or without including a hand prosthesis device. *Across technologies:* To deliver the electrical stimulation sequences and also to obtain quantitative and qualitative measures on the effect of the microstimulation, a semi-automatic and computerized platform was developed (Psychophysical Testing Platform).

Clinical trials outcomes. *Route 1: Direct peripheral nerve sensory feedback*. Two upper limb amputee volunteers participated in to receive ‘direct’ peripheral sensory feedback. *Route 2: Non-invasive sensory feedback.* 29 volunteer subjects enrolled in the non-invasive trials, including upper limb amputees, lower limb amputees and subjects with complex regional pain syndrome (CRPS)**.** *Across technologies.* The group analysis indicated that there was, on average, a significant reduction in the phantom limb pain. Upper extremity subjects showed the largest effect as a group (as measured by the VAS and NAP of VAS measures). The lower limb amputees did not show a change in pain (as measured by the VAS and NAP of VAS measures), however they showed significant reductions in neuropathic pain (burning, paresthesia as measured by the NPSI) and reduction in pain interference on daily activities (as measured by the BPI). Contraindication is suggested for subjects with Complex Regional Pain Syndrome (CRPS) as the therapy appeared to increase the paroxysmal pain in some CRPS subjects (too few subjects to reach a definitive conclusion). Due to the heterogeneity of the subjects, it was not possible to achieve conclusive, joint results on the cortical organization/re-organization.

Exploitation and impact. The consortium has built novel technological systems based on existing technologies emerging from previous EU funded research and demonstrated the technologies in clinical trials with overall positive results. Business model cases were developed and the IPR situation analysed as the framework for brining the technologies to market. In case of the invasive clinical trials it proved challenging to obtain approval by the relevant competent authorities throughout different European countries, and it was highly difficult to identify volunteer subjects for this part of the study. However, we believe that the proposed work has laid a foundation for translating the basic research results into real clinical market applications and thereby provide long-term, patient-specific solutions to a large group of patients suffering from phantom limb pain.

Project Context and Objectives

Context

Amputation of a limb may result from trauma or surgical intervention. The amputation traumatically alters the body image, but often leaves sensations that refer to the missing body part. In 50-80% amputees, neuropathic pain develops, also called phantom limb pain (PLP). Both peripheral and central nervous system factors have been implicated as determinants of PLP. Also, PLP may be triggered by physical (changes in the weather) and psychological factors (emotional stress). Recent evidence suggests that PLP may be intricately related to neuroplastic changes in the cortex, and that these changes may be modulated by providing sensory input to the stump or amputation zone. However, the understanding of why PLP occurs is still poor, the basic research results have not been tested on a large scale in the clinic, and there are no fully effective, long-term treatments readily available on the market.

<u>*Hypothesis (Figure 1).*</u> We aim to challenge the status-quo of PLP therapy by offering technological solutions that will invasively or non-invasively induce natural, meaningful sensations to the amputee to restore the neuroplastic changes in the cortex and thereby control and alleviate PLP. We will assess the effect of cortical neuroplastic, psychological and cognitive components of pain and integrate the knowledge into clinical guidelines.

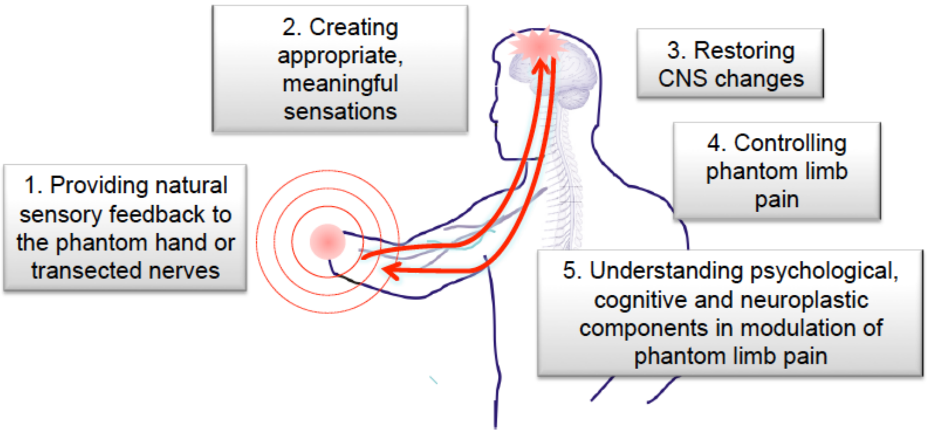


Figure 1. EPIONE hypothesis

Grand objectives

<u>*Objective I: Treatment of PLP.*</u> No effective, long-term treatments are currently available for PLP. In addition, 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 the amputees. We aim to provide clinical guidelines that include a recommended protocol for delivering sensory feedback therapy, methods for assessment of the PLP, factors determining the degree of PLP experienced by the individual subject and the sensory augmentation method. Through coordinated, multi-center clinical trials, we will deliver 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. Both solutions may be integrated with the operation of a hand prosthesis which many subjects already use on a daily basis.

<u>*Objective II: Understanding PLP.*</u> The mechanisms underlying the painful perception of a missing body part are still unclear. We aim to investigate if generation of PLP can be explained by changes in the cortical map that follows amputation, and whether PLP can be quenched by restoring the cortical map. We aim to assess the associated cortical neuroplastic, psychological and cognitive components of pain.

<u>*Objective III: Innovative solutions.*</u> There are no dedicated medical technologies available on the market with the aim to provide sensory feedback to control and alleviate pain. We aim to build novel innovative technological pre-industrial systems for delivering invasive/non-invasive sensory feedback based on existing solutions emerging from previous funded EU research.
The methodologies and outcomes are summarized in Figure 2.

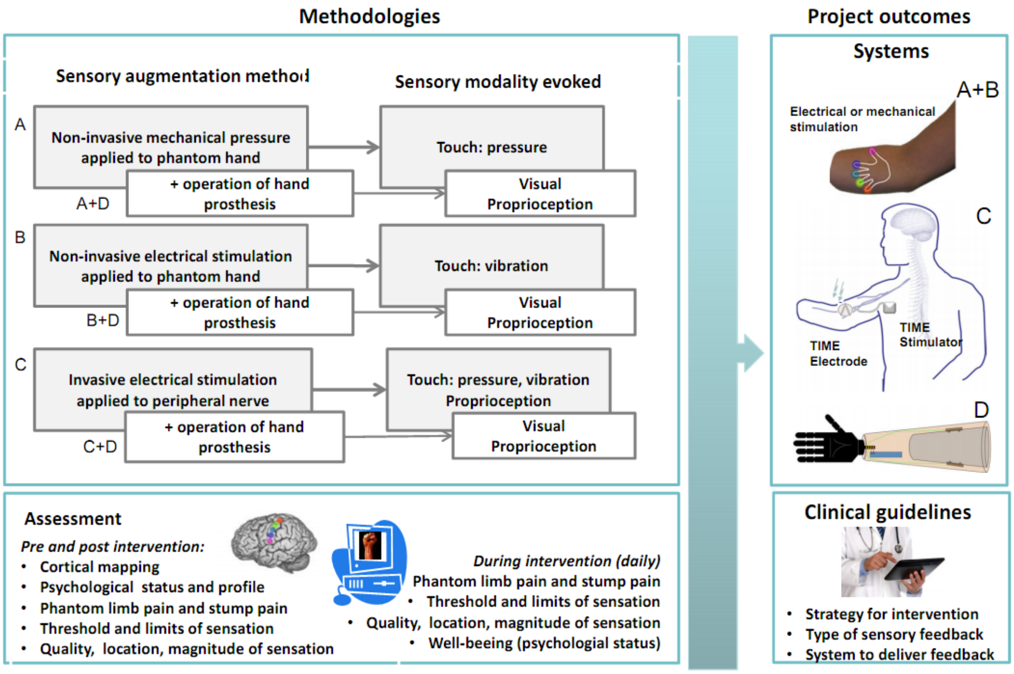


Figure 2. Methodological approaches to be investigated, prototype systems developed and assessment methods.

Organization of the work

The ultimate outcomes of the EPIONE project are to deliver clinical guidelines and prototype technologies for the use of natural sensory feedback for phantom limb pain modulation and therapy. Although the solutions offered by the consortium will be based on existing technologies and clinical protocols we aim to investigate multiple factors as possible determinants of PLP (e.g. cognitive and psychological) and assess multiple aspects of providing sensory feedback (e.g. different sensory modalities and technologies for delivering sensory feedback) that are unprecedented in the literature. As a consequence of this, it is believed that it will be important to evaluate the obtained results and possibly refine the clinical protocol and technologies during the project lifetime. To address the objectives and reach the defined milestones, the work is structured in three main, sequential phases, where a level of iteration is incorporated in the second phase. '

- *Phase I: Design and development (month 0-12):* In phase I, the preparatory work for the clinical trials will be carried out. A common clinical protocol will be defined for all clinical trials (across type of sensory feedback to be provided and type of technology to be used) (WP1). Technologies to deliver invasive/non-invasive sensory feedback will be adjusted / refined to meet the clinical protocol requirements and market needs (WP2+ WP3). To efficiently drive the EPIONE technologies towards the market, a preliminary market analysis will carried out during the first phase to map the market needs and requirements (WP6).
- *Phase II: Test, evaluate and revise (month 12-38):* A large portion of the work will be invested in phase II. After the necessary approvals for the clinical trials have been obtained, the first group of clinical trials will be carried out (WP4 + WP5) and results will be collected and evaluated across the different clinical trials (WP1). In parallel, a full market analysis will be carried out (WP6). Based on the preliminary scientific outcomes ('lessons learned') and the results of the market analysis, the clinical protocol and technologies may be refined before the second group of clinical trials is initiated. During the last part of this phase, specific exploitation strategies will be developed.
- *Phase III: Deployment (month 38-48):* In the final phase, all results will be integrated to deliver the clinical guidelines (WP1) and demonstrate prototype specifications and technologies (WP6)

1.3 Main S&T Results/foreground

WP1. Clinical Trials Governance

WP leader: THE TRUSTEES OF INDI
Partners involved: All

Objectives
The overarching objective of WP1 is to oversee, harmonize and coordinate multi-centre clinical trials of multiple neuromodulatory treatments and evaluations of phantom limb pain (PLP) such that statistical evidence of their differential efficacy can be tested, and based upon this evidence develop and establish good practices guidelines of effective treatment and evaluation. The work package was broken down into four tasks. The first task aimed to establish, maintain, shepherd and refine a common clinical protocol to be used across the multi-centre clinical trial. The second task aimed to collect and evaluate the group results to measure whether the therapeutic arms of the trial resulted in a change in the phantom limb pain experienced by the subject. The third task aimed to collect the experiences from the clinical partners to retrospectively establish a common set of guidelines and practices for delivering the effective therapies for treating PLP. And, the fourth task aimed to observe, monitor and facilitate the theoretical ethical framework within which the clinical trial and its participants operated.

Overview of main results

- **A common clinical protocol which guided the development of the testing platforms, and the common execution of the multi-center clinical trial was established.** The common protocol, furthermore, defined measures for group analyses which were used to determine the therapeutic outcomes and evaluate their effect sizes.
- **The group analysis from the trial indicates that there was, on average, a significant reduction in the phantom limb pain experienced by the amputee subjects that participated in the trial.**
  - Upper extremity subjects showed the largest effect as a group as measured by the VAS and NAP of VAS measures.
  - Although lower extremity subjects did not show a change in pain measured by the VAS and NAP of VAS measures, they showed significant reductions in neuropathic (burning, paresthesia) pain as measured by the NPSI measure and reduction in pain interference on daily activities as measured by the BPI measure. This contradictory outcome comes with the added observation of an increase in prosthetic limb use. This leads us to hypothesize that the therapy reduced PLP to enable increase use of their prosthetic limb which resulted in an increase in non-neuropathic residual limb pain. Thus we believe that the increase in non-neuropathic pain masked the reduction in neuropathic pain.
  - The therapy appears to have a strong positive effect in reducing phantom limb pain for subjects with amputated toes.
  - Contraindication is suggested for subjects with Complex Regional Pain Syndrome (CRPS) as the therapy appeared to increase the paroxysmal pain in some CRPS subjects. Although there were too few CRPS subjects to reach a definitive conclusion, future experiments with CRPS subjects should proceed with caution.
- **The therapy showed to have a short carry over, and thus analysis of the group was made in the period between baseline (i.e. before initiating therapy) and the final week of therapy (therapy week 4). Effect measured at the outcome showed some reversion in some cases, which reduced the average outcome of the therapy.**
- **All therapy arms as measured in the final week of therapy vs baseline showed, on average, a positive effect in reducing phantom limb pain.**
- **The ethical framework underlying the project and its execution was developed by an independent ethical advisor.**

Details of Main results

Establish and adjust/refine clinical protocol

The protocol defined the inclusion/exclusion criteria, timeline and phases of the trial, minimum durations and composition of the sessions, and the self-report instruments that measured the magnitude and extent pain, change of phantom sensations, emotion, interference by pain on activities of daily living, and objective instruments that aimed to measure changes in the cortical representations of sensation. The protocol served as the roadmap for the site-to-site protocols that were submitted by each clinical partner for ethical approval

of their respective clinical trial, as well as the specifications blueprint for the computer based psychophysical testing platform (a tool to systematically collect data) developed as part of the EPIONE project. Finally, the protocol defined the common instruments to be used to assess the change in PLP experienced conditioned by the therapeutic intervention arms across the multi-center trial.
The refinement of the protocol, which came between the defined Round 1 and Round 2 of clinical trials, extended the inclusion criteria to include other classes of subjects that experienced phantom limb pain (lower extremity amputees) and neuropathic pain (CRPS) to address recruitment difficulties of upper extremity unilateral amputees, loosened the calendaring rigidity to minimize the day to day intrusion on the subject's lives, and increased the measurement frequency for measures that were susceptible to drop outs. The general timeline and integrity of the measurements were otherwise unchanged to enable compatibility of the two trials to a combined analysis. The successful application of the common clinical protocol ensured compatibility of the protocols conducted at the various clinical trial sites, ensured compatibility of the data collected at each site, and enabled a combined group analysis to be undertaken.

Collect, integrate and evaluate all results from the clinical trials

During the course of the project, six clinical trial sites ran the study following the common clinical protocol defined in Task 1. A total of 31 total participants were enrolled, 23 started the therapy phase and 20 completed the protocol. At the time of this report one participant is still undergoing therapy. The data of this final subject is not included in the group analysis, and heretofore not included in the participant counts.
The subjects included in the analyses were those who started the therapy phase. The subject pool consisted of 11 upper extremity amputees (UE), 8 lower extremity amputees (LE), 3 subjects with complex regional pain syndrome (CRPS), and 1 subject with all 10 toes amputated (BLT). Summary of the subjects, site, therapy modality and measures received by IU for group analysis are summarized in Table 1.
Preliminary analyses between groups indicated that upper extremity and lower extremity subjects responded differently based on the psychometric measures, thus the subjects were grouped into four diagnoses: upper extremity amputees, lower extremity amputees, CRPS, and bilateral toes amputee.
The 24-hour Visual Analogue Scale of Pain (VAS) and the Non-overlap of All Pairs (NAP) of VAS, as well as the total measures and sub-scales of the Neuropathic Pain Symptom Inventory (NPSI), Brief Pain Inventory (BPI), and Profile of Mood States (POMS) were analysed to calculate the difference in measures as a function of protocol phase (1-4 weeks in therapy, outcome and follow-up weeks) to quantify whether the therapy resulted in a measurable change in the nature of pain (VAS, NAP of VAS, NPSI), interference of pain in the subject's activities of daily living (BPI), and emotional status (POMS).
Although fMRI was included as an objective measure, due to the grouping of the subjects into upper and lower extremity groups, a sufficient number of subjects, $n<10$, was not achieved to enable group analysis of the fMRI.
The overall results are summarized in Table 2, which shows the average change by group in the scores from the primary psychophysical instruments. These results were cross-validated using a longitudinal statistical measure, the Linear Mixed Effects and Tukey post hoc. The effect, and significance of the effect are indicated in Table 3.
Although the table only shows the difference in score change from baseline to the last week of therapy, the changes indicated here are indicative of the general overall change seen longitudinally.
The statistical significance of the effect size was estimated using the Linear Mixed Effects (LME) longitudinal analysis coupled to a within-design analysis of variance (ANOVA). In all cases, $p<0.05$ was used as the standard level of significance. A p-value ~0.1 was used as the threshold to indicate trending changes that could become significant with the inclusion of more subjects. The overall results from the psychophysical instruments are summarized in Table 3.
The table further shows the p-values from a between-design 1-way ANOVA and within-measures repeated measures (RM) ANOVA. The 1-way ANOVA does not link change to subject, and thus was not used. RM ANOVA was limited in possibilities to run post-hoc analyses, but was retained as a cross validation of the LME+ANOVA method used.

Subject				Tx Mode			PsyP Measures Analysis: VAS			PsyP Measures Analysis: POMS	PsyP Measures Analysis: NPSI	PsyP Measures Analysis: BPI	fMRI Groups			CMPL Tx
Round	Diagnosis	Code	Site	i/ni	E/M	HP	0HR	1HR	24HR	All	All	All	UE	LE	CRPS	
2	*BLT*	*a06*	*a*	*ni*	*E*											
1	*CRPS*	*a04*	*a*	*ni*	*E*											
1	*CRPS*	*a05*	*a*	*ni*	*E*											
2	*CRPS*	*c02*	*c*	*ni*	*E*											
2	LE	a08	a	ni	E											
2	LE	a10	a	ni	E											
2	LE	a12	a	ni	E											
2	LE	a15	a	ni	E											
2	LE	a16	a	ni	E											
2	LE	i01	i	ni	E											
2	LE	i02	i	ni	E											
2	LE	a18	a	ni	E											
1	**UE**	**a03**	**a**	**ni**	**E**											
2	**UE**	**a09**	**a**	**ni**	**E**											
2	**UE**	**a17**	**a**	**ni**	**E**											
1	**UE**	**c01**	**c**	**ni**	**E**											
2	**UE**	**cp01**	**p**	**ni**	**E**	**H**										
1	**UE**	**l01**	**l**	**ni**	**M**	**H**										
2	**UE**	**l02**	**l**	**ni**	**M**	**H**										
2	**UE**	**l04**	**l**	**ni**	**M**	**H**										
2	**UE**	**l05**	**l**	**ni**	**M**											
1	**UE**	**r01**	**r**	**i**	**E**											
2	**UE**	**r02**	**r**	**i**	**E**	**H**										
2	*LE*	*a07*	*a*	*ni*	*E*		*Withdrew Before Tx Phase*									
2	*UE+CRPS*	*a13*	*a*	*ni*	*E*											
2	*LE hip*	*a14*	*a*	*ni*	*E*											
2	*LE*	*i000*	*i*	*ni*	*E*											
2	*LE*	*i001*	*i*	*ni*	*E*											
2	*LE*	*i002*	*i*	*ni*	*E*											
1	*UE*	*l03*	*l*	*ni*	*M*	*H*										
2	*UE*	*l06*	*l*	*ni*	*M*	*H*										
	Count	**31**					**22**	**22**	**23**	**17**	**18**	**14**	**7**	**7**	**2**	**20**

Table 1: Summary of subjects and group analysis measures for group analysis. The subject information includes the de-identified subject code, diagnosis, round site and mode of therapy. LE = lower extremity amputee, UE = upper extremity amputee, CRPS = complex regional pain syndrome, BLT = bilateral toes amputee. 31 subjects were recruited for the study. 7 subjects withdrew (W) before the therapy (Tx) phase. 1 subject's data was lost, leaving 23 subjects who underwent the trial. 3 of these subjects withdrew during the therapy phase and 20 subjects completed the trial. The Notes indicate details on drop-outs or withdrawals of subject. W TxN for the 3 subjects who entered the therapy phase indicate the last week in which they received therapy (i.e. Tx2 indicates the 2nd week of therapy). The blocked out fields indicate the data set received for group analysis. Empty fields indicate missing data.

#Subject	Average Group Change	dNAP 24HR	dVAS 24HR	dPOMS Total	dNPSI Total	dBPI Total
23	All	0.10	-0.62	0.20	-4.90	-0.36
1	10 Toes (BLT)	*0.36*	*-2.03*			
3	CRPS	*-0.10*	*0.51*	*-2.00*	*4.16*	*0.05*
8	LE	*0.00*	*-0.22*	*3.94*	*-4.17*	*-0.60*
11	UE	*0.21*	*-1.08*	*-3.00*	*-7.56*	*-0.13*
19	LE+UE	*0.12*	*-0.72*	*0.47*	*-5.97*	*-0.42*

Clinical Effect Th	dNAP 24HR	dVAS 24HR	dPOMS Total	dNPSI Total	dBPI Total
Strong +	-0.42		-4	-16	-2.1
Medium +	*-0.16*		*-2*	*-10*	*-1.3*
Positive					
No Change					
Negative					
Medium -	*0.16*		*2*	*-1*	*2.1*
Strong -	0.42		4	16	1.3

Table 2: Summary of the average change in primary psychophysical outcome measures instruments. This table shows the change in score at the last week of therapy from the baseline measure for all subjects that entered the therapy phase. The lower table is a legend showing the values for clinical effect thresholds. Green indicates positive change, while red indicates negative change

	Measure	1-way ANOVA (Between)		RM ANOVA (Within)		LME+ANOVA (Within)	Tukey PostHoc					
	Incl Wks	*B->F*	*B->Tx4*	*B->F*	*B->Tx4*	*B->F*	*Tx1-B*	*Tx2-B*	*Tx3-B*	*Tx4-B*	*O-B*	*F-B*
UE	NAP_24HR	**0.097**	**0.016**	**0.037**	**0.009**	**0.002**						
UE	VAS_24HR	0.170	**0.109**	**0.012**	**0.007**	**0.002**	**0.011**	**0.019**	**0.004**	**0.012**	**0.040**	**0.001**
UE	NPSI_Total	**0.105**	0.145	**0.057**	**0.068**	**0.038**	0.919	0.740	**0.067**	**0.102**	0.618	**0.055**
UE	BPI_Total	0.843	0.890	0.241	0.848	0.672	1.000	0.943	0.999	1.000	0.832	0.999
UE	POMS_Total	0.530	0.756	0.718	0.441	0.772	0.996	0.989	0.999	0.713	1.000	0.995
						p-values						
LE	NAP_24HR	0.829	0.793	0.949	0.957	0.995						
LE	VAS_24HR	0.308	0.292	0.996	0.690	0.908	1.000	1.000	1.000	0.968	0.999	0.997
LE	NPSI_Total	0.736	0.982	0.277	0.349	**0.009**	**0.004**	**0.002**	0.205	0.559	0.146	0.150
LE	BPI_Total	**0.089**	0.157	0.196	0.119	**0.070**	0.560	0.395	**0.040**	0.185	**0.052**	0.905
LE	POMS_Total	0.892	0.429	0.360	0.856	0.239	1.000	0.943	1.000	1.000	0.971	0.178
						p-values						
UE+LE	NAP_24HR	0.230	**0.066**	0.156	**0.052**	**0.051**						
UE+LE	VAS_24HR	**0.093**	**0.054**	**0.103**	**0.045**	**0.041**	**0.106**	0.190	**0.071**	**0.032**	0.154	0.211
UE+LE	NPSI_Total	0.171	0.304	**0.032**	**0.038**	**0.002**	**0.049**	**0.009**	**0.004**	**0.025**	**0.094**	**0.004**
UE+LE	BPI_Total	0.247	0.594	0.576	0.114	0.495	0.960	0.997	0.290	0.861	0.957	1.000
UE+LE	POMS_Total	0.619	0.431	0.454	0.737	0.367	0.999	1.000	1.000	0.966	0.991	0.667
						p-values						
CRPS	NAP_24HR	0.994	0.978	0.996	0.982	0.767						
CRPS	VAS_24HR	0.519	0.923	0.722	0.811	0.695	1.000	1.000	0.992	0.981	1.000	0.917
CRPS	NPSI_Total	0.705	0.623	0.234	0.446	0.175	0.900	0.927	0.986	0.860	1.000	0.572
CRPS	BPI_Total	0.701	0.799	0.527	0.465	**0.016**	**<.001**	**0.020**	**0.001**	0.930	**<.001**	**0.004**
CRPS	POMS_Total	0.957	0.611	0.102	0.132	0.214	1.000	0.449	0.967	0.939	0.148	0.304

Table 3: Results of the statistical tests from the primary psychophysical instruments to measure pain (24hr VAS, 24hr NAP of VAS, NPSI), pain interference on activities of daily living (BPI), and emotional state (POMS), grouped by diagnoses. Results indicate the p-values of the change. A p-value < 0.05 was considered significant, and is highlighted in green if the direction of the change was a positive effect. Changes trending in the positive direction that did not meet the significance criteria are highlighted in yellow.

Task 3. Provide therapy guidelines

Based on the results and collected clinical observations from the consortium, a guidelines document was authored that provides a retrospective guidance on the delivery of the therapy and suggestions for best practices. The overall outcome from the trial indicated that all arms of therapy showed some degree of positive effect on PLP for the amputee subject groups (UE, LE, BLT). CRPS showed mixed but negatively trending results suggesting contraindication for this diagnosis. Given the positive outcome for amputees, the guidelines suggest that non-invasive methods be applied first to determine efficacy for the patient. In cases where there is limited residual limb for electrode placement and access to hot spots, the implanted approach could be indicated. Caution is indicated in assessing pain in lower extremity amputees due to the possibility of interference with residual limb pain resulting from increased use of weight bearing prostheses.

Task 4. Ethical issues management

The ethical considerations during EPIONE have been thorough and consistent throughout the whole project. The IEA has initiated, facilitated and executed several different activities.

The following regulatory activities have been carried out during the project EPIONE.

1. Acknowledgment of relevant laws, principals and regulations
2. Identifying the relevant ethical field, in moral philosophy as well as in medical ethics / bioethics
3. Checking up on all ethical approvals
4. Analysis of the applied procedures of informed consent
5. Observation of cooperation, and work flow
6. Interview with participating patient

The following advisory activities have been carried out during the project EPIONE.

1. Developing an adequate method for relevant ethical reflection
2. Identifying adequate moral concerns, theoretically thickened and practically recognizable
3. Discussing appropriate learning strategies
4. Questionnaire disturbed amongst the partners, and analysis of the survey
5. A lecture on ethics and medical ethics for the partners

6. Workshop session with the partners
7. Evaluation with EPIONE management

It is the opinion of the IEA, that the partners in the project EPIONE have clearly demonstrated a more than adequate ethical awareness, of principals, in character and in judgment.
Ethical guidelines, principals and regulations have been adequately identified and satisfactory applied. Issues of relational ethics have been addressed and acknowledge, and to some extent also soundly developed. The partners have demonstrated a respectful behaviour and sufficient moral concern in their interaction with the participating patients. The partners have been taught medical ethics and normative theory, and they have verified appropriate interest, knowledge and competencies in these fields. The partners have also competently taken active part in practised ethical deliberation relevant for EPIONE.

WP2. Technologies for non-invasive sensory feedback

WP leader: EPFL
Partners involved: EPFL, AAU, THE TRUSTEES OF INDI, LUNDS UNIVERSITET, CHUV

Objectives
The objective of WP2 was the development of several non-invasive sensory feedback strategies for humans, designed to alleviate the symptoms of phantom limb pain. Different types of non-invasive feedback systems were developed, including (1) non-invasive mechanical stimulation, (2) non-invasive electrical nerve stimulation (TENS) without prosthesis, and (3) TENS used in conjunction with a prosthesis. Furthermore, relevant steps needed to be taken to facilitate future commercialisation of the new systems.

Overview of main results
- A system for non-invasive mechanical stimulation of the skin was successfully developed, including a hand prosthesis with integrated sensors, a custom socket/liner with mechanical actuators contained within.
- A custom system for non-invasive TENS, integrating a commercial TENS stimulator (INOMED), a computer and a custom developed stimulation software.
- A system for TENS sensory feedback with a hand prosthesis, incorporating a commercial TENS stimulator (REHASTIM), a single board computer running a custom control software, a commercial robotic hand (PRENSILIA) and an sEMG acquisition device.
- Preparatory work on commercialisation of devices was carried out to facilitate further development and exploitation.

Details of main results
The main goal of WP2 was to prepare three research setups for further clinical tests, these included (1) a non-invasive mechanical stimulation device with a hand prosthesis, (2) a non-invasive TENS stimulation device with a hand prosthesis, and (3) an open-loop TENS setup. All three systems were successfully developed. Additional details regarding each system are introduced here.
First, a system capable of conveying sensory feedback via mechanical skin stimulation was developed. This system was composed of a prosthetic hand with incorporated sensors. The readout from these sensors triggered mechanical stimulation of the forearm, thus delivering physiologically relevant feedback information to the wearer. Furthermore, the relevant performance metrics of the system were tested for various variants, and the most appropriate set of parameters were selected for use in the clinical studies (such as minimal force threshold).

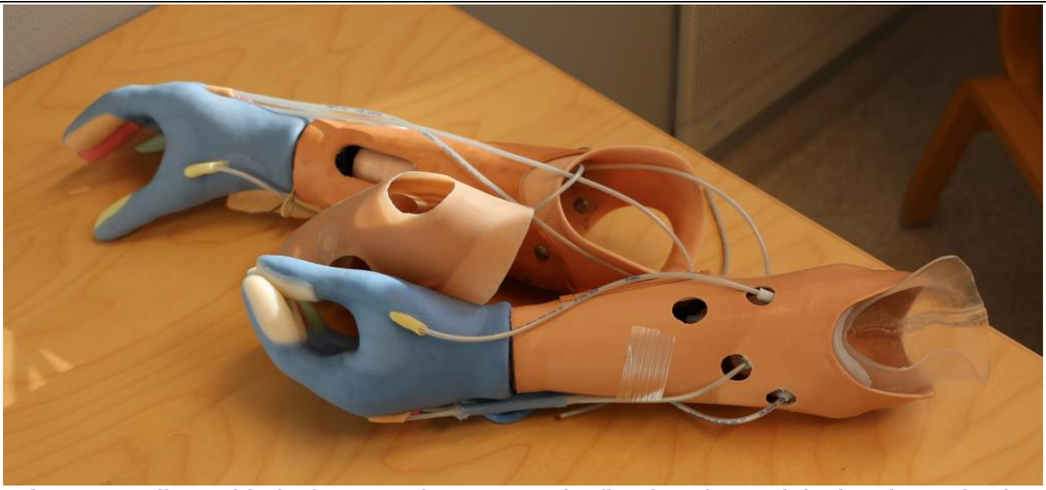
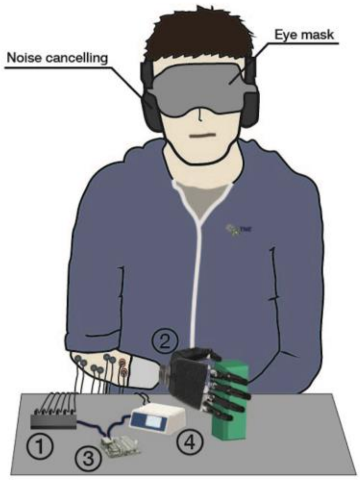


***Figure 3: The custom liner with the integrated actuators, the fitted socket and the hand prosthesis with force sensors*.**

The sensory feedback system includes a "bubble-sensor" matrix, where silicone encapsulated gas bubble are connected via a thin silicone tube to pressure sensors or directly to pneumatic actuators. A pneumatic actuator is used to transfer sensations to the forearm skin from a hand prosthesis equipped with sensors.
Second, a system for open loop TENS was developed. In this case, the surface electrical stimulation was delivered independently of a robotic hand. To successfully control stimulation therapy sessions, a complete control software was developed: the psychophysical testing platform. The 'Psychophysical testing platform' is a dedicated software with the aim to provide time sensitive control over all aspects of the experimental setup. The setup was composed of surface electrodes applied to the stump. The computer controlled two screens, one for displaying information to the experimenter, and the second for displaying patient specific information.
The complete system, including the software platform and stimulator, were tested together and shown to work optimally for a wide range of operating conditions and therapy types.
Third, a system for TENS feedback during hand prosthesis use was developed. This system was composed of a hand with incorporated tensions sensors, connected to a central processing unit (a single board computer).



F*igure 4: an overview of the components used in the system for non-invasive electrical stimulation, including the hand prosthesis: (1) the sEMG acquisition device, connected to the forearm via gel electrodes, (2) the prosthetic hand, (3) the single-board computer, and (4) the TENS stimulator, connected to the skin via gel electrodes.*

The overall system was tested extensively on healthy individuals, to fine tune the various parameters and timing issues which arose from the complex interplay of several independent components exchanging data in real-time. The system was found to be robust, and the best parameters were selected for use in the clinical study.

Finally, initial preparatory steps for the future commercialisation of the system were carried out during the project's timeframe. These included preliminary market research, as well as initial considerations considering CE marking and relevant regulations. Overall, clear steps have been defined for the future work needed regarding commercialisation.

WP3. Technologies for direct, invasive peripheral nerve sensory feedback

WP leader: ALU-FR
Partners involved: AAU, RN-Aalborg UH, UCSC, CHUV, ALU-FR, UM2, EPFL, THE TRUSTEES OF INDI, UAB, MXM-OBELIA

Objectives
The objective of WP3 was to develop a platform applicable for invasive peripheral nerve sensory feedback studies on human subjects. The platform should be applied in patients suffering from phantom limb pain using either sensory feedback without or with an additional hand prosthesis.. The platform should include (1) intrafascicular nerve electrodes for chronic implantation, (2) a wearable electrical stimulator connected either to (3) a psychophysical testing platform and/or (4) a hand prosthesis.

Overview of main results
- Technologies to drive direct, nerve sensory feedback (TIME-4H, STIMEP and hand prosthesis) were adjusted, refined and successfully integrated with focus on long-term stability.
- A psychophysical testing platform was developed.
- The technical teams assisted to establish and refine clinical protocol and provided technical support to the clinical test teams during the surgeries and afterwards.
- Preparatory work for commercialization of the system was done.

Details of main results
The main goal of WP3 was to develop, refine and adjust the technical devices for the invasive clinical trials. The whole technical setup consists of four sub systems, (1) the transversal intrafascicular multichannel electrode (TIME), which is implanted in the median and/or ulnar nerve, (2) the stimulator STIMEP, which is capable of driving four electrodes in parallel, (3) a hand prosthesis equipped with sensors for haptic feedback and (4) a psychophysical platform to apply therapy and to obtain quantitative and qualitative measures of the effect of the therapy (Figure 5)
Partner ALU-FR has adjusted and refined the previous TIME-3H from the EU-FP7 project called TIME (sub chronic application) to end up in the current version, TIME-4H (chronic application). In depth analysis of the TIME-3H explants led to the following optimization steps:
First, the design and positioning of active sites and ground sites was changed, but the established outer dimensions of the electrode (width and thickness) remained within the previous version. Changes included the segmentation of the ground electrode to reduce intrinsic stress and delamination. Furthermore, the location of active stimulation sites on the substrate was shifted and additional adhesion promotion layers without access to the material-tissue-interface were included (layer setup was examined according to the ISO 10993 standard on cytotoxicity and passed) and tested with the partner UAB in the small animal model. Electrode sites proved to be more stable during continuous stimulation in vivo with adhesion layers compared to sites without. On the other hand, the packaging of the system was changed in some details, like the linkage between cable and connector or the identification tags. Furthermore, the restricted materials, which are in contact with the tissue after implantation of the devices, have been exchanged to non-restricted ones. These changes have also been integrated in the quality management system of the partner ALU-FR (fully ISO 13485 certified). Based on suggestion of US FDA guidance, ASTM F2503, IEC 62570 and for CE marking, the TIME-4H implants were investigated on MR compatibility by the company MR:comp. This non-clinical testing has demonstrated, that the TIME-4H implant is MR conditional in clinical relevant position and orientation according to the specification of ALU-FR. A patient with this device can be safely scanned in an MR system meeting the conditions specified in the manual. Essential validations for usage of the implants within invasive clinical trials, like washing and sterilization validation, were accomplished as well.
After design freeze the implants were constantly further improved in detailed parts (e.g. epoxy encapsulation, plasma treatment) to increase the long-term stability for the clinical trials (e.g. after analysis of the first round).
Both French partners, MXM-OBELIA and UM, refined the stimulator and stimulation paradigms according to the clinical requirements and to the performances of the considered system. The development, design and

manufacturing of the miniaturized multichannel stimulator STIMEP included:

- 1 base board: BAISE_EP supporting power supplies, peripherals and insulated communication links and carrying
- 4 x 24xEP: independent 14 channels stimulator front-end, based on dedicated MXM-OBELIA KF24 ASIC component
- 1 M2S-FG484 —off the shelf microcontroller board
- Design and manufacturing of the miniaturized STIMEP packaging
- All accessories (cables, switchboard etc.) have been specified according to these specifications as commercially available components
- Interconnect box has been designed and manufactured

Miniaturized devices were tested and integrated before final delivery according to the corresponding EU directives and international standards.

The partner UM designed and partially developed the controller-embedded software, as well as communication protocols with third parties (PLPP and HPC). UM has also co-designed with MXM-OBELIA, the global STIMEP architecture as well as the digital architecture of stimulation units. As the partner UM does not have an established quality management system special care was devoted to comply with the harmonized standard EN 62304 “Medical device software - Software life-cycle processes”.

The performance of different stimulation strategies for intraneural stimulation was assessed using TIME electrodes and the Stimn‘D stimulator (from the TIME project, delivered by UM and MXM-OBELIA) in experiments in rats at the UAB. The results showed that the inclusion of a 100 µs delay between the cathodic and the anodic phase of the stimulus allows to reduce charge requirements by around 30% without affecting stimulation selectivity. Further *in vivo* studies, were made to determine to which extent the stimulation charge might be decreased by delaying the discharge phase, depending on pulse duration and the way discharge is performed. The results demonstrated that delaying the discharge phase allows to gain more charge for shorter pulses. The difference in the gain between waveforms with passive and active discharge is lower.

In order to investigate the physiological bases and the most efficient therapeutical pattern of nerve stimulation for reduction of neuropathic pain, experiments on stimulus patterns have been performed in animal models of peripheral nerve lesions that cause hyperalgesia and pain.

Data generated by the small animal model testing was delivered to the partner UM for optimization of the STIMEP stimulation parameters.

EPFL was mainly responsible to integrate a sensor equipped hand prosthesis for the sensory feedback. Therefore, EPFL has developed encoding algorithms to transduce the readout of sensors embedded in the prosthetic hand in stimulation parameters. Moreover, EPFL has implemented decoding algorithms and the control of the prosthetic hand.

These algorithms have been ported on a small controller that can be powered with a battery (Odroid U3). Two systems can be used for acquiring sEMG signals which are Grapevine (Ripple) and TeleMyo (Noraxon). Moreover, two robotic hands were available: Azzurra (Prensilia) or the Robotic hand from Wessling Robotics. As planned, the control of the STIMEP, for driving the current injection in the intraneural electrodes, has been implemented. The chosen controller was able to virtually interface to every device wirelessly or with wires (USB or SPI connection).

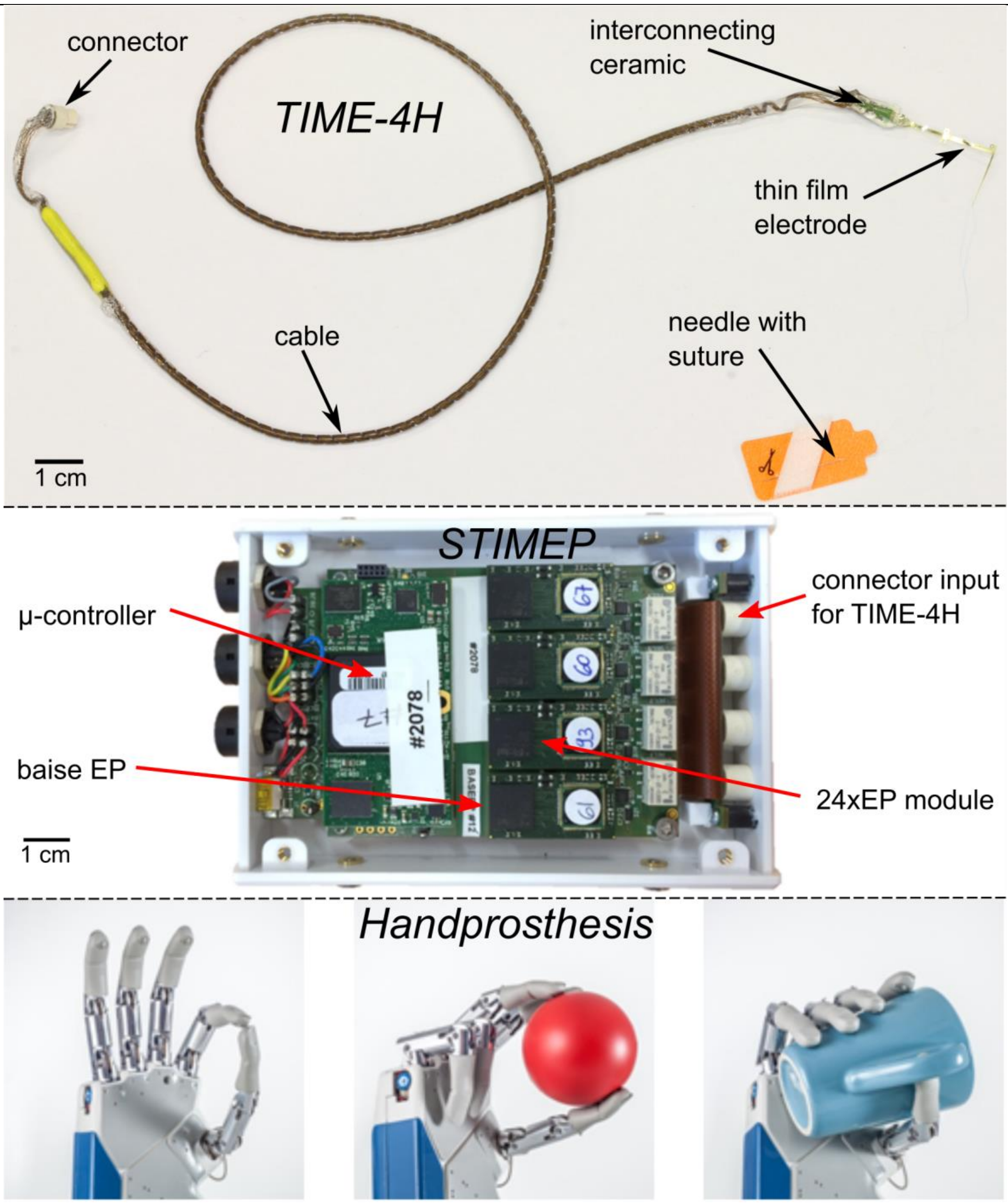


Figure 5. ALU-FR developed, refined and adjusted the transverse intrafascicular multichannel electrode to the newest version TIME-4H, which was used during the clinical trial to interface the median and ulnar nerves electrically. The STIMEP stimulator, developed by UM (software) and MXM-OBELIA (hardware), was used for driving the TIME-4H. Moreover, EPFL developed the possibility to link the STIMEP with a sensor equipped hand prosthesis to realize sensory feedback.

The Psychophysical Testing Platform developed by the partner AAU is a computer based system developed to apply therapy to modulate painful and non-painful phantom limb sensations and to obtain quantitative and qualitative measures of the effect of the therapy. The Platform also assists to secure that the therapy is delivered and the data is collected in a systematic and time efficient way across clinical test sites.
Since the Psychophysical Testing Platform was intended to control the STIMEP, which drives electrical stimulation administered by the implanted TIME-4H devices, the software was therefore classified as IIb according to directive 93/42/EEC annex IX.
Function included to the platform were:

- Log in control of administrators, experimenters and experimental subjects
- Keeping track of the experimental phase of each subject and which questionnaires and test to

present to
- Monitoring the subjects
- All questionnaires included in common protocol (D1.1) in Danish, English, Italian and French.
- Different images for left/right and arm/leg amputation.
- Save logs for conducted procedures and results of questionnaires.
- Facilities for planning and conducting stimulation using the STIMEP (iE) or InoMed (niE)
- Review functions

In accordance to prove the functionality of the all devices and systems, animal tests were performed on rats (UAB) and pigs (AAU). All the procedures used by the psychophysical testing platform (PSYP / USB), the hand prosthesis (HP / SPI) and SYNERGY (USB) software (testing software used by UM) were fully assessed using the whole EPIONE system (TIME-4H implanted on the sciatic nerve of the rat, STIMEP and final versions of software). Typical measurements with both EMG recordings and synchronization output, and evoked EMG on 3 muscles (PL, GM, TA) were performed. Safety embedded procedures was also successfully tested. During the use of STIMEP and third party software within the clinical trial, no critical bugs were reported. ALU-FR fabricated according to the quality management system requests more than 60 implantable TIME-4H devices. They are all listed in the system and traceable. MXM completed manufacturing (12 pieces), verification and validation of all STIMEP systems (10 systems in total) before dispatch to the partners. Each device and accessories were thoroughly tracked and traced to ensure traceability as requested by the quality management system. The WP3 teams provided technical assistance in two human implantations. A technical dossier is set up as documentation and prerequisite for further clinical trials and commercialization steps.

WP4. Clinical trials: Efficacy of non-invasive sensory feedback

WP leader: LUNDS UNIVERSITET
Partners involved: LUNDS UNIVERSITET, AAU, EPFL, THE TRUSTEES OF INDI, UAB and NOVOSENSE AB

Objectives
The main objective of this work package was to assess efficacy of the non-invasive feedback to reduce phantom limb pain (PLP) using electrical or mechanical sensory feedback with or without the simultaneous operation of a hand prosthesis device.

Overview of main results
- Assist to establish and refine EPIONE clinical protocol
- Testing the non-invasive system/methods with the developed EPIONE clinical protocol
- Analysing and reporting clinical result of the non-invasive clinical therapies.
- Mechanical and electrical stimulation of referred sensation areas provided consistent positive non-painful evoked sensations, qualified for sensory input for therapy of phantom limb pain.
- Experience of phantom limb pain was highly individual, however, common features of the types of pain could be identified for groups of patients.
- Out of 23 subjects completing the therapy session we observed a consistent decrease of pain in 10 subjects as indicated by the VAS measure questionnaire during or after the therapy session, and a significant short-term relief of phantom limb pain has been observed in 12 subjects during the therapy session.
- Selective effective relief of specific components of pain associated with changes in the unnatural perception of the phantom limb associated with pain relief were reported.

Details of main results
Four types of non-invasive sensory feedback were used during a four week therapy session in the clinical tests electrical and mechanical feedback with or without the operation of a hand prosthesis device. The patient groups included upper limb amputees, lower limb amputees and different type of nerve injury patients experiencing phantom limb pain. Only the upper limb amputees worked with the handprosthesis device. A variety of clinical observations were reported that indicated a strong correlation between the stimulus delivered, characteristics of the referred sensation areas, external factors and the type of pain experienced. The outcome from the clinical trials was feed back to WP1 (Clinical trials governance) where a joint group analysis was performed. In WP4 the analysis and reports was instead done by a case-by-case analysis.

Stimulation strategy – utilizing the referred sensation areas

Before initiating the therapy phase we examined and mapped the referred sensation areas (RSA) for each subject. The RSAs were highly specific to each subject, depending on e.g. level of amputation, on the condition that led to amputation, and on the type, intensity, and duration of the stimulus. RSAs occur as nerve endings sprout following amputation connecting to existing skin sensors, representing a gate to the nervous system to provide sensory input to the brain. If the subject had a phantom map referred sensation area, this was then used as stimulation zone for the therapeutic stimulation. The phantom map referred sensation area was defined as an area of skin on the amputee that is if touched gives the amputee the sensation of touching part of the amputated limb.

In some subjects RSAs could be determined as larger areas on the skin, whereas in the other subjects RSAs were characterized as smaller spots. We found that the RSAs maps typically changed slightly over time with respect to in both location and type of sensation. Also, we found that a majority of the subjects would at first report not to experience any referred sensations, while this changed after some sessions.

Characteristics of the experienced phantom limb pain

Individual experiences of phantom limb pain (PLP) were reported, as perception of pain is highly individually and it may be affected by a great variety of factors. However, common features were noticed with subjects experiencing similar injury types (arm or leg amputees, as well as brachial plexus nerve damage) described the type and pattern/dynamics of PLP such as:

- Hard or partial clenched fist (upper limb amputees)
- Stretched / compressed (like small shoe, tight ring, or vice like clamping), or cramps in muscle of phantom limb (lower limb amputees)
- Short but very intense iron bar/needle piercing or current
- Constant continuous pain
- Continuous pain with relative fast and large variations within seconds/minutes
- Additional factors affecting dynamics of phantom limb pain: weather (warm, cold, pressure), stump load during physical activity, associated with use of prosthesis, intake of medicine on demand.

The naturally occurring dynamics of the experienced pain (i.e. the changes in pain over time), especially the frequent variations, posed additional demands when evaluation of evoked/induced sensations.

Short-term effects of therapy by surface electrical stimulation

The type of stimulus, location for delivery (i.e. the referred sensation area), and dosage proved to affect the type and intensity of phantom pain experienced. The following were noticed during repeated/randomized stimulus delivery:

- *Relative long delayed occurrence of significant pain reduction*. A sub-group of upper-limb amputee subjects initially had the feeling of a hard clenched fist. The 'clenched fist' opened after several session and were associated with a pain reduction by approximately 30-40%.
- *Immediate pain modulation*. A sub-group of subjects experienced immediate reduction of pain between 40 to 100%, with long-lasting effect, i.e. after stop of stimulus delivery, pain increased after a few minutes to the level experienced just before stimulus delivery.
- *Short-medium delayed pain modulation.* A sub-group of subjects experienced a delayed (seconds to minutes, dependent on pain level before stimulus delivery) pain reduction that lasted up to 3 hours.
- *General minor reduction of pain during and after the therapy phase*. A sub-group of subject not report any of the effects listed above, however mild reduction in pain level and less frequent pain episodes were reported during and after the therapy phase that correlated with an improvement in their general mood.

WP5. Clinical trials: Efficacy of direct, peripheral nerve sensory feedback

WP leader: UCSC
Partners involved: UCSC, CHUV, RN-Aalborg UH

Objectives

The main objective of this work package is to assess efficacy of direct, peripheral nerve sensory feedback to reduce/suppress phantom limb pain (PLP) with or without the simultaneous operation of a hand prosthesis device.

Overview of main results

- We confirmed the possibility to use TIME electrodes for delivering intraneural stimulation and PLP treatment.
- Following the intraneural stimulation one of the two recruited patients experienced a statistically significant decrease of PLP intensity. In this patient the multimodal analysis for brain plasticity showed significant changes following the treatment, mainly on brain regions corresponding to the amputated side.
- Recommended procedures for surgical TIME electrodes implantation and for the intraneural stimulation process were provided.
- Some important lessons were learned regarding difficulties on patient recruitment and ethical and legal approval in this field.

Details of main results

By the end of the project it was only possible to recruit two out six planned patients. The two patients were recruited by UCSC. Despite strong efforts made, CHUV and RN-Aalborg UH were not able to find patients for the invasive trial. RN-Aalborg screened more that 30 subjects but nobody was recruited due to the inclusion/exclusion criteria. CHUV, due to the late approval from Swiss Medic, started the recruitment with delay and had the possibility to screen few patients. Also in this case the patients did not fulfil the inclusion/exclusion criteria.

PLP treatment

The first patient was a 37-year-old male from Ecuador with a traumatic transradial (proximal third of the forearm) amputation of the left arm occurred about 3 years ago. The second patient was an Italian 54-year-old female with a traumatic very proximal trans-radial amputation of the left arm occurred about 1 year and 6 months ago.

We confirmed the possibility to use TIME electrodes for delivering intraneural stimulation for PLP treatment.

Following the intraneural stimulation one of the two patients experienced a statistically significant decrease of PLP intensity (Figure 6 and Figure 7) measured with VAS (in the 24 hours) and NPSI. In this patient the simple intraneural stimulation was able to reduce the pain, while in the other patient PLP remained unchanged so far (the trial with this patient is presently on-going) also after prolonged session of continuous intraneural stimulation (VAS and NPSI score not statistically significant). Due to the low number of patients it is impossible to identify factors (e.g. like time from amputation, level of amputation, degree of functionality of the residual stump) linked to a possible success or failure of the treatment.

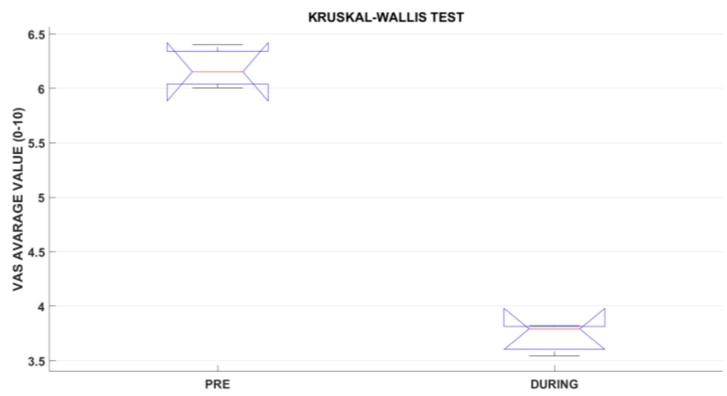


Figure 6. Graphic showing the comparison of VAS score before the implant and during the treatment.

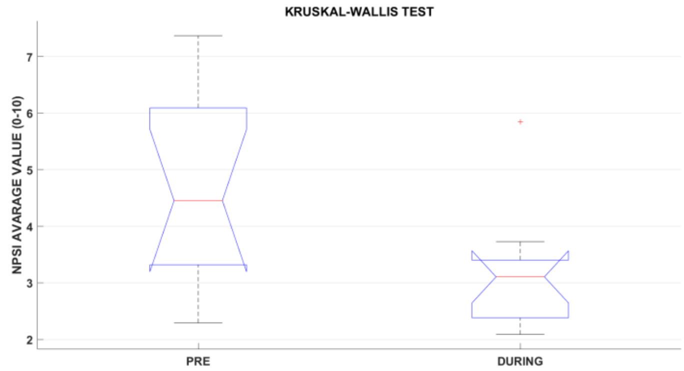


Figure 7. Graphic showing the comparison of NPSI score before the implant and during the treatment.

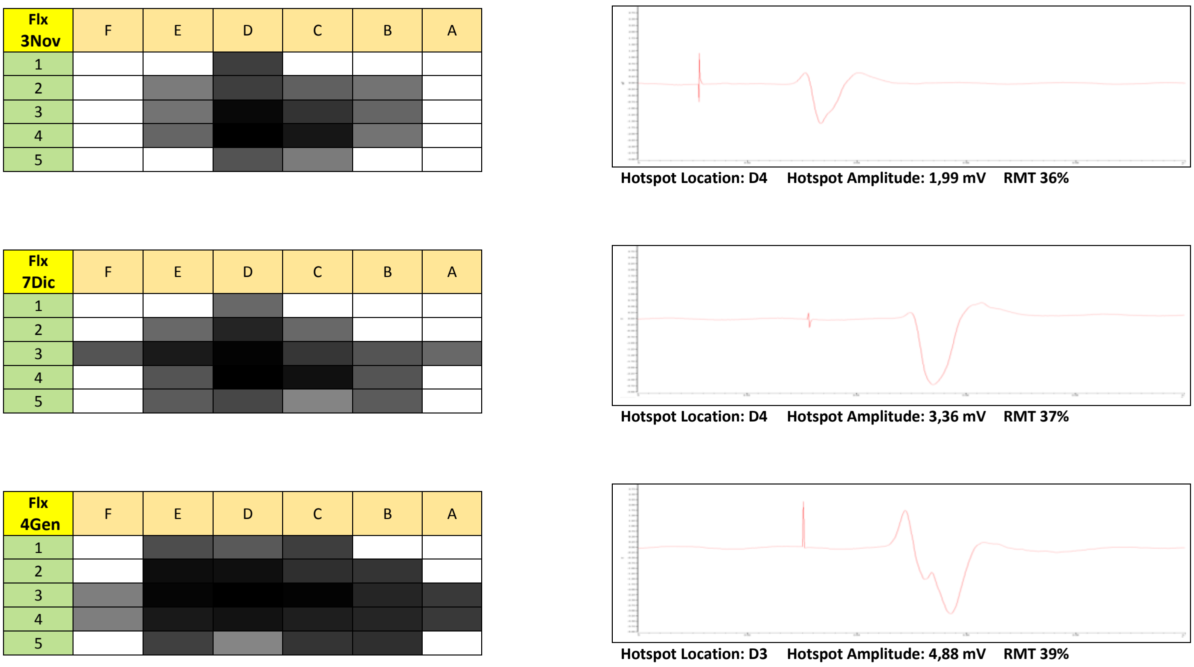


Figure 8. MEP maps. A progressive enlargement of the excitable area of forearm muscles on the hemisphere contralateral to the amputation is evident during the trial.

Brain plasticity

The multimodal analysis for brain plasticity assessment has been completed in the fist patient, and it is being performed in the second patient whose trial is on going (in this case during the first five weeks of treatment it was possible to perform only the baseline evaluation). In this first patient TMS pre-therapy showed a slight abnormal inter-hemispheric asymmetry of motor cortex topography, resulting in a smaller area of representation of muscles governing the amputated limb compared to the area for the intact limb. Following therapy, cortical maps showed a partial reversal of this asymmetry because of an enlargement of the excitable area on the right hemisphere, contralateral to the stump, leading towards a more symmetrical muscle representation in the two hemispheres, as in normal subjects (Figure 8).

EEG analysis showed a progressive increase of alpha 1 power density during the trial, and a consensual decrease of delta band power density, mainly located in the parietal, occipital, temporal and central areas of the brain. The network analysis showed a statistically significant increase of the Path Length index in the sensory-motor network involving both hemispheres with a preferential increase on the right hemisphere (the contralateral to the amputation in this case). Functional MRI results showed a progressive reduction of motor areas needed to perform a task of phantom hand movement during the trial, indicating the presence of a motor learning process involving the amputated arm. On the other side structural MRI was not able to show significant changes of corticospinal tract and thickness of S1-M1 cortex suggesting that in our experiment the brain changes globally observed in our patients were mainly due to functional plastic phenomenon acting at synaptic level.

Lessons learned

The process of ethical and especially legal approval of the invasive part of EPIONE project was complicated. First of all, every European nation has is own legislation, meaning similar but not equal documentation had to be prepared by clinical partner in the project and no recruitment was possible until the study was legally approved some precious time was lost. Moreover it proved more difficult than expected to recruit patients for the invasive clinical trial mainly because of the combination of some issues: 1) Few potential subjects experience strong PLP and the numbers available in the literature may be overestimated; 2) The defined inclusion criteria (e.g. site and level of injury, etc to allow space for the implants), made it difficult to include most of the interested patients, so future studies focused on PLP treatment should include also lower limb amputees; 3) The temporary effect (if any) of the treatment, the hypothetical risk related to the trial (in particular because the system was percutaneous and therefore prone to mechanical damage and infection) and the need to perform two surgical interventions (the first to implant and the second to explant the TIME electrodes); a completely implantable system could have been more acceptable. These experiences will be important to speed up the approval process in eventual future studies.

WP6. Exploitation and dissemination

WP leader: Novosense AB
Partners involved: All partners.

Objectives

The RTD developments within EPIONE was expected to produce several important knowledge and technology-based results. Implementation of active strategies for the exploitation and dissemination of the results is fundamental for bringing the results and developments to the market in the future. The objectives of the exploitation has therefore been to develop a sound set of business models around the EPIONE technologies being developed. The objective of the dissemination is to develop a plan to facilitate the translation of the research results to the general public and other stakeholders.

Overview of main results and finalised tasks

- Dissemination plan for patient recruitment established
- Established dissemination plan for communication with the scientific community and industry
- A market analysis
- A competitor landscape analysis
- A IPR strategy analysis report for project partners
- Developing a concrete business model base on EPIONE results

Details of main results

Dissemination

Plan for pt recruitment

The following channels were identified for communicating to the target group.

- EPIONE website
- Partner local websites
- Press release
- News spots: Television
- News spots: newspapers
- Personal communication
- News spots: Radio
- News spots: magazines
- Conference
- Brochure
- Newsletter
- Social media

- Clinical trials registration

An plan was set up for utilising these channels and the general planning was to;

- Step 1 - Press releases
- Step 2 - Information on clinical trials and opportunities on EPIONE website
    - for volunteers
    - for medical and scientific community
- Step 3 – Partner level dissemination
- Step 4 – Evaluate
- Step 5 – Revise if necessary and iterate step 2 and 5 again.

More details on partners efforts for PT-recruitment has been reported in the earlier period reports.

Dissemination plan

The first version of the EPIONE dissemination plan was reported M14 and it has thereafter periodically been updated. The overall plan is shown in table below.

No.	Title	Description of Activities	Main leader	Date	Place	Audience	Countries addressed
1.	Home page	Raise awareness	AAU	Oct 2013	Internet	www	all
2.	Logo	Raise awareness	AAU	Oct 2013	Internet	www	all
3.	Advertisement for clinical trial	Raise awareness of the trial and potential treatment	Clinical trials team	Pending ethical committee and PO approval	Internet, Print, Mail	Clinicians and prospective subjects	
4.	Press release	Inform the public	UAB	July 2014	Public media (newspaper, radio)	General public	Spain
5.	Meeting presentation	Communication to the FENS meeting	UAB	July 2014	Milano, IT	Neuroscientists	EU
6.	Hospital and University Journals/Newsletters	Raise awareness	CHUV	Jan 2015		Switzerland University and patients	Switzerland
7.	CHUV Intranet/Department website	Raise awareness	CHUV	Jan 2015	Intranet	CHUV employees	Switzerland
8.	EPIONE - workshop at international conference		AAU/entire consortium	year 3 and/or year 4	Do be determined	Scientific community	all

Table 4. Dissemination planning

The last joint dissemination task, “8. EPIONE - Workshop…” was later decided to be to set up a special session at International Conference on NeuroRehabilitation, ICNR2016 and at the RehabWeek in London 2017.

Exploitation

Competitive landscape

The work in regards to mapping the competitive landscape led to the identification of 90 organisations that very diverse in nature, including research companies, larger medical companies and research universities. These were then analysed according to the business model configurations that they apply. For various reasons, including bankruptcy, M&A’s and secrecy, not all of these could be mapped in practice. This left a total sample of 80 companies.

Currently, the competition regarding Non-Invasive Technologies solutions for reducing PLP is relatively limited. Most of the solutions offered today are still at in a research and development phase. But nonetheless, given the positive impact of these technologies in reducing PLP (as indicated by pilot tests conducted), an increasing interest by various research centres to enter into this emerging industry, which, evidently was identified. This indicates a future potential growth in this industry. Because of the early stage of industry, the review does not always provide reliable data on the most probable business models and as such the next phase in this regard will take its outset in the understanding of the medico-tech sector.

Competition within the invasive technology segment varies depending on the market. In the USA, competition is strong, and mainly lead by Medtronic and the major hospitals, who offer various pain treatment options. This is partly because of the liberal healthcare system, which compared to Canada and most of Europe, is

not financed by public funds. The general competition is also very much dependent upon whether or not the clinics offer treatment using their own product developments or health care technologies developed elsewhere. Access to these markets is regulated through national health authorities, who approve/reject use of new health technologies.
Strong competition exists within Orthopaedics Prosthetics, where the two largest companies hold 75% of the total market share. Products in this category have been on the market for several years. With new innovative products, it could be possible to gain market access as there are many companies with similar products today.
Currently all pharmaceutical approaches in the medical segment will be offered as first line of therapy for reducing PLP, and may thus not be considered direct competitors for the EPIONE project technologies. The medication is generally inexpensive compared to the other types of treatment, as they are non-invasive and the prices of these are unlikely to increase in the future. However, it has been difficult to establish any proven substantial clinical effect of these on PLP, and thus EPIONE may be expected to acquire market share from these treatment options.

Identified EPIONE IPRs
The EPIONE exploitables was identified early in the project and an analysis regarding strategy, owner, etc. was delivered at month 16, see Table 10.2. The list of exploitable has been update a few time during the duration of project.

Business models
The work with the EPIONE business models included several subtasks such as identifying exploitable EPIONE outcomes and stake holders, the making of market analysis, investigating competitors, IPR strategies and product cost analysis. All these activities have then lead to the final development of the EPIONE business models. In short the following strategies was suggested.

- *The clinic-based business model:* Here the technologies would be sold directly to PLP patients through direct contact in clinics. This disintermediates the existing structures, where PLP patients mainly are treated through university hospitals. Such clinics take on the business model of being trusted advisors. They can either be core-focused (i.e. only on PLP), or they can have a diversified more full-service orientation towards pain treatment.
- *The prosthetics-based business model:* In essence, this business model differentiates itself from the clinic-based business model by being a product-based, with three possible routes. (1) a long-tail scenario for selling a wider scope of "non-hit" products in low quantity, (2) a cell-phone scenario offering different plans in relation to a product featuring a range of prices depending on varying levels of usage, or (3) reverse bait and hook offering a low-margin product at low or no cost to encourage sales of the initial higher-margin product
- *The data-driven business model:* A third opportunity of a business model configuration was identified as the 'data-driven business model'. Being a data-based model the scalability is much higher than man-hour and product-based business models, making it easier to achieve true scalability. This business model would entail developing the software platform where the EPIONE technologies would provide the basis of a trusted advisor position and a trusted product/service leadership strategy.

1.4 Potential Impact

The potential impact of EPIONE has been analysed in relation to 1) Science and Technology, 2) Economy and Society, 4) The political landscape, 4) Exploitation and IPR and 5) Dissemination

Science and Technology

The originally defined expected impact of the HEALTH 2013.2.2.1-5 topic was: *''(a) Successful projects are expected to deepen our knowledge of how pain is generated, propagated and quenched, (b) work towards the identification of more effective diagnostic and/or treatment approaches and (c) help translate pre-clinical and clinical results into solutions for the patients''*

The EPIONE consortium provided input to the expected impact of the topic through the following.

a) *Clinical trials outcomes.* We investigated if generation of PLP may be explained by changes in the cortical map that follows amputation, and whether PLP may be quenched by restoring the cortical map through sensory feedback therapy. We compared two main routes for providing a more long-term or permanent solution for the amputees, i.e. a non-invasive sensory feedback solution that could be integrated with the operation of a hand prosthesis and an invasive sensory feedback solution that in the future may offer the ultimate, permanent, invisible and cosmetically acceptable interface.

A total of 31 volunteer subjects were enrolled in the studies, 23 subjects started the therapy phase and 20 subjects completed the full study (the remaining withdrew during different phases of the study). Initially our focus was on upper limb amputees only, however, it was difficult to recruit subjects across Europe and the USA. The inclusion criteria were therefore widened to also include and lower limb amputees and subjects with complex regional pain syndrome that experience phantom limb symptoms in the trials where this was possible.

The group analysis from the trial indicated that there was, on average, a significant reduction in the phantom limb pain. It was not possible to do a group analysis on the effect of the therapy on the cortical organization due to the large heterogeneity of the included subjects.

We summarized our clinical experiences in a guideline for delivering sensory feedback.

b) *Technological developments.* Before EPIONE was initiated, the specific technologies were only available as experimental units and have only been tested on very few subjects. Implementation of EPIONE allowed a translation of experimental work and results previously funded by EU (www.project-time.eu) into the clinic for further validation. The validation is an important step to move the technologies into the medical market.
   - In case of the invasive technologies, the research conducted within this project showed that thin-film electrodes embedded in polyimide can be safely and reliably implanted for stimulation purposes in a human peripheral nerve. Intuitive sensory feedback can be restored with this type of intrafascicular neural multichannel electrodes (TIME 4H). The results that we achieved regarding the TIME electrode performance in two human volunteer subjects and use for phantom limb pain treatment are very important for applications of these electrodes in the closely related field of sensorised robotic hand prosthesis in amputees. To transfer into a permanent solution and thereby make the system commercially available will be dependent on finding a solution to connect single TIME 4H electrodes via a detachable plug system to implantable electrical stimulators. Further clinical validation and assessment would be needed for the invasive system, where it showed only possible to recruit 2 of planned 8 participants.
   - In case of the non-invasive sensory feedback we developed novel non-invasive technologies (electrical or mechanical systems with or without hand prosthesis integration) for delivering sensory. A dedicated software platform was developed to implement the clinical protocol and gather the clinical data. In addition dedicated software was developed to extract and analyse the common clinical data. In case of the non-invasive systems, system miniaturisation and human factor engineering are the main requirements to effectively translate the non-invasive technologies developed during the EPIONE project into commercial products. The focus of these efforts would be to transform research prototypes into standalone therapeutic devices, easily useable by the patient or medical personnel. Preliminary steps for the preparation of commercialisation were carried out during this project, which could be leveraged by a party willing to pursue the successive steps.

Economy and society

The originally defined overarching objective of the call was to ''*(a) improve the health of the EU citizens and (b) increase the competitiveness and boosting the innovative capacity of European health-related industries while addressing global health issues''.*

We believe that EPIONE provided direct input to this objective through the following.

a) There are currently more than 1.6 million persons in the US and more than 400.000 persons within Europe that are living with the loss of a limb (2005 numbers) and many of these are living with phantom limb pain. A potential means to treat PLP to those suffering from its effect was demonstrated. For both upper and lower extremity who benefitted from the therapy, the therapy represents a means to reduce the impact of PLP on their lives through the reduction or potentially elimination of the use of drugs prescribed to control pain. In the case of the lower extremity subjects who benefited from the therapy, the therapy represents an opportunity to use their prosthetic legs and regain mobility and freedom that they lost as a result of amputation and PLP. The successful deployment of the therapy could represent an improved quality of life to these subjects, which could result in the decrease of time lost from work due to PLP, time spent in out-patient care to treat pain, and the reduction in the prescription of prescription analgesics which come with the potential side-effect of addiction and substance abuse.

b) In case of the invasive system, the technical system opens new therapy options for subjects with amputation trauma to increase their quality of life in long-term perspectives. Sensory feedback is a first step for better embodiment of prostheses and more frequent use.

c) In case of the non-invasive system**,** the various non-invasive sensory feedback systems developed during the project have great potential for socio-economic impact. Indeed, the developed systems could serve as the basis for commercial devices which may help alleviate phantom limb pain symptoms with minimal invasiveness, limited side effects and relatively low cost. This contrasts with approaches requiring surgical intervention or based on pharmaceutical. Preparatory work for the commercialisation of such devices was carried out during the project, facilitating future impact of these non-invasive technologies.
d) Even though that EPIONE provided a proof of concept, the developed systems are not yet mature enough for immediate commercialization. However, identified short term effects include; 1) Opportunities for younger scientist to learn and network with other European scientist, 2) Established scientific cooperation between several European and one American scientist group. 3) Increased knowledge of scientists regarding medical regulations

The political landscape
Within the political landscape as defined in Horizon 2020 and the Europe 2020 strategy, one of the seven identified flagships is 'The Innovative Union' [weblink 1, weblink 2, weblink 3], where there is a focus on fostering new ideas to tackle societal challenges and ensuring that EU investments can be properly exploited. One of the identified challenges is 'Health – demographic change and well being' [weblink 2]. In particular the Innovative Union should ''respond to the major health-related socio-economic and societal challenges in view of the new orientations given by the EUROPE 2020 strategy''

We believe that EPIONE provided direct input to this objective through the following.

- Science. A better understanding of which factors are affecting the degree of phantom limb pain and pain management
- Science. Which sensory feedback type is efficient in quenching PLP
- Technology. Dedicated technologies to deliver different types of sensory feedback developed, delivered and tested.
- Technology. Preparation of technologies closer to the medical market
- Economy and society. Assist to maintain knowledge and expertise within EU (the brain drain problem)
- Economy and society. Knowledge transfer from academia to industry
- Economy and society. Better positioning of SMEs within the European health-related industry (partners MXM and NS)
- Economy and society. Training of younger researchers
- Economy and society. Opportunity for younger researchers to establish a European/US network

In EPIONE we carried out clinical trials in 4 European Countries (Denmark, Sweden, Switzerland, Italy) and in the US. The realization of the project has shown, that the project duration of four years is a strict timeframe to refine technologies, obtain approval and implement the clinical trials. Since medical device directives have always to be transferred into national law with national legal bodies, it is therefore a highly labour intensive and challenging task to plan clinical trials in several European countries. Even though non-approval studies are now separately addressed in the new European Medical Device Regulation (EC 2017/745) for all European companies, detail specification what has to be done beyond the "essential requirements" has to be delegated to the member states and their specific national laws.

Exploitation and IPR
EPIONE has resulted in two filed patents and two registered software applications. The exploitation framework was analysed during the project and dedicated business models for the EPIONE specific technologies were devised. Although the different non-invasive technologies need final development and validation this is key knowledge in taking the final step to bring the technologies to the medical market. Due to the low number of subjects recruited for the invasive technologies, this system must undergo further clinical validation.

Dissemination
The EPIONE work has resulted in 31 peer reviewed articles/conference proceedings, with a number of pending and planned publications. The consortium has disseminated their work at more than 160 events during the project life-time, including several tv/radio/press coverage for the general public, and two organized special-sessions at international conferences.

1.5. Contact Details and further information

Project Homepage: www.project-epione.eu
Project Logo:

Part. no	Participant organization name	Part. Short name	Country
1	AALBORG UNIVERSITY	AAU	Denmark
2	REGION NORDJYLLAND (NORTH DENMARK REGION)	RN-Aalborg UH	Denmark
3	UNIVERSITA CATTOLICA DEL SACRO CUORE	UCSC	Italy
4	HOSPICES CANTONAUX CHUV	CHUV	Switzerland
5	ALBERT-LUDWIGS-UNIVERSITAET FREIBURG	ALU-FR	Germany
6	UNIVERSITE MONTPELLIER 2 SCIENCES ET TECHNIQUES	UM2	France
7	ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE	EPFL	Switzerland
8	LUNDS UNIVERSITET	LUNDS UNIVERSITET	Sweden
9	THE TRUSTEES OF INDIANA UNIVERSITY	THE TRUSTEES OF INDI	United States
10	UNIVERSITAT AUTONOMA DE BARCELONA	UAB	Spain
11	NOVOSENSE AB	NOVOSENSE AB	Sweden
12	OBELIA SARL	MXM-OBELIA	France

Contact information:

Scientific Project Coordinator:

Prof. Winnie Jensen, wj@hst.aau.dk, Aalborg University, Sensory-Motor Interaction, Dept. Health Science and Technology, Fredrik Bajersvej 7D, 9220 Aalborg, Denmark

Project Manager:

Diana Mardare, dm@adm.aau.dk, The Fundraising and Project Management Office, Aalborg University, Niels Jernes Vej 10, 9220 Aalborg, Denmark

1.6 Bibliography

[weblink 1]: Innovation priorities for Europe:
http://ec.europa.eu/commission_2010-2014/president/news/documents/pdf/innovation_en.pdf

[weblink 2]: State of the innovative union 2011
http://ec.europa.eu/research/innovation-union/pdf/state-of-the-union/2011/state_of_the_innovation_union_2011_brochure_en.pdf#view=fit&pagemode=none

[weblink 3]: Enhancing and focusing EU international cooperation in research and innovation: A strategic approach
https://ec.europa.eu/research/iscp/pdf/policy/com_2012_497_communication_from_commission_to_inst_en.pdf

2. Use and dissemination of foreground

Section A (public)

A1 Peer Reviewed materiel

Table A1 below includes a list of peer-reviewd material. The list is ranked according to impact factor, with the highest impact factor listed first.

D.	Main partner	Title	Main Author	Title of periodical or series	Number, date or frequency	Publisher	Place of publication	Year	Pages	Permanent Identifier	Open Acces	Impact factor
1	EPFL	A somatotopic bidirectional hand prosthesis with transcutaneous electrical nerve stimulation based sensory feedback	D'Anna E, Petrini FM, Artoni F, Popovic I, Simanić I,Raspopovic S, Micera S	Scientific Reports	7:10930	Springer Nature	International	2017	1-15	10.1038/s41598-017-11306-w	yes	40,137
2	UAB	NKCC1 activation is required for myelinated sensory neurons regeneration through JNK-dependent pathway	Mòdol L, Santos D, Cobianchi S, González-Pérez F, López-Alvarez V, Navarro X	The Journal of Neuroscience	35(19)	Society for Neuroscience	USA	2015	7414-7427	10.1523/JNEUROSCI.4079-14.2015	no	5,988
3	UAB	Endogenous modulation of TrkB signaling by treadmill exercise after peripheral nerve injury	Arbat-Plana A, Cobianchi S, Herrando-Grabulosa M, Navarro X, Udina E	Neuroscience	340	International Brain Research Organization; Elsevier	International	2017	188-200	10.1016/j.neuroscience.2016.10.057	no	5,988
4	UAB	Botulinum neurotoxin A promotes functional recovery after peripheral nerve injury by increasing regeneration of myelinated fibers	Cobianchi S, Jaramillo J, Luvisetto S, Pavone F, Navarro X	Neuroscience	359	International Brain Research Organization; Elsevier	International	2017	82-91	10.1016/j.neuroscience.2017.07.011	no	5,988
5	UAB	Prevention of NKCC1 phosphorylation avoids downregulation of KCC2 in central sensory pathways and reduces neuropathic pain after peripheral nerve injury	Mòdol L, Cobianchi S, Navarro X	Pain	155(8)	International Association for the Study of Pain; Elsevier	International	2014	1577-1590	10.1016/j.pain.2014.05.004	no	5,445
6	UAB	Early increasing-intensity treadmill exercise reduces neuropathic pain by preventing nociceptor collateral sprouting and disruption of chloride cotransporters homeostasis after peripheral nerve injury	López-Álvarez VM, Modol L, Navarro X, Cobianchi S	Pain	156(9)	International Association for the Study of Pain; Elsevier	International	2015	1812-1825	10.1097/j.pain.0000000000000268	no	4,519

o.	Main partner	Title	Main Author	Title of periodical or series	Number, date or frequency	Publisher	Place of publication	Year	Pages	Permanent Identifier	Open Acces	Impact factor
7	**UAB**	Fascicular topography of the human median nerve for neuroprosthetic surgery	Delgado-Martinez I, Badia J, Pascual-Font A, Rodríguez-Baeza A, Navarro X	Frontiers in Neuroscience	10:286	Frontiers	International	2016	1-13	10.3389/fnins.2016.00286	yes	3,566
8	**UAB**	Sensory symptom profiles of patients with neuropathic pain after spinal cord injury	Soler MD, Moriña D, Rodríguez N, Saurí J, Vidal J, Navarro A, Navarro X.	The Clinical Journal of Pain	33(9)	Wolters Kluwer Health	International	2017	827-834	10.1097/AJP.0000000000000467	no	3,492
9	**UAB**	Spatial and functional selectivity of peripheral nerve signal recording with the transversal intrafascicular multichannel electrode (TIME)	Badia J, Raspopovic S, Carpaneto, J, Micera S, Navarro X	IEEE Transactions on Neural Systems and Rehabilitation Engineering	24 (1)	IEEE	International	2016	20-27	10.1109/TNSRE.2015.2440768	no	3,41
10	**UAB**	Functional evaluation of peripheral nerve regeneration and target reinnervation in animal models : a critical overview	Navarro X	European Journal of Neuroscience	43(3)	Federation of European Neuroscience Societies, FENS; Wiley-Blackwell	International	2016	271-286	10.1111/ejn.13033	no	2,941
11	**UAB**	Changes of voltage-gated sodium channels in sensory nerve regeneration and neuropathic pain models	Casals-Díaz L, Casas C, Navarro X	Restorative Neurology and Neuroscience	33(3)	IOS Press	International	2015	321-334	10.3233/RNN-140444	no	2,526
12	**MXM-OBELIA**	Delaying discharge after the stimulus significantly decreases muscle activation thresholds with small impact on the selectivity : an in vivo study using TIME	Maciejasz P, Badia J, Boretius T, Andreu D, Stieglitz T, Jensen W, Navarro X, Guiraud D	Medical and Biological Enginering and Computing	53(4)	International Federation for Medical and Biological Engineering; Springer Nature	International	2015	371-379	10.1007/s11517-015-1244-4	no	1,916
13	**CHUV**	Return of the cadaver: Key role of anatomic dissection for plastic surgery resident training	Krähenbühl SM, Čvančara P, Stieglitz T, Bonvin R, Michetti M, Flahaut M, Durand S, Deghayli L, Applegate LA, Raffoul W	Medicine	96(29):e7528	Wolters Kluwer Health	International	2017	1-7	10.1097/MD.0000000000007528	yes	1,803

No.	Main partner	Title	Main Author	Title of periodical or series	Number, date or frequency	Publisher	Place of publication	Year	Pages	Permanent Identifier	Open Acces	Impact factor
14	**UAB**	Neuroprotective effects of exercise treatments after injury : the dual role of neurotrophic factors	Cobianchi S, Arbat-Plana A, López-Álvarez VM, Navarro X	Current Neuropharmacology	15(4)	Bentham Science	International	2017	495-518	10.2174/1570159X14666160330105132	Will be available in PMC on November 1, 2017	1,68
15	**ALU-FR**	On the stability of implanted thin-film stimulation electrodes	Čvančara P, Boretius T, Stieglitz T, Maciejasz P, Guiraud D	Biomedical Engineering / Biomedizinische Technik	59(S1)	Walter de Gruyter	International	2014	S1089	10.1515/bmt-2014-5014	no	1,263
16	**ALU-FR**	In-vivo investigation on the improvement of thin-film metallization adhesion in neural electrodes	Čvančara P, Stieglitz T, López V, Navarro X	Biomedical Engineering / Biomedizinische Technik	60 (S1)	Walter de Gruyter	International	2015	S396	10.1515/bmt-2015-5016	no	1,263
17	**ALU-FR**	Investigations on stability of implanted nervous thin-film electrodes	Cvancara P, Boretius T, Stieglitz T	2014 IEEE 19th International Functional Electrical Stimulation Society Annual Conference (IFESS)	ISBN 978-1-4799-6483-3	IEEE	International	2014	1-4	10.1109/IFESS.2014.7036747	no	
18	**EPFL**	Controlling prostheses using PNS invasive interfaces for amputees	Carpaneto J, Citi L, Raspopovic S, Rigosa J, Micera S	Introduction to Neural Engineering for Motor Rehabilitation	ISBN 9780470916735 / 9781118628522 Chapter 16	IEEE; Wiley	International	2013	311-326	10.1002/9781118628522.ch16	no	
19	**UM2**	Automatic handling of conflicts in synchronous Interpreted Time Petri nets implementation	Leroux H, Godary-Dejean K, Coppey G, Andreu D	Proceedings, 2014 IEEE Computer Society Annual Symposium on VLSI		IEEE	International	2014	100-105	10.1109/ISVLSI.2014.44	no	
20	**EPFL**	Recording properties of an electrode implanted in the peripheral nervous system : a human computational model	Jehenne B, Raspopovic S, Capogrosso M, Arleo A, Micera S	7th International IEEE/EMBS Conference on Neural Engineering, NER		IEEE	International	2015	482-485	10.1109/NER.2015.7146664	no	
21	**UAB**	Decreasing stimulation charge by delaying the discharge phase : comparison of efficacy for various stimulation waveforms	Maciejasz P, Badia J, Souquet G, Čvančara P, Picq C, Stieglitz T, Navarro X, Guiraud D	7th International IEEE/EMBS Conference on Neural Engineering, NER		IEEE	International	2015	402-405	10.1109/NER.2015.7146644	no	

D.	Main partner	Title	Main Author	Title of periodical or series	Number, date or frequency	Publisher	Place of publication	Year	Pages	Permanent Identifier	Open Acces	Impact factor
22	ALU-FR	Neuroprothetik heute und morgen	Stieglitz T, Schüttler M, Plachta D	Orthopädie Technik - ISSN 0340-5591	66(6)	Verlag Orthopädie-Technik	Dortmund	2015	32-37	Not available. See https://www.confairmed.de/verlag-ot/content/fachzeitschrift/fachartikel_suche/index_ger.html?aid=295	no	
23	ALU-FR	Investigations on different epoxies for electrical insulation of microflex structures	Cvancara P, Lauser S, Rudmann L, Stieglitz T	38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society		IEEE	International	2016	1963-1966	10.1109/EMBC.2016.7591108	no	
24	LUNDS UNIVERSITET	Superior tactile discrimination in the phantom hand map in forearm amputee	Wijk U, Björkman A, Antfolk C, Björkman-Burtscher, Rosen B	Hand	11(1)Supplement	Sage	International	2016	131S	10.1177/1558944716660555ja	no	
25	UM2	Advanced 56 channels stimulation system to drive intrafascicular electrodes	Guiho T, Andreu D, López-Alvarez VM, Cvancara P, Hiairrassary A, Granata G, Wouters L, Jensen W, Divoux JL, Micera S, Stieglitz T, Navarro X, Guiraud D	Converging Clinical and Engineering Research on Neurorehabilitation II : Proceedings of the 3rd International Conference on NeuroRehabilitation, ICNR 2016	Biosystems and Biorobotics; 15	Springer	International	2017	743-747	10.1007/978-3-319-46669-9_122	no	
26	AAU	Natural sensory feedback for phantom limb pain modulation and therapy	Jensen W	Converging Clinical and Engineering Research on Neurorehabilitation II : Proceedings of the 3rd International Conference on NeuroRehabilitation, ICNR 2016	Biosystems and Biorobotics; 15	Springer	International	2017	719-723	10.1007/978-3-319-46669-9_118	no	
27	ALU-FR	On biocompatibility and stability of transversal intrafascicular multichannel electrodes—TIME	Stieglitz T, Boretius T, Cvancara P, Guiraud D, Guiho T, Lopez-Alvarez VM, Navarro X	Converging Clinical and Engineering Research on Neurorehabilitation II : Proceedings of the 3rd International Conference on NeuroRehabilitation, ICNR 2016	Biosystems and Biorobotics; 15	Springer	International	2017	731-735	10.1007/978-3-319-46669-9_120	no	

D.	Main partner	Title	Main Author	Title of periodical or series	Number, date or frequency	Publisher	Place of publication	Year	Pages	Permanent Identifier	Open Acces	Impact factor
28	**THE TRUSTEES OF INDI**	Evaluation of the effect of sensory feedback on phantom limb pain in multi-center clinical trials	Yoshida K, Malec J, Comoglio C, Mosier K, Lontis R, Larsen K, Navarro X, Jensen W	Converging Clinical and Engineering Research on Neurorehabilitation II : Proceedings of the 3rd International Conference on NeuroRehabilitation, ICNR 2016	Biosystems and Biorobotics; 15	Springer	International	2017	725-730	10.1007/978-3-319-46669-9_119	no	
29	**UM2**	Complex digital system design : A methodology and its application to medical implants.	Leroux H, Godary-Dejean K, Andreu D	Proceedings, 18th International Workshop on Formal Methods for Industrial Critical Systems, FMICS 2013	Lecture Notes in Computer Science; 8187	Springer	International	2013	94-107	10.1007/978-3-642-41010-9_7	no	
30	**EPFL**	Efferent microneurography recordings : a tool for motor control study and hand-prosthesis decoding	Petrini FM, Raspopovic S, Bonizzato M, Giambattistelli F, Zollo L, Guglielmelli E, Micera, S	6th International IEEE/EMBS Conference on Neural Engineering, NER	ISBN 978-1-4673-1969-0	IEEE	International	2013	383-386	10.1109/NER.2013.6695952	yes	
31	**UM2**	Integrating implementation properties in analysis of Petri nets handling exceptions	Leroux H, Godary-Dejean K, Andreu D	12th IFAC/IEEE International Workshop on Discrete Event Systems (WODES'14)		IFAC, Elsevier	International	2014	406-411	10.3182/20140514-3-FR-4046.00032	yes	

A2 Dissemination

No.	Acitivty type	Main lead	Title	Date	Place	Audience	Audience size	Countries addressed
1	Internal university presentation	CHUV	Project description and organization for invasive sensory biofeedback for phantom limb pain	09.03.2014	Department role and collaboration (CHUV)	presentation to determine department interaction with the Direction	20	Switzerland
2	MS Thesis	THE TRUSTEES OF INDIANA UNIVERSITY	Comoglio, C.C., "A system for studying the effectiveness of treatment for phantom limb pain in amputees", Masters Thesis, Purdue University, Indianapolis, Indiana, 16 Mar 2017 (2017)	16.03.2017	IUPUI	Faculty, Scientific Community	10	US
3	Popular press	AAU	Hjerne-Madsen underholder fuld AAU-sal	2014	University Homepage: http://mo.infomedia.dk/ShowArticle.aspx?Duid=e4a7dc2a&UrlID=6b1166c7-0e52-4fb3-bb32-3c88e33110fe&Link=	General public	Unknown	Denmark
4	Popular press	AAU	Danske forsøgspersoner skal have elektroder opereret ind i nerverne	2014	Magazine_ http://www.infomedia.dk/mo/ShowArticle.aspx?Duid=e4534db9&UrlID=6b1166c7-0e52-4fb3-bb32-3c88e33110fe&Link=	General public	Unknown	Denmark
5	Popular press	AAU	En robotarm og to bioniske øjne, tak!	2015	Newspaper_ http://mo.infomedia.dk/ShowArticle.aspx?Duid=e544bafd&UrlID=6b1166c7-0e52-4fb3-bb32-3c88e33110fe&Link=	General public	Unknown	Denmark
6	Popular press	AAU	Medicinske muligheder	2015	Newspaper_ http://mo.infomedia.dk/ShowArticle.aspx?Duid=e52dd50f&UrlID=6b1166c7-0e52-4fb3-bb32-3c88e33110fe&Link=	General public	Unknown	Denmark
7	Popular press	AAU	Fremtidens menneske kan trække på to typer reservedele	2015	Magazine_http://mo.infomedia.dk/ShowArticle.aspx?Duid=e4f319d9&UrlID=6b1166c7-0e52-4fb3-bb32-3c88e33110fe&Link=	General public	Unknown	Denmark
8	Popular press	AAU	Jagten på supermennesket	2015	Newspaper_ Jyllands-Posten	General public	Unknown	Denmark
9	Popular press	AAU	EU funds 6 million Euro for new tech solutions to combat phantom limb pain	01.12.2013	Aalborg University homepage	General public	Unknown	Denmark
10	Popular press	AAU	10 teknologiske tendenser, du bør kende: #4. Trådløse signaler mellem hjerne og muskel erstatter ødelagt rygmarv	03.05.2017	ing.dk Magazine for engineers	Scientific Community, Research	Unknown	Denmark
11	Popular press	AAU	Spørg Scientariet: Hvor meget elektricitet kan menneskekroppen holde til?	06.05.2017	ing.dk Magazine for engineers	Scientific Community, Research	Unknown	Denmark

No.	Acitivty type	Main lead	Title	Date	Place	Audience	Audience size	Countries addressed
12	Popular press	AAU, RN-Aalborg UH	Banebrydende metode kan hjælpe amputerede	2016	Videnskab.dk_ http://mo.infomedia.dk/ShowArticle.aspx?Duid=e594c27e&UrlID=6b1166c7-0e52-4fb3-bb32-3c88e33110fe&Link=	General public	Unknown	Denmark
13	Popular press	ALU-FR	„Neuroimplantate". Spektrum der Wissenschaft?Spezial, Physik?Mathematik?	2015	Mansch Maschine Visionen?Wenn Biologie und Technik verschmelzen	General public	Unknown	Germany
14	Popular press	CHUV	Thérapies: Les cellules font des miracles pour réparer les corps abîmés	2016	popular journal ("Le Matin Dimanche")	General public	Unknown	Switzerland
15	Popular press	LUNDS UNIVERSITET	Fantomsmärtan försvinner med ny känslig handprotes	2016	dagens medicin nr 4/16 onsdag 27 januari 2016	Scientific Community, Research	Unknown	International
16	Popular press	LUNDS UNIVERSITET	Phantom pain disappears with new sensitive hand prosthesis	27.01.2016	"Dagens medicin" nr4/16. Swedish newspaper targeting medical employees	General public	Unknown	Sweden
17	Presentation	AAU	Implanterbare teknologier til at interface det perifere eller central nervesystemet'	2013	Communication to seminar at Aalborg University Hospital, DK	Scientific Community, Research	40	Denmark
18	Presentation	AAU	Invasiv og ikke-invasiv sensorisk feedback til lindring af fantomsmerter	2014	Pain symposium at Health and Rehab Scandinavia conference, Sept. 11, 2014, Copenhagen	Scientific Community, Research	300	Denmark
19	Presentation	AAU	Sensory modulation of cortical neuroplasticity in phantom limb pain	2015	Pain symposium/Ph.D course at Aalborg University, Denmark, May 22, 2016	Scientific Community, Research	30	Denmark
20	Presentation	AAU	DEN 'FØLENDE' HÅNDPROTESE. Er implanterbare nerveelektroder det næste skridt for fremtidens rehabiliteringsteknologier?	2015	Dansk Almen Medicinsk Forskningsdag, Århus Universitet, Denmark	Scientific Community, Research	100	Denmark
21	Presentation	AAU	Natural Sensory Feedback for Phantom Limb Pain Modulation and Therapy	2016	International conference on neurorehabilitation (ICNR2016) Segovia, Spain	Scientific Community, Research	500	International
22	Presentation	AAU	Sensory modulation of cortical neuroplasticity in phantom limb pain	2016	Rehabilitation Institute of Chicago, Chicago, USA,	Scientific Community, Research	30	International
23	Presentation	AAU	Sensory modulation of cortical neuroplasticity in phantom limb pain	2016	Indiana University – Purdue University Indianapolis, USA	Scientific Community, Research	50	International
24	Presentation	AAU	Surface electrical stimulation in modulation of phantom limb pain	2016	The International conference on neurorehabilitation (ICNR2016), Segovia, Spain	Scientific Community, Research	500	International
25	Presentation	AAU	Invasiv og ikke-invasiv sensorisk feedback til lindring af fantomsmerter	11.09.2014	Communication to International Workshop	Scientific Community, Research	Unknown	Denmark

No.	Acitivty type	Main lead	Title	Date	Place	Audience	Audience size	Countries addressed
26	Presentation	ALU-FR	Miniaturized neural interfaces and implants	2013	DEMOVE Symposium, Translational Engineering in Neurorehabilitation 2013, October 22-23, 2013, Goettingen (2013).	Scientific Community, Research	75	International
27	Presentation	ALU-FR	Flexible neural probes in fundamental and translational research	2013	International Conference on Biomedical Technology, November 20-22, 2013, Hannover (2013)	Scientific Community, Research	30	Germany
28	Presentation	ALU-FR	Miniaturized neural interfaces and implants DEMOVE Symposium	2013	Translational Engineering in Neurorehabilitation 2013, October 22-23, 2013, Goettingen	Scientific Community, Research	75	International
29	Presentation	ALU-FR	Flexible neural probes in fundamental and translational research	2013	International Conference on Biomedical Technology, November 20-22, 2013, Hannover	Scientific Community, Research	50	Germany, Austria,Switzerl and
30	Presentation	ALU-FR	On the stability of implanted thin-film stimulation electrodes	2014	Proceedings of the annual conference DGBMT, Hannover, Germany	Scientific Community, Research	50	Germany
31	Presentation	ALU-FR	Investigations on stability of implanted nervous thin-film electrodes	2014	Proceeding of the annual conference IFESS, Kuala Lumpur, Malaysia,	Scientific Community, Research	25	International
32	Presentation	ALU-FR	On the stability of implanted thin-film stimulation electrodes	2014	Proceedings of the annual conference DGBMT, Hannover, Germany	Scientific Community, Research	50	Germany
33	Presentation	ALU-FR	Investigations on stability of implanted nervous thin-film electrodes	2014	Proceeding of the annual conference IFESS, Kuala Lumpur, Malaysia	Scientific Community, Research	30	International
34	Presentation	ALU-FR	Miniaturized Neural Interfaces and Implants in Neurological Rehabilitation	2014	Biosystems &Biorobotics	Scientific Community, Research	50	International
35	Presentation	ALU-FR	In-vivo investigation on the improvement of thin-film metallization adhesion in neural electrodes	2015	Proceedings of the annual conference DGMBT, Luebeck, Germany	Scientific Community, Research	50	Germany
36	Presentation	ALU-FR	Neural Interfaces – From Basic Research to Clinical Applications	2015	The US-Turkey Advanced Study Institute on Global Healthcare Challenges, 22.-25.06.2015, Izmir, Turkei (2015)	Scientific Community, Research	30	Turkey, USA
37	Presentation	ALU-FR	Darf Technik den Nerv treffen ? –Ein Streitgespräch" moderiert von Tom Hegemann. BMBF-Zukunftskongress Demografie?	2015	Technik zum Menschen bringen, 29.-30.06.2015, Berlin (2015).	Scientific Community, Research	250	Germany
38	Presentation	ALU-FR	Strom hilft heilen – Neurotechnik in Therapie und Rehabilitation	2015	Lange Nacht der Wissenschaft, 24. Juli 2015, Technische Fakultät der Albert-Ludwigs-Universität Freiburg, (2015)	Scientific Community, Research	100	Germany
39	Presentation	ALU-FR	Neural implants in basic and translational research	2015	Microalliance Meeting- Kyoto-Michigan-Freiburg, 24.-25.09.2015, Freiburg (2015)	Scientific Community, Research	40	USA, Japan, Germany

No.	Acitivty type	Main lead	Title	Date	Place	Audience	Audience size	Countries addressed
40	Presentation	ALU-FR	Miniaturisierte Implantate zwischen Grundlagen und klinischer Anwendung	2015	Workshop für Unternehmer: Medizintechnik der Zukunft. Neue Technologien und Werkstoffe, Spitzmüller AG, 01.10.2015, Gengenbach (2015).	Scientific Community, Research	100	Germany
41	Presentation	ALU-FR	Neurotechnik – trifft den Nerv und geht unter die Haut	2015	VDE Fachtagung mit Ausstellun "Albert-Keil-Kontaktseminar", 08.10.2015, KIT, Karlsruhe (2015)	Scientific Community, Research	150	Germany
42	Presentation	ALU-FR	FES:Stretching the boundaries	2015	FES: The interdisciplinary Dialogue, IFESS, 15.-16.10.2015, IIT, Chicago, USA (2015)	Scientific Community, Research	30	international
43	Presentation	ALU-FR	Wenn Technik den Nerv trifft – Neurotechnik in Therapie und Rehabilitation	2015	Lecture,Festvortrag an der Univeristät des Saarlandes, 22.10., Saarbrücken (2015).	Scientific Community, Research	100	Germany
44	Presentation	ALU-FR	Neural Implants in Translational Research and Clinical Applications	2015	Annual Liability Regimes Conference. The Geneva Association. 04.-05.11.2015, Rüschlikon, Schweiz	Scientific Community, Research	50	Germany, CH, Austria
45	Presentation	ALU-FR	Technik hilft Heilen-Vom Hörimplantat zum Hirnschrittmacher. Tagung Alter(n) und Gesellschaft	2015	Bürgerhaus Zähringen, Freiburg	General public	50	Germany
46	Presentation	ALU-FR	Cyborgs und Maschinen-Menschen zwischen Therapie und Utopie	2015	Jubiläum 25 Jahre wissenschaftliche Politikberatung Technikfolgen-abschätzung beim Deutschen Bundestag, 02.12.2015, Paul-Löbe-Haus, Berlin (2015)	General public	150	Germany
47	Presentation	ALU-FR	Technik unter der Haut-Elektronische Pillen oder Ersatzteile für Maschinenmenschen ?	2015	Dialog im Museum, Daimler und Benz Stitung, Mecedes Benz Museum, 08.12.2015, Stuttgart	Industry	150	Germany
48	Presentation	ALU-FR	On Biocompatibility and Stability of Transversal Intrafascicular Multichannel Electrodes—TIME. In Converging Clinical and Engineering Research on Neurorehabilitation II	2015	International Conference on Neurorehabilitation	Scientific Community, Research	30	International
49	Presentation	ALU-FR	On Biocompatibility and Stability of Transversal Intrafascicular Multichannel Electrodes—TIME. In Converging Clinical and Engineering Research on Neurorehabilitation II	2015	International Conference on Neurorehabilitation	Scientific community	300	International
50	Presentation	ALU-FR	Investigations on Different Epoxies for Electrical Insulation of Microflex Structures	2016	2016 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)	Scientific Community, Research	50	International

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51	Presentation	ALU-FR	Neurotechnische Schnittstellen und Implantate	27/02/14	Neurotechnische Schnittstellen und Implantate. Aesculap, Tuttlingen	Industry	10	Germany
52	Presentation	ALU-FR	Miniaturized Neural Implants. Meet & Match Workshop „Neurological Implants	04.04.2014	Biovalley Trinational and NEUREX	Scientific Community, Research	30	Germany, France
53	Presentation	ALU-FR	Neuroimplantate – Technische Systeme an der Material Gewebe Schnittstelle	04.06.2014	Kolloquium der Daimler und Benz Stiftung mit dem Thema „Mensch-Maschine Visionen; Technik,die unter die Haut geht	Scientific Community, Research	200	Germany
54	Presentation	ALU-FR	Investigations on the integrity of epoxy - silicone rubber interfaces	04.10.2016 - 06.10.2016	"Dreiländertagung" Swiss, Austrian and German Societies for Biomedical Engineering	Scientific community - Research	200	Germany, Switzerland, Austria
55	Presentation	ALU-FR	Proof of concepts study of non-destructive component validation in neural implant manufacturing	04.10.2016 - 06.10.2016	"Dreiländertagung" Swiss, Austrian and German Societies for Biomedical Engineering	Scientific community - Research	200	Germany, Switzerland, Austria
56	Presentation	ALU-FR	Technik, die unter die Haut geht – Neurotechnische Implantate im peripheren und zentralen Nervensystem" Reihe „Hirnforschung was kannst Du ? –Potentiale und Grenzen	05.06.2014	Frankfurt	Scientific Community, Research	300	Germany
57	Presentation	ALU-FR	Flexible Neural Interfaces in Fundamental and Translational Research	05.12.2016	University of Florida	Scientific community - Research	30	USA
58	Presentation	ALU-FR	Polymer-basierte Schnittstellen zum Nervensystem	06.07.2017	Hector Fellow Symposium "Medizin 4.0 - Organische Elektronik in der modernen Medizin"	Scientific community - Research and general pubilc	230	Germany
59	Presentation	ALU-FR	Neuronale Steuerung von Handprothesen	08.05.2014	Freiburg Akademie; Germany	General public	75	Germany
60	Presentation	ALU-FR	Is this me ? Interfaces with the nervous system control prostheses and treat diseases and disorders	10.02.2017	" Séminaire «Corps et prothèses : vécus, usages, contextes», Séance 1: «Vulnérabilité et capabilité»	Scientific community - Research	30	France
61	Presentation	ALU-FR	Technik unter der Haut : Elektronische Pillen und Ersatzteile für Maschinenmenschen	12.10.2016	Erlebnispark Fördertechnik	General public	25	Germany
62	Presentation	ALU-FR	Prothesen: von der Vision zur Wirklichkeit	13.03.2014	Café Scientifique, Bernstein Center Freiburg	General public	50	Germany
63	Presentation	ALU-FR	Neurotechnik", Technologien im sozialen Kontext	13.12.2016	Kontroversen und Konvergenzen: Wissenschaften an ihren Schnittstellen	Scientific community - Research	75	Germany
64	Presentation	ALU-FR	Neural Implants. Medical Cyber Physical Systems Workshop 2014 - Medical Device Interoperability, Safety, and Security Assurance	14.04.2014	Medical Cyber Physical Systems Workshop	Scientific Community, Research	50	International

No.	Acitivty type	Main lead	Title	Date	Place	Audience	Audience size	Countries addressed
65	Presentation	ALU-FR	On Biocompatibility and stability of transversal intrafascicularmultichannel electrodes— TIME	18.-21.10.2016	the 3rd International Conference on NeuroRehabilitation	Scientific community - Research	20	International
66	Presentation	ALU-FR	Influence of Different Plasma Activation Treatments on Polyimide Thin-Film Electrodes	18.07.2017 - 20.07.2017	International Functional Electrical Stimulation Society 21st Annual Conference	Scientific community - Research and Industry	300	Europe
67	Presentation	ALU-FR	Development, prototyping, fabrication and testing individualized long-term safe electrode arrays	18.10.2016 - 21.10.2016	3rd International Conference on NeuroRehabilitation (ICNR2016)	Scientific community - Research	25	International
8	Presentation	ALU-FR	Miniaturisierte Systeme für die Neurotechnologie	20.02.2014	Materials Valley Workshop	Scientific Community, Research	50	Germany
69	Presentation	ALU-FR	Neuroprothetik	20.09.2016 -21.09.2016	Herbsttagung der Sektion "Electronics, Micro and Nano Technologies"	Scientific community - Research	50	Germany
70	Presentation	ALU-FR	Why Neurotechnologies? About the Purposes for Developing Clinical Applications of Neurotechnologies	20/01/2017 - 21/01/2017	Freiburg Institute of Advanced Studies	Scientific community - Research	100	Germany
71	Presentation	ALU-FR	Neural Arrays – between Fundamental Research and Clinical Applications	21-23.07.2014	CSNE & BrainLinks-BrainTools, Joint Roundtable Workshop: "Clinical Applicability of BMIs"Freiburg, Germany	Scientific Community, Research	50	USA, Germany
72	Presentation	ALU-FR	Miniaturized neural interfaces and implants DEMOVE Symposium	22-23.10.2013	Translational Engineering in Neurorehabilitation	Scientific Community, Research	70	International
73	Presentation	ALU-FR	Flexible neural probes in fundamental and translational research	22-23.11.2013	International Conference on Biomedical Technology	Scientific Community, Research	50	International
74	Presentation	ALU-FR	Miniaturized Neural Interfaces and Implants in Neurological Rehabilitation	24-26.06.2014	2nd International Conference on Neural Rehabilitation (ICNR), Plenary talk, Aalborg	Scientific Community, Research	50	International
75	Presentation	ALU-FR	Miniaturized Neural Interfaces and Implants in Neurological Rehabilitation	24.06.2014	ICNR, Aalborg	Scientific Community, Research	250	International
76	Presentation	ALU-FR	Miniaturized Neural Interfaces and Implants in Fundamental and Translational Research	25.04.2014	Massachussetts Institute of Technology (MIT)	Scientific Community, Research	50	USA
7	Presentation	ALU-FR	Stability and functionality of flexible electrode arrays in chronic applications	25.05.2017	IEEE Brain Initiative Workshop on Advanced NeuroTechnologies for BRAIN Initiatives (ANTBI): Challenges and Opportunities	Scientific community - Research	50	International
78	Presentation	ALU-FR	Laser-Structured Small Ceramic Plates for Reliable Assembly of Commercial Connectors with Customized Cables	25.05.2017 - 28.05.2017	8th International IEEE EMBS Conference on Neural Engineering	Scientific community - Research	150	International

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79	Presentation	ALU-FR	Invasive Mensch-Maschine-Schnittstellen	26.-27.06.2017	3. Zukunftskongress zur Mensch-Technik Interaktion "Technik zum Menschen bringen" des BMBF	Scientific community - Research	50	Germany
80	Presentation	ALU-FR	Wenn Technik den Nerv trifft...	26.09.2016	Lehrerfortbildung "Neurotechnik-An der Schnittstelle zwischen Mensch und Technik"	General public	30	Germany
81	Presentation	ALU-FR	Prüfverfahren für hermetische und nicht-hermetische Implantat-Komponenten	27.01.2017	Fachgruppe Intelligente Implantate, MicroTEC Südwest	Scientific community - Research and Industry	40	Germany
82	Presentation	ALU-FR	The Influence of Temperature on Hydrated Sputtered Iridium Oxide Films	27.11.2016 - 02.12.2016	2016 MRS Fall Meeting & Exhibit	Scientific community - Research and Industry	500	International
83	Presentation	ALU-FR	Long-Term Performance of Flexible Thin-Film Electrode Arrays in Neural Implants	28.06.2016 - 30.06.2016	International Conference BrainLinks-BrainTools	Scientific community - Research	200	International
84	Presentation	ALU-FR	Aktive Neuroimplantate	29.03.2017	Gesundheitskongress 2017, Hochschule Furtwangen	Scientific community - Research	50	Germany
85	Presentation	ALU-FR	Thin-film electrodes to interface with the nervous system	29.10.2016	The Össur and OttobockTreaty on Neural Controlled Man-Machine Interface	Industry	60	Selected countries
86	Presentation	ALU-FR	Stability and Selectivity of PNS interfaces	4-5.12.2013	Symposium on Grand Challenges on Neurotechnology (SGCNT)	Scientific Community, Research	50	international
87	Presentation	ALU-FR	From Prototypes to approved devices: challenges to setup a production	4-5.12.2013	Symposium on Grand Challenges on Neurotechnology (SGCNT)	Scientific Community, Research	50	International
88	Presentation	CHUV	EPIONE: a solution to combat phantom limb pain	2016	A poster describing the EPIONE study has been presented during a "Swiss Clinical Trial Organisation Symposium" at the CHUV on 2016/06/16.	Scientific Community, Research	100	Switzerland
89	Presentation	CHUV	Hand rehabilitation: from amputation to the central lesion. Can we dream of new technological solutions?	2017	Symposium organised by "Le Centre de la Main", CHUV, Switzerland	Scientific Community, Research	100	EU
90	Presentation	CHUV	Workshop, Phantom pain in amputees: from theory to practice	2017	Pain Forum	Scientific Community, Research	15	Switzerland

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91	Presentation	CHUV	Invasive and Non-invasive sensory feedback for Phantom Limb Pain- solutions for our amputees?	19.09.2015	CHUV	presentation to Department and public- Department of Musculoskeletal Medicine Seminar Series	70	Switzerland
92	Presentation	EPFL	Neuroprosthetics for sensory-motor function restoration	01.10.2015	BrainDisC PhD Conference – Freiburg	Scientific Community, Research	30	Germany
93	Presentation	EPFL	Neuroprosthetics for sensory-motor function restoration	06.04.2016	Summer school on Neuroscience and Neural Repair – Cambridge	Scientific Community, Research	100	England
94	Presentation	EPFL	Intraneural interfaces restore sensory feedback in hand prostheses	06.05.2014	European Commission (Future and Emerging Technology area)	Policy makers	100	Europe
95	Presentation	EPFL	The quest for a bionic limb	07.11.2016	Neurotechnix International Conference – Porto	Scientific Community, Research	30	Portugal
96	Presentation	EPFL	Neuroprosthetics for sensory-motor function restoration	08.07.2016	Summer school of the Scuola Normale Superiore - San Miniato	Scientific Community, Research	50	Italy
97	Presentation	EPFL	Closing the loop in neuroprosthetics	09.09.2014	Glaxo-SmithKline workshop on "Closing the loop in neuroprosthetics" - London (UK)	Scientific Community, Research	50	England
98	Presentation	EPFL	Intraneural interfaces restore sensory feedback in hand prostheses	09.09.2016	IBSA Workshop on "New technologies to treat neurodisorders" – Geneva	Scientific Community, Research	200	Switzerland
99	Presentation	EPFL	Closing the loop in neuroprosthetics	09.11.2015	Max Planck Institute for Biological Cybernetics – Tuebingen	Scientific Community, Research	50	Germany
100	Presentation	EPFL	The quest for a bionic limb	1-4.7.2014	MEA Meeting 2014 9th International Meeting on Substrate-Integrated Microelectrode Arrays, Mainz	Scientific Community, Research	300	Germany
101	Presentation	EPFL	The quest for a bionic limb	11.10.2015	Bergamo Science Festival – Bergamo	Scientific Community, Research and General Public	200	Italy
102	Presentation	EPFL	The quest for a bionic limb	12.10.2014	Annual meeting of the Italian Society of Neurology - Cagliari	Scientific Community, Research	200	Italy
103	Presentation	EPFL	Neuroprosthetics for sensory-motor function restoration	13.03.2014	Workshop on Neurorehabilitation organized by the Geneva University Hospital- Geneva (CH)	Scientific Community, Research	100	Switzerland

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104	Presentation	EPFL	Intraneural interfaces restore sensory feedback in hand prostheses	14.02.2014	DARPA workshop on Neuroprosthetics - Scottsdale (AZ, US)	Policy makers	100	USA
105	Presentation	EPFL	Neuroprosthetics for sensory-motor function restoration	14.05.2015	Annual symposium of the Institute of Neuroscience of CNR – Pisa	Scientific Community, Research	40	Italy
106	Presentation	EPFL	Neuroprosthetics for sensory-motor function restoration	16.06.2014	5th US-Turkey Advanced Study Institute on Global Healthcare - Antalya	Scientific community, Reserach and Policy makers	50	Turkey
107	Presentation	EPFL	Intraneural interfaces restore sensory feedback in hand prostheses	16.10.2014	"BrainFET workshop" organised by the FET area of EU Commission - Genoa	Policy makers	200	Italy
108	Presentation	EPFL	The quest for a bionic limb	17.09.2015	Summer school on Neurorehabilitation – Valencia	Scientific Community, Research	50	Spain
109	Presentation	EPFL	The quest for a bionic limb	17.10.2015	Bertarelli Symposium on Translational Neuroengineering and Neuroscience – Geneva	Scientific Community, Research	300	Switzerland
110	Presentation	EPFL	Neuroprosthetics for sensory-motor function restoration	18.10.2016	Workshop on The IEEE Brain Initiative Workshop on Advanced NeuroTechnologies for NeuroRehabilitation- Segovia	Scientific Community, Research	100	Spain
111	Presentation	EPFL	The quest for a bionic limb	21.04.2015	Workshop on Advanced NeuroTechnologies for NeuroRehabilitation - Milan	Scientific Community, Research	40	Italy
112	Presentation	EPFL	Neuroprosthetics for sensory-motor function restoration	21.06.2016	Summer school of the Scuola Normale Superiore - San Miniato	Scientific Community, Research	50	Italy
113	Presentation	EPFL	Neuroprosthetics for sensory-motor function restoration	22.09.2014	Annual School of the Italian Group of Bioengineering - Bressanone	Scientific Community, Research	400	Italy
114	Presentation	EPFL	Closing the loop in neuroprosthetics	23.03.2015	Summer School on Neural Engineering (University of Padoa) – Padoa	Scientific Community, Research	50	Italy
115	Presentation	EPFL	Neuroprosthetics for sensory-motor function restoration	23.11.2016	Joint Symposium on Stroke Plasticity – Geneva	Scientific Community, Research	150	Switzerland
116	Presentation	EPFL	Neuroprosthetics for sensory-motor function restoration	24.04.2014	University of Twente	Scientific Community, Research	50	Holland
117	Presentation	EPFL	Closing the loop in neuroprosthetics	24.04.2016	Max Planck Institute workshop on Biological Information Processing – Tuebingen	Scientific Community, Research	50	Germany

No.	Acitivty type	Main lead	Title	Date	Place	Audience	Audience size	Countries addressed
118	Presentation	EPFL	Intraneural interfaces restore sensory feedback in hand prostheses	26.08.2014	Life Science EPFL workshop on Translational Medicine - Lausanne	Scientific Community, Research	300	Switzerland
119	Presentation	EPFL	Neuroprosthetics for sensory-motor function restoration	30.05.2016	Summer School Advanced Innovation Methods– Vinci	Scientific Community, Research	40	Italy
120	Presentation	IUPUI	Yoshida, K., Malec, J., Comoglio, C., Mosier, M., Lontis, R., Larsen, K., Navarro, X, Jensen, W., "Evaluation of the effect of sensory feedback on phantom limb pain in multicenter clinical trials", RehabWeek 2017 pre conference Workshop "Novel technologies & natural sensory feedback for phantom limb pain modulation and therapy", 17 July 2017, London, UK (2017)	17.07.2017	QE2 Centre, London	Scientific community - Research and Industry	25	International
121	Presentation	LUNDS UNIVERSITET	Superior tactile discrimination in the phantom hand map in forearm amputee	2016	IFSHT, Buenos Aires	Scientific Community, Research	50	International
122	Presentation	LUNDS UNIVERSITET	Superior tactile discrimination in the phantom hand map in forearm amputee	26.09.2016	IFSHT, Buenos Aires	Scientific Community (higher education, Research), Industry, and Media	700	International
123	Presentation	LUNDS UNIVERSITET	The phantom hand map - a possible target for non-invasive sensory feedback in hand prostheses	8-11.05.2017	ISPO 16TH WORLD CONGRESS, Cape Town	Scientific Community (higher education, Research), Industry, and Media	>4000	International
124	Presentation	MXM-OBELIA	Quels défis pour notre communauté?	2015	Congrès Club Electronique, Electrotechnique, Automatique	Scientific Community, Research	150	France
125	Presentation	MXM-OBELIA	Decreasing Stimulation Charge by Delaying the Discharge Phase - Comparison of efficacy for various Stimulation Waveforms	2015	Proc. 7th International IEEE EMBS Conference on Neural Engineering. Montpellier	Scientific Community, Research	100	International
126	Presentation	MXM-OBELIA	Decreasing Stimulation Charge by Delaying the Discharge Phase - Comparison of efficacy for various Stimulation Waveforms	01.04.2015	Proc. 7th International IEEE EMBS Conference on Neural Engineering. Montpellier	Communication to International Workshop	100	International
127	Presentation	RN-Aalborg UH	Invasiv og ikke-invasiv sensorisk feedback til lindring af fantomsmerter' – Presentation at 'Forskningens Døgn'	23/04/15	Communication to general public at Aalborg University Hospital, DK	Scientific Community	<50	Denmark

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128	Presentation	THE TRUSTEES OF INDIANA UNIVERSITY	Evaluation of the effect of sensory feedback on phantom limb pain in multi-center clinical trials	2016	International Conference on Neurorehabilitation (ICNR2016), Segovia, Spain	Scientific Community, Research	500	International
129	Presentation	THE TRUSTEES OF INDIANA UNIVERSITY	Yoshida, K., Malec, J., Comoglio, C., Mosier, M., Lontis, R., Larsen, K., Navarro, X, Jensen, W., "Evaluation of the effect of sensory feedback on phantom limb pain in multicenter clinical trials", RehabWeek 2017 pre conference Workshop "Novel technologies & natural sensory feedback for phantom limb pain modulation and therapy", 17 July 2017, London, UK (2017)	17.07.2017	QE2 Centre, London	Scientific, Corporate	25	International
130	Presentation	UAB	Early intense exercise activity reduces neuropathic pain by preventing nociceptor collateral sprouting and spinal KCC2 down-regulation after peripheral nerve injury	2014	9th FENS Forum of Neuroscience, Milan, It	Scientific community - Research	6000	Europe
131	Presentation	UAB	Frequency-dependent acute electrical stimulation as a modulator of hyperexcitability and pain in the spared nerve injury model	2015	5th International Congress on Neuropathic Pain (NeuPSIG 2015)	Scientific community - Research	50	International
132	Presentation	UAB	Role of TrkB and noradrenergic descendent projections in the modulatory effects induced by treadmill exercise on the spinal changes that motoneurons suffer after peripheral nerve injury in rats	2015	3rd International Symposium on Peripheral Nerve Regeneration, Hanover,	Scientific community - Research	50	International
133	Presentation	UAB	Early increasing-intensity treadmill exercise reduces neuropathic pain by preventing nociceptor collateral sprouting and disruption of chloride cotransporters homeostasis after peripheral nerve injury	2015	3rd International Symposium on Peripheral Nerve Regeneration, Hanover,	Scientific community - Research	50	International
134	Presentation	UAB	Role of TrkB and noradrenergic descendent projections in the modulatory effects induced by treadmill exercise on the spinal changes that motoneurons suffer after peripheral nerve injury in rats	2015	Society for Neuroscience Meeting 2015, Chicago,	Scientific community - Research	50	International
135	Presentation	UAB	Early increasing-intensity treadmill exercise reduces neuropathic pain by preventing nociceptor collateral sprouting and disruption of chloride cotransporters homeostasis after peripheral nerve injury	2015	3rd International Symposium on Peripheral Nerve Regeneration, Hanover, 24-25 September 2015.	Scientific community - Research	50	International
136	Presentation	UAB	Neural interfaces for the control of neuroprosthetic device	2015	IV DEMOVE Symposium TEN2015, Göttingen, 11-12 June 2015.	Scientific community - Research	100	International
137	Presentation	UAB	Functional and electrophysiological evaluation of peripheral nerve regeneration and target reinnervation	2015	3rd International Symposium on Peripheral Nerve Regeneration, Hanover, September 2015.	Scientific community - Research	50	International

lo.	Acitivty type	Main lead	Title	Date	Place	Audience	Audience size	Countries addressed
138	Presentation	UAB	Decreasing stimulation charge by delaying the discharge phase - Comparison of efficacy for various stimulation waveforms	2015	7th Annual International IEEE EMBS Conference on Neural Engineering, Montpellier, France, 22-24 April, 2015.	Scientific community - Research	50	International
139	Presentation	UAB	Noradrenergic modulation of neuropathic pain induced by increasing-intensity treadmill exercise after peripheral nerve injury	2016	10th FENS Forum of Neuroscience, Copenhagen, DK, July 2016	Scientific community - Research	50	International
140	Presentation	UAB	Noradrenergic and serotonergic modulation of neuropathic pain induced by increasing-intensity treadmill exercise after peripheral nerve injuries	15-18.06.2017	6th International Congress on Neuropathic Pain (NeuPSIG), Gothenburg, Sweden.	Scientific community - Research	1000	International
141	Presentation	UAB	Navarro X. Interfases neurales para el control de prótesis biónicas. Papel de la neurofisiología.	15.05.2017	Barcelona, Spain	Scientific community - Research	250	Spain
142	Presentation	UAB	Neuropathic pain. A maladaptive reaction of the nervous system	16.10.2014	XXVI Technical Meeting of the Institute Guttmann on "Therapeutic innovations in neuropathic pain". Barcelona	Scientific community - Research	50	International
143	Presentation	UAB	Navarro X. Regenerative nerve electrodes. Meeting electronics and neurobiology.	18–21.10.2016	Segovia, Spain	Scientific community - Research	1000	International
144	Presentation	UAB	Puigdomenech M, Lopez-Alvarez VM, Navarro X, Cobianchi S. Central modulation of neuropathic pain after peripheral nerve injury induced by treadmill exercise	6-8.07.2017	Barcelona, Spain	Scientific community - Research	120	International
145	Presentation	UCSC	Robotic hand prosthesis and phantom limb pain	30.08.2017-02.09.2017	ECCN 2017, Budapest	Scientific Community, Research	100	International
146	Presentation	UM2	Complex digital system design: A methodology and its application to medical implants.	2013	International Workshop on Formal Methods for Industrial Critical Systems (FMICS'13), Spain	Scientific Community, Research	< 200	International
147	Presentation	UM2	Automatic handling of conflicts in synchronous Interpreted Time Petri nets implementation.	2014	12th IFAC - IEEE International Workshop on Discrete Event Systems (WODES'14), France	Scientific Community, Research	< 500	International
148	Presentation	UM2	Integrating implementation properties in analysis of Petri nets handling exceptions.	2014	IEEE Computer Society Annual Symposium on VLSI (ISVLSI'14, USA	Scientific Community, Research	< 500	International
149	Presentation	UM2	4 invited talks (C. Azevedo, D. Guiraud, W. Raffoul, Lee Ann) about Epione	03.03.2017	Lausanne, CHUV	Medical Community	200	Switzerland
150	Presentation	UM2	Presentation of EPIONE stimulation device	17-21.7.2017	Rehabweek 2017. London, UK	Scientific Community, Research	50	International

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151	Presentation	UM2	Advanced 56 channels stimulation system to drive intrafascicular electrodes	18-21.10.2016	International Conference on Neurorehabilitation. Segovia, Spain	Scientific Community, Research	300	International
152	Presentation	UM2	Selective stimulation could help to get bidirectional control of movement of the upper limb	28-29.04.2017	IFRH, 2017, Nagoya, Japan	Medical community	<1000	International
153	Press release	UAB	La UAB participa en un projecte europeu per mitigar el dolor que apareix després d'una amputació	04.07.2014	UAB homepage	Scientific community - Research	Unknown	Spain
154	Radio	AAU	Nyt forskningsprojekt skal komme fantomsmerter til livs	2014	Radio: http://www.infomedia.dk/mo/ShowArticle.aspx?Duid=e453adc3&UrlID=6b1166c7-0e52-4fb3-bb32-3c88e33110fe&Link=	General public	Unknown	Denmark
155	Radio	CHUV	Radio spot on National radio ("Radio Suisse Romande, RSR")	2016	National Radio	Civil Society	Unknown	Germany
156	Radio	LUNDS UNIVERSITET	New hand prosthesis simulates sensation	24.12.2016	P1, Swedish national radio	General public	Unknown	Sweden
157	Science Brochure	ALU-FR	Intelligent Implants in Neural Engineering: from tool in neuroscience to new treatment options in an ageing society	2016	Microsystems Technology in Germany 2016	Industry	2000	Germany
158	Science Fair	ALU-FR	Strom hilft heilen – Neurotechnik in Therapie und Rehabilitation	14.07.2017 - 15.07.2017	Science market	General public	500	Germany
159	Science Fair	ALU-FR	Wenn Technik den Nerv trifft	27.09.2016 - 01.10.2016	Highlights der Physik	General public	500	Germany
160	Social media	AAU	Projekt EPIONE	2016	Facebook	General public	Unknown	Denmark
161	Social media	THE TRUSTEES OF INDIANA UNIVERSITY	EPIONE-Indiana Facebook page: http://www.facebook.com/epioneindiana	2013-2016	Facebook	General public	Unknown	International
162	TV	AAU	Bionisk protese	2015	TV_ http://mo.infomedia.dk/ShowArticle.aspx?Duid=e4e0b1de&UrlID=6b1166c7-0e52-4fb3-bb32-3c88e33110fe&Link=	General public	Unknown	Denmark
163	TV	AAU	Aalborg Universitet vil behandle fantomsmerter	2016	TV_ http://mo.infomedia.dk/ShowArticle.aspx?Duid=e5890c90&UrlID=6b1166c7-0e52-4fb3-bb32-3c88e33110fe&Link=	General public	Unknown	Denmark
164	TV	AAU	Aalborg-forskere fjerner fantomsmerter med strøm	14.11.2016	tv2nord.dk Local newa	General public	Unknown	Denmark
165	TV	RN-AalborgUH	Grise hjælper forskere med at bekæmpe fantomsmerter	2016	Tv_ http://mo.infomedia.dk/ShowArticle.aspx?Duid=e59e9b47&UrlID=6b1166c7-0e52-4fb3-bb32-3c88e33110fe&Link=	General public	Unknown	Denmark

No.	Acitivty type	Main lead	Title	Date	Place	Audience	Audence size	Countries addressed
166	TV	AAU	Moderne mirakler	27.03.2017	Dr.dk National televison	General public	Unknown	Denmark
16	Video	UCSC	Video Tape of experiments for the two recruited patients	2015-2017	Rome, UCSC	Media	Unknown	International

Section B
Part B1 (PUBLIC

B1: LIST OF APPLICATIONS FOR PATENTS, TRADEMARKS, REGISTERED DESIGNS, ETC.

No.	Type of IP Rights	Confidential	Embargo date	Application reference(s)	Title	Applicant (s)	Partner
1	Patent	no	NA	US 20160331561 A1	Bidirectional Limb Neuro-Prosthesis	Stanisa RASPOPOVIC, Francesco Maria PETRINI, Marco CAPOGROSSO, Marco Bonizzato, Silvestro Micera	EPFL
2	Patent	yes	When approved	6.1346.1-US — US Provisional Patent Application n° US 62/403,727	Intrafascicular Electrode Implant	ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE (EPFL)	EPFL
3	Registered software	no	NA	IDDN.FR.001.380008.001.S.P.2011.000.31235 - 11/06/2016	HILECOP (HIgh LEvel hardware COmponent Programming), Software tool to formally develop complex digital architectures, with model based checking	UM/INRIA	UM2
4	Registered software	no	NA	IDDN.FR.001.060026.000.S.P.2016.000.31230 - 03/02/2016	SYNERGY NEUROMODULATION SOFTWARE, Software tool to remotely configure and control a set of four 24 poles neural stimulator device	UM / INRIA	UM2
5	Technical documentation	yes	no	NA	STIMEP tehnical documents (Software Life Cycle Processes (IEC 62304))	Université de Montpellier (UM)	UM2

Part B2 (CONFIDENTIAL)

No.	Type of Exploitable Foreground (**1)	Description of exploitable foreground	Confidential	Foreseen embargo date	Exploitable product(s) or measure(s)	Sector of application (**2)	Timetable, commercial or other use	Patents or other IPR exploitation (licences)	Owner & Other beneficiary(s) involved
1	Mechanical sensory feedback system	System for hand prosthesis	yes	2019	Part of Hand prosthesis	C32.5.0 - Manufacture of medical and dental instruments and	Planned	Patent if possible	LUNDS UNIVERSITET and NOVOSENSE
2	Sensor technology for hand prosthesis	Tactile sensor	yes	2019	Part of Hand prosthesis	C32.5.0 - Manufacture of medical and dental instruments and supplies	Planned	Patent if possible	LUNDS UNIVERSITET and NOVOSENSE
3	Therapy of phantom limb pain with surface electrical stimulation	Software	yes	2025	Part of medical device	C32.5.0 - Manufacture of medical and dental instruments and supplies	Planned	Patent if efficacy shown and if possible	AAU and IUPUI
4	Computer-based assessment and evaluation of sensation and pain related to amputation	Software	yes	2025	Part of medical device	C32.5.0 - Manufacture of medical and dental instruments and supplies	Planned	Patent if efficacy shown and if possible	AAU and IUPUI
5	Neural stimulation system (external)	External Stimulator	yes	2018	Medical device for thearapy	C32.5.0 - Manufacture of medical and dental instruments and supplies	Planned	Patent if possible	AAU
6	Neural stimulation system (implantable)	Implantable stimulator	yes	2021	Medical device for thearapy	C32.5.0 - Manufacture of medical and dental instruments and supplies	Planned	Patent if possible	MXM-OBELIA and UM2
7	Guidelines for the use of EPIONE invasive system for treating Phantom Limb Pain	Service	yes	2017	Service	C32.5.0 - Manufacture of medical and dental instruments and supplies	Planned	Patent if possible	MXM-OBELIA and UM2
9	Bidirectional prosthesis that restores sensory feedback by means of transcutaneous nerve stimulation	Microcontroller handling the closed loop control of the bidirectional prosthesis	yes	2019	Part of Hand prosthesis	C32.5.0 - Manufacture of medical and dental instruments and supplies	Planned	Patent pending (related to background activities)	EPFL

No.	Type of Exploitable Foreground (**1)	Description of exploitable foreground	Confidential	Foreseen embargo date	Exploitable product(s) or measure(s)	Sector of application (**2)	Timetable, commercial or other use	Patents or other IPR exploitation (licences)	Owner & Other beneficiary(s) involved
10	Therapy of phantom limb pain with direct, intraneural stimulation	System including electrodes, stimulator, platform and therapy guidelines	yes	2020	Medical device for thearapy	C32.5.0 - Manufacture of medical and dental instruments and supplies	Planned	Patent if possible	CHUV
12	Commercial exploitation of R&D results	NEURINNOV startup	no	NA	Implantable Active Medical Device	C26.6 - Manufacture of irradiation, electromedical and electrotherapeutic equipment	2018	Software deposit (HILECOP)	UM2

3. Report on societal implications

A. General Information *(completed automatically when **Grant Agreement number** is entered.*	
Grant Agreement Number:	**FP7-HEALTH-2013-INNOVATION 602547**
Title of Project:	**EPIONE Natural sensory feedback for phantom limb pain**
Name and Title of Coordinator:	Professor Winnie Jensen

B Ethics	
1. Did your project undergo an Ethics Review (and/or Screening)? • If Yes: have you described the progress of compliance with the relevant Ethics Review/Screening Requirements in the frame of the periodic/final project reports? Special Reminder: the progress of compliance with the Ethics Review/Screening Requirements should be described in the Period/Final Project Reports under the Section 3.2.2 *'Work Progress and Achievements'*	***NO***
2. Please indicate whether your project involved any of the following issues (tick box) :	***YES***
RESEARCH ON HUMANS	
• Did the project involve children?	***NO***
• Did the project involve patients?	***YES***
• Did the project involve persons not able to give consent?	***NO***
• Did the project involve adult healthy volunteers?	***NO***
• Did the project involve Human genetic material?	***NO***
• Did the project involve Human biological samples?	***NO***
• Did the project involve Human data collection?	***NO***
RESEARCH ON HUMAN EMBRYO/FOETUS	
• Did the project involve Human Embryos?	***NO***
• Did the project involve Human Foetal Tissue / Cells?	***NO***
• Did the project involve Human Embryonic Stem Cells (hESCs)?	***NO***
• Did the project on human Embryonic Stem Cells involve cells in culture?	***NO***
• Did the project on human Embryonic Stem Cells involve the derivation of cells from Embryos?	***NO***
PRIVACY	
• Did the project involve processing of genetic information or personal data (eg. health, sexual lifestyle, ethnicity, political opinion, religious or philosophical conviction)?	***YES***
• Did the project involve tracking the location or observation of people?	***NO***
RESEARCH ON ANIMALS	
• Did the project involve research on animals?	***YES***
• Were those animals transgenic small laboratory animals?	***NO***
• Were those animals transgenic farm animals?	***NO***
• Were those animals cloned farm animals?	***NO***
• Were those animals non-human primates?	***NO***
RESEARCH INVOLVING DEVELOPING COUNTRIES	
• Did the project involve the use of local resources (genetic, animal, plant etc)?	***NO***
• Was the project of benefit to local community (capacity building, access to healthcare, education etc)?	***NO***
DUAL USE	
• Research having direct military use	***NO***
• Research having the potential for terrorist abuse	***NO***

C	Workforce Statistics	
3. Workforce statistics for the project: Please indicate in the table below the number of people who worked on the project (on a headcount basis).		
Type of Position	**Number of Women**	**Number of Men**
Scientific Coordinator	1	0
Work package leaders	1	6
Experienced researchers (i.e. PhD holders)	11	19
PhD Students	4	8
Other	15	17

4. How many additional researchers (in companies and universities) were recruited specifically for this project?	**11**
Of which, indicate the number of men:	7

D Gender Aspects		
5. Did you carry out specific Gender Equality Actions under the project?	 X	Yes No

6. Which of the following actions did you carry out and how effective were they?

	Not at all effective				Very effective
❑ Design and implement an equal opportunity policy	○	○	○	○	○
❑ Set targets to achieve a gender balance in the workforce	○	○	○	○	○
❑ Organise conferences and workshops on gender	○	○	○	○	○
❑ Actions to improve work-life balance	○	○	○	○	○

X Other: No specific gender equality actions were carried out under the project

7. Was there a gender dimension associated with the research content – i.e. wherever people were the focus of the research as, for example, consumers, users, patients or in trials, was the issue of gender considered and addressed?

Yes- please specify

X No

E Synergies with Science Education

8. Did your project involve working with students and/or school pupils (e.g. open days, participation in science festivals and events, prizes/competitions or joint projects)?

Yes- please specify

X No

9. Did the project generate any science education material (e.g. kits, websites, explanatory booklets, DVDs)?

Yes- please specify

X No

F Interdisciplinarity

10. Which disciplines (see list below) are involved in your project?

Main discipline[1]: 2.3

Associated discipline[1]: 2.2 | Associated discipline[1]: 3.2

G Engaging with Civil society and policy makers

11a Did your project engage with societal actors beyond the research community? *(if 'No', go to Question 14)*	X	Yes No

11b If yes, did you engage with citizens (citizens' panels / juries) or organised civil society (NGOs, patients' groups etc.)?

No

Yes- in determining what research should be performed

X Yes - in implementing the research

Yes, in communicating /disseminating / using the results of the project

11c In doing so, did your project involve actors whose role is mainly to organise the dialogue with citizens and organised civil society (e.g. professional mediator; communication company, science museums)?	X	Yes No

12. Did you engage with government / public bodies or policy makers (including international organisations)

X No

[1] Insert number from list below (Frascati Manual).

	Yes- in framing the research agenda
	Yes - in implementing the research agenda
	Yes, in communicating /disseminating / using the results of the project

13a Will the project generate outputs (expertise or scientific advice) which could be used by policy makers?

	Yes – as a **primary** objective (please indicate areas below- multiple answers possible)
	Yes – as a **secondary** objective (please indicate areas below - multiple answer possible)
X	No

13b If Yes, in which fields?

Agriculture Audiovisual and Media Budget Competition Consumers Culture Customs Development Economic and Monetary Affairs Education, Training, Youth Employment and Social Affairs		Energy Enlargement Enterprise Environment External Relations External Trade Fisheries and Maritime Affairs Food Safety Foreign and Security Policy Fraud Humanitarian aid		Human rights Information Society Institutional affairs Internal Market Justice, freedom and security Public Health Regional Policy Research and Innovation Space Taxation Transport	

13c If Yes, at which level?

Local / regional levels
National level
European level
International level

H Use and dissemination	
14. How many Articles were published/accepted for publication in peer-reviewed journals?	**31**
To how many of these is open access[2] provided?	**6**
How many of these are published in open access journals?	**6**
How many of these are published in open repositories?	**0**
To how many of these is open access not provided?	**0**
Please check all applicable reasons for not providing open access:	
❑ publisher's licensing agreement would not permit publishing in a repository ❑ no suitable repository available ❑ no suitable open access journal available ❑ no funds available to publish in an open access journal ❑ lack of time and resources ❑ lack of information on open access ❑ other[3]: ……………	
15. How many new patent applications ('priority filings') have been made? *("Technologically unique": multiple applications for the same invention in different jurisdictions should be counted as just one application of grant).*	**5**

16. Indicate how many of the following Intellectual Property Rights were applied for (give number in each box).	Trademark	
	Registered design	**2**
	Other	**1**

17. How many spin-off companies were created / are planned as a direct result of the project?	**0**
Indicate the approximate number of additional jobs in these companies:	

18. Please indicate whether your project has a potential impact on employment, in comparison with the situation before your project:

❑	Increase in employment, or	❑	In small & medium-sized enterprises
❑	Safeguard employment, or	❑	In large companies
❑	Decrease in employment,	❑	None of the above / not relevant to the project
x	Difficult to estimate / not possible to quantify		

19. For your project partnership please estimate the employment effect resulting directly from your participation in Full Time Equivalent (*FTE = one person working fulltime for a year*) jobs: x Difficult to estimate / not possible to quantify	*Indicate figure:*

[2] Open Access is defined as free of charge access for anyone via Internet.
[3] For instance: classification for security project.

I	Media and Communication to the general public		
20.	**As part of the project, were any of the beneficiaries professionals in communication or media relations?**		
	X Yes		No
21.	**As part of the project, have any beneficiaries received professional media / communication training / advice to improve communication with the general public?**		
	Yes	X	No
22	**Which of the following have been used to communicate information about your project to the general public, or have resulted from your project?**		
X	Press Release	X	Coverage in specialist press
❑	Media briefing	X	Coverage in general (non-specialist) press
X	TV coverage / report	X	Coverage in national press
X	Radio coverage / report	X	Coverage in international press
X	Brochures /posters / flyers	X	Website for the general public / internet
X	DVD /Film /Multimedia	X	Event targeting general public (festival, conference, exhibition, science café)
23	**In which languages are the information products for the general public produced?**		
X	Language of the coordinator	X	English
X	Other language(s)		