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**Direct Nerve Stimulation for  
Induction of Sensation and  
Treatment of Phantom Limb Pain**

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# **Direct Nerve Stimulation for Induction of Sensation and Treatment of Phantom Limb Pain**

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**Editor**

**Winnie Jensen**

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## Preface

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Phantom limb pain (PLP) is a frequent consequence of amputation, and it is notoriously difficult to treat. Despite isolated reports of success, no medical/non-medical treatments have been beneficial on more than a temporary basis. While the majority of the treatments currently offered seek to actively suppress the pain, we embarked on a journey back in 2008 to challenge the status-quo of PLP treatment by instead supplying meaningful sensations that will restore the neuroplastic changes in the cortex and thereby control and alleviate pain. We designed, implemented and tested a novel ‘human-machine interface’ that included a ‘first-in-human’ clinical trial of the system. In this book we report on the first steps and results from this journey to demonstrate and provide a proof of concept of our ideas.



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June 2019, Winnie Jensen





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## List of Abbreviations

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AG	assembly groups
AP	action potential
API	application programming interface
AS	active sites
ASICS	acid sensing channels
ASIP	application-specific instruction-set processor
BOLD	Blood oxygen level dependent
BPA	brachial plexus avulsion
BPI	brief pain inventory
BPI-IS	Brief Pain Inventory – Interference Scale
BPI-SF	brief pain inventory – short form
CES-D	Center for Epidemiological Studies – depression questionnaire
CGRP	calcitonin gene-related peptide
CMAP	compound muscle action potentials
CNAP	compound nerve action potentials
CNS	Central nervous system
CPG	chronic pain grade
CRPS	complex regional pain syndrome
cVLM	caudal ventrolateral medulla
cw	constant weighing
d	device
DACC	digital to analog current converter
DBS	deep brain stimulation
Deg/ENaC	degenerin family
DN4	the neuropathic pain four questions
DNIC	diffuse noxious inhibitory control
DRt	dorsal reticular nucleus
EDM	electrical discharge machining
EEG	electroencephalogram
EES	epidural electrical stimulation
EIS	electrochemical impedance spectroscopy

EMG	electromyogram
ES	electrical stimulation
FBR	foreign body response
FEM	finite element method
FEP	flourinated ethylene propylene
FES	functional electrical stimulation
FFC	flexible flat cable
FIR	finite impulse response
fMRI	functional magnetic resonance imaging
FPGA	programmable electronic device
FRAP	non-peptidergic ones possess fluoride-resistant acid phosphatase
FTIR	fourier transform infrared spectroscopy
GALS	Globally Asynchronous Locally Synchronous
GDNF	glial cell line-derived neurotrophic factor
GM	gastrocnemius medialis
GMI	Graded motor imagery
GND	ground
GQPAA	Groningen questionnaire problems after arm amputation
GUI	graphical user interface
H&E	Hematoxylin and Eosin
HCNS	heterotopic noxious conditioning stimulation
HCP	health care provider
HMI	Human machine interface
HRF	hemodynamic response function
IASP	International Association for the Study of Pain
ICA	independent component analysis
IMMPACT	the initiative on methods, measurement and pain assessment in clinical trails
IPA	isopropyl alcohol
ISI	interactive subject interface
LANSS	Leeds assessment of neuropathic symptoms and signs
LEF	laboratory for electrode manufacturing
LEP	laser evoked potential
LIFE	Longitudinal Intrafascicular electrode
LTD	long-term depression
LTP	long-term potentiation
M1	primary motor cortex
MAC	medium access control

MAV	mean absolute value
MFI	microflex interconnector
MP	micro program
MPI	West Haven-Yale multidimensional pain inventory
MPQ	McGill pain question
NGF	nerve growth factor
NMDA	N-methyl D-aspartate
NOS	NO synthase
NP	neuropathic pain
NPC	nano plastic circular
NPQ	neuropathic pain questionnaire
NPS	Neuropathic pain scale
NPSI	neuropathic pain symptom inventory
NRS	numeric rating scale
PAG	periaqueductal gray matter
PAP	Post amputation pain
PBS	phosphate buffered saline
PECVD	plasma enhanced chemical vapour deposition
PEI	polyesterimide
PEQ	prosthesis evaluation questionnaire
PKC $\gamma$	protein kinase Cgamma
PL	plantar interosseus
PLP	Phantom limb pain
PLS	Phantom limb sensation
PN	petri nets
PNS	peripheral nervous system
POMS-SF	profile of mood states – short form
PPI	present pain intensity
Pt	platinum
PVCN	posteroventral cochlear nucleus
QMS	quality management system
RCT	randomized controlled trials
RIE	reactive ion etching
RL	recruitment level
RLP	Residual limb pain
RMN	raphe magnocellular nucleus
RMS	root mean square
ROI	region of interest
RS	referred sensation

S1	Primary somatosensory cortex
S2	Secondary somatosensory cortex
SEC	stimulator and experiment control
SEP	somatosensory evoked potential
SEP	somatosensory evoked potential
sfMcGill	McGill pain questionnaire
SF-MPQ	short-form McGill pain questionnaire
Sias	best active site in each electrode
Sid	Selectivity index – device
SIDNE	stimulation-induced depression of neuronal excitability
SiN <sub>x</sub>	silicon nitride
SIROF	sputtered iridium oxide films
Sias	selectivity index
sLORETA	standardized Low Resolution Electromagnetic Tomography Algorithm
SMA	shape memory alloys
SNR	signal-to-noise ratio
SOM	somatostatin
SP	substance P
SVM	support vector machine
TA	tibialis anterior
TENS	transcutaneous electrical nerve stimulation
TEP	tactile evoked potential
tf-LIFE	thin-polymer-based electrodes longitudinally in the nerve
tf-LIFE	Thin-film Intrafascicular Multichannel electrode
TIME	Thin-film Intrafascicular Multichannel electrode
TIME	Transversal intrafascicular multichannel electrodes
TIME-3H	Transversal intrafascicular multichannel electrodes – human
TMR	targeted muscle reinnervation
TNF- $\alpha$	tumor-necrosis factor- $\alpha$
tr	training set
TRP	transient receptor potential
TRPV1	vanilloid receptor
USEA	Utah slanted electrode array
VAS	visual analog scale
VE	multi site stimulation
VPL	ventral posterior lateral
WDR	wide dynamic range neurons
ZIF	zero insertion force