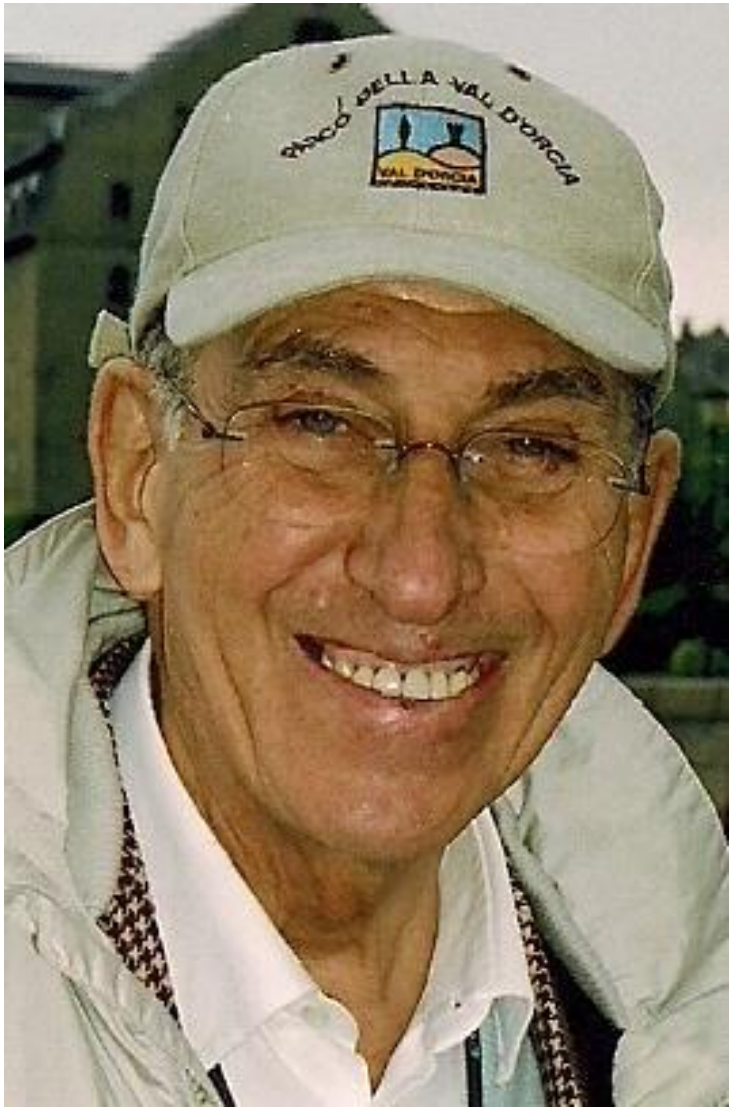


In Commemoration

of our departed colleague

Giorgio Brunelli

AMN Founding Honorary Member

By Klaus RH von Wild

Born October 21,1925 – Died September 29, 2018

Cellatica (BRESCIA), Italy

Giorgio Brunelli - Curriculum Vitae

- **Professor emer. of Orthopaedics** and Chair School of Specialisation in Orthopaedics and Traumatology, Univ. Brescia, Medical School until 1997; more than 25.000 ops**. 3.500 of which in microsurgery;**
- **Author** of 466 papers in previewed journals, 30 chapters,10 textbooks;
- **Distinguished Prof.** Philadelphia; **Dr.hon.causa** Univ. of Wroslaw, PL.
- Member of the Academy of Sciences, New York, US.
- **Founder member**: The International Society for Reconstructive Microsurgery, The International Society of Microsurgery, French Groupe d' Etude des Nerfs, The Italian Society of Hand Surgery, The Italian Society for Microsurgery, The European Society for research in microsurgery. Founding member World AMN, Society for clinical Neuromusicology; Honorary Member of national/intern. Sc. Societies;
- **Founder of Giorgio Brunelli Foundation** for the Experimental Research on Spinal Cord Repair and Regeneration.

We met first in 1997, when G.B. has focused already a great part his professional life on experimental research for the development of reconstructive techniques and new clinical concepts in microsurgery. He has become known and estimated worldwide for his surgical talent and great experience. His numerous studies in experimental surgery in animals including primates were translated successfully into human peripheral nerve and spinal cord repair, e.g. brachial plexus lesions and severance of spinal cord lesions.

CNS- PNS nerve grafting in human became his challenge.

SCI rehabilitation is a multidisciplinary challenge
People becoming involved in SCI issues should approach **all category groups in** a ***humanistic*** **way**
Based & balanced on academic rules & best practise

- To exchange knowledge in specific fields
- To learn from the experience of experts - *evidence based*
- To check the reputation of the own teamwork
- To make use of new technologies
- To plan / take part in experimental (clinical) trials
- To guarantee quality management/ rehabilitation evidence
- To enhance prestige in SCI neuroscience and the public
- To create new partners, teams, data sets & sponsors
- To foster social competence and re-entry after SCI

Implantation of neuroprosthesis in paraplegics:

BIOMED II European Comm.1996–2000: Computer added locomotion by implated electrical stimulation in paraplegic patients (SUAW)
K.von Wild, P.Rabischong,**G.Brunerlli** et al A**cta Neurochir,2001 Suppl.79 99-10**

Giorgio **Brunelli** (left) & SUAW Surgeons with P. Rabischong (3rd from right) in front Anatom .Inst. Univ. Montpellier, **Oct.1997**: **Cadaver studies & scientific discussion**

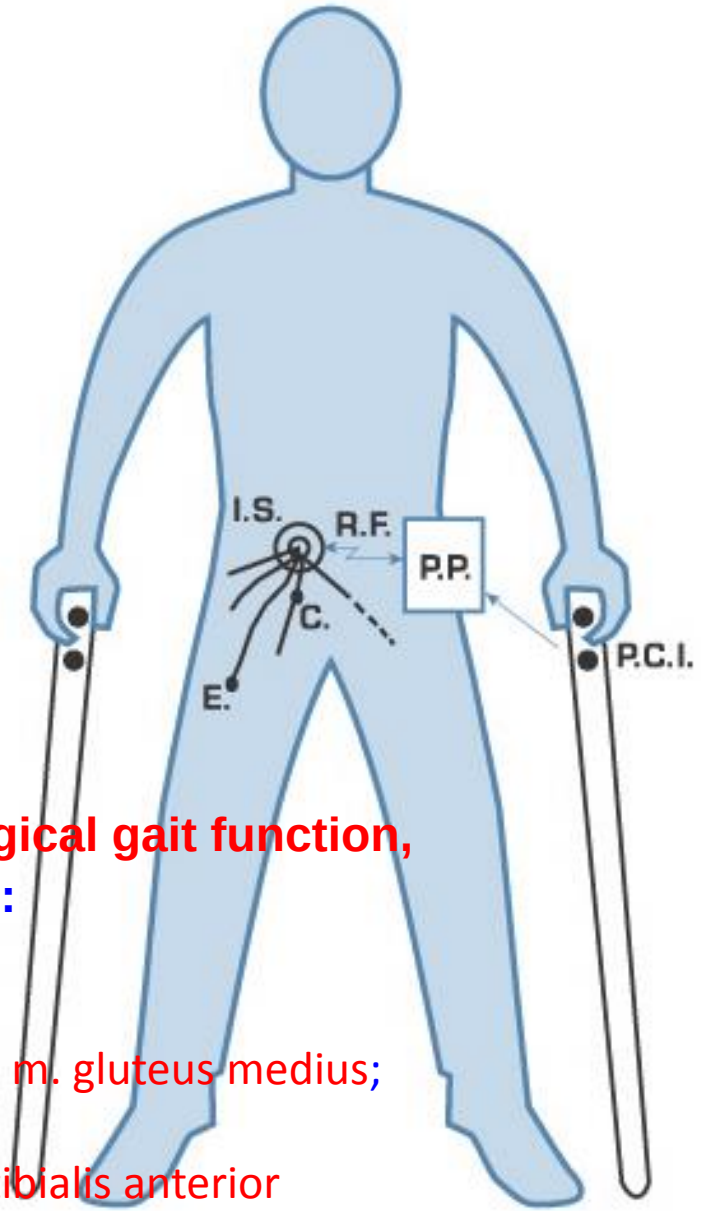
Giorgio Brunelli

Pierre Rabischong Kris Krishnan †

Michel Benichou Klaus von Wild

Implementation of SUAW technical FES package on a Patient

I.S.	Implanted Stimulator
C.	Connector
E.	Electrode
P.P.	Portable Programmer
R.F.	Radio Frequency link
P.C.I.	Patient Command Interface



6 muscles- **upright mobility & physiological gait function, stimulated according to Kobecic R (1997):**

Hip extensor- m.gluteus maximus;

Hip flexors- m. satorius & m. rectus femoris;

Lateral hip stabilisation & knee abduction- m. gluteus medius;

Knee extension- m. quadriceps**;**

Knee flexion- m. hamstrings**; Foot extension-** m. tibialis anterior

Neuromedics® implant,

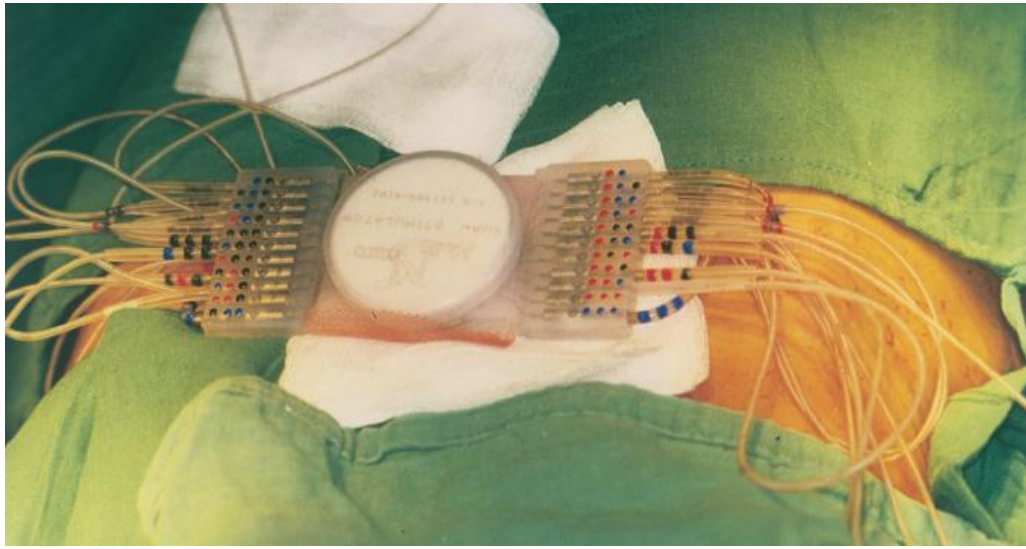
70mm diameter, contains the

ASIC® chip of 3,9x45mm

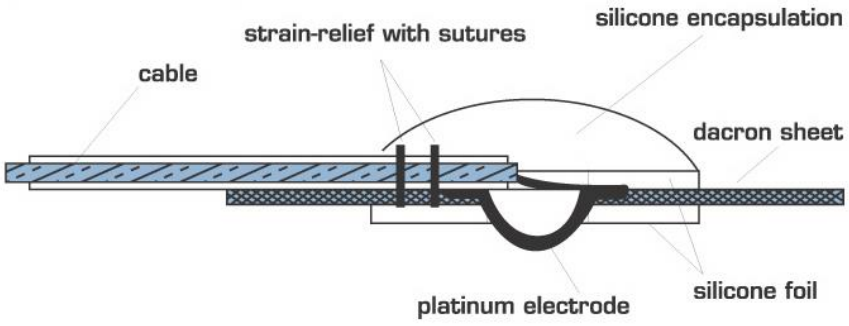
70 wire pads bounded to a

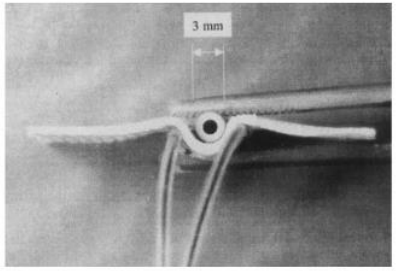
9 x 9 mm ceramic package.

16 output channels on both sides



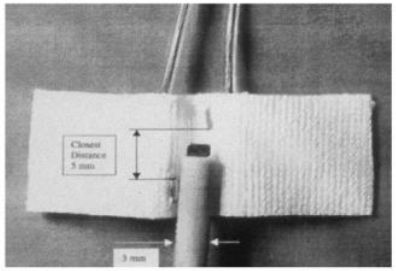
Epimysial electrodes to be fixed over the motor point of the gluteal hip muscles for monopolar stim.20mA





Perineural electrodes (Fig. 3) ARTOTECH®

(1,5kOhm) threshold. **Only one electrode should be stimulated at a given time**.



SUAW 28. 09.99.1. implantation Marc M, 38 ys, T8

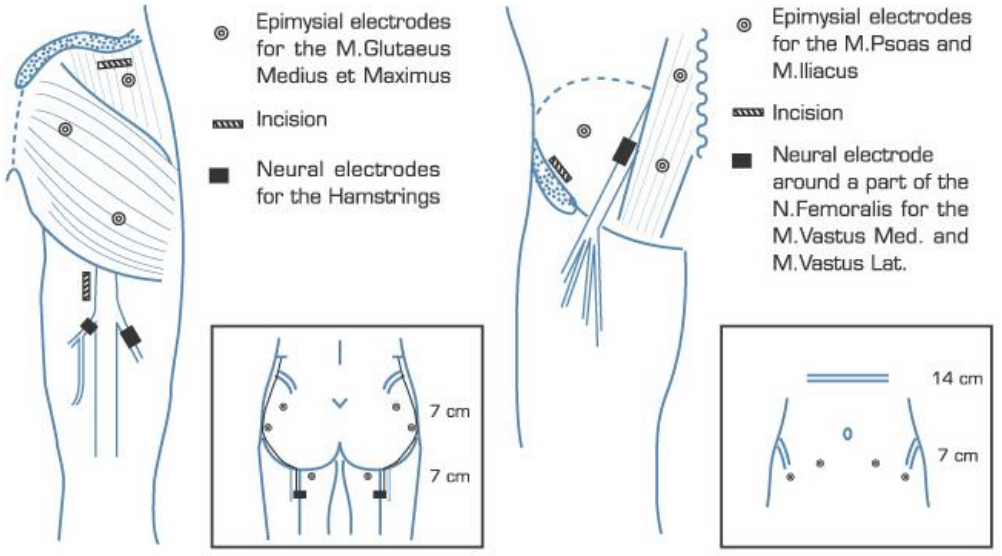
9 yrs car accident; married, two children; banker.

Surgical team: Dr. BENICHOU, **Prof. BRUNELLI**, Prof. K. von WILD

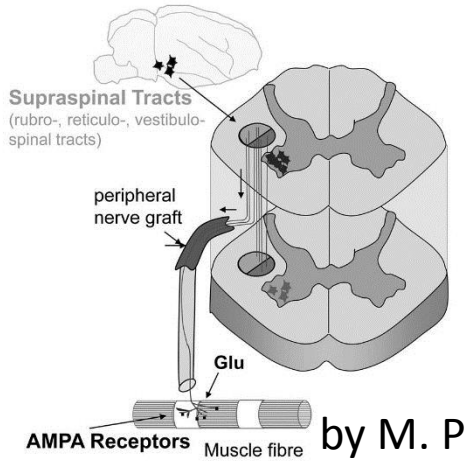
Engineers P. Couderc, D. Guitaud, Stieglitz, Koch Physio.(Exostim®) Marc Vivent

Technical complications: Postoperative **cross talk** during FES by all four neuronal empimysial electrodes at 10mA

Second complication: Following scar tissue fibrosis current intensity for both epimysial (10mA) and neuronal electrodes (0.2mA) turned out to be too low according to the threshold of the receiver



Marc M. after implantation walking by Stimulation - TV show



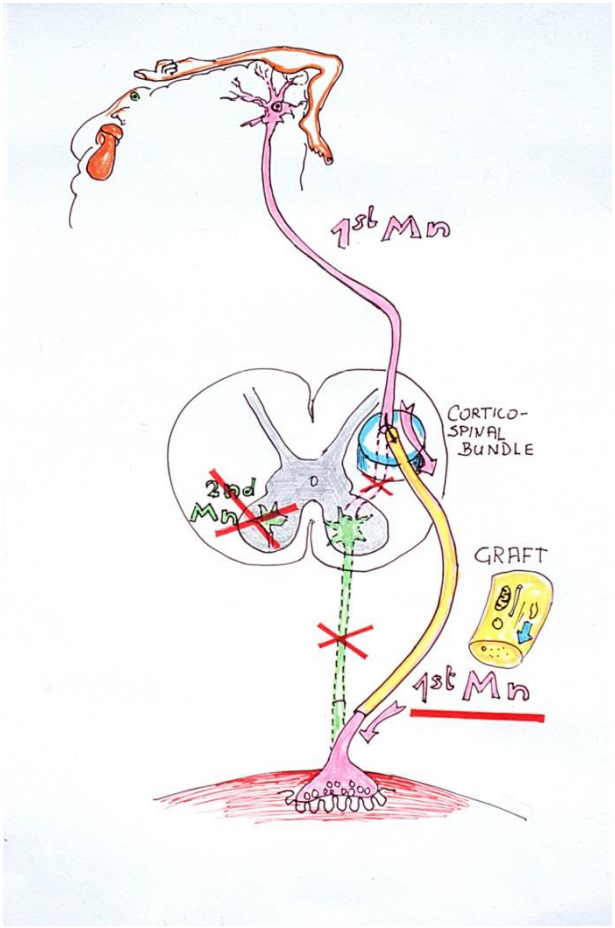
by M. Pizzi

BRUNELLI's PARADIGM –

DIRECT CNS – PNS CONNECTION:

THE MUSCLES ARE RE-INNERVATED BY THE UPPER (1st) MOTO-NEURON WHILE THE LOWER (2nd) MOTO-NEURON IS EXCLUDED

Sketch by Giorgio Brunelli



PNAS PNAS PNAS

Glutamatergic reinnervation through peripheral nerve graft dictates assembly of glutamatergic synapses at rat skeletal muscle

Giorgio Brunelli*†, PierFranco Spano†‡§, Sergio Barlati†¶, Bruno Guarneri‖, Alessandro Barbon¶, Roberto Bresciani**, and Marina Pizzi†††

*Foundation for Experimental Spinal Cord Research, Divisions of †Pharmacology and Experimental Therapeutics, ¶Biology and Genetics, and **Biochemistry and Clinical Biochemistry, Department of Biomedical Sciences and Biotechnologies, School of Medicine, University of Brescia, 25123 Brescia, Italy; ‖Division of Neurophysiology, Spedali Civili of Brescia, 25123 Brescia, Italy; and §Istituto Ricovero e Cura a Carattere Scientifico, S. Camillo Hospital, 30100 Venice, Italy

Edited by Gerald D. Fischbach, Columbia University College of Physicians and Surgeons, New York, NY, and approved April 26, 2005 (received for review January 21, 2005)

Acetylcholine is the main neurotransmitter at the mammalian neuromuscular junction (NMJ) where nicotinic acetylcholine receptors mediate the signaling between nerve terminals and muscle fibers. We show that under glutamatergic transmission, rat NMJ switches from cholinergic type synapse to glutamatergic synapse. Connecting skeletal muscle to the lateral white matter of the spinal cord by grafting the distal stump of the transected motor nerve produced functional muscle reinnervation. The restored neuromuscular activity became resistant to common curare blockers but sensitive to the glutamate α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor antagonist. Analysis of the regenerated nerve disclosed new glutamatergic axons and the disappearance of cholinergic fibers. Many axons belonged to the supraspinal neurons located in the red nucleus and the brainstem nuclei. Finally, the innervated muscle displayed high expression and clustering of α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor subunits glutamate receptors 1 and 2. Our data suggest that supraspinal neurons can target skeletal muscle, which retains the plasticity to generate functional glutamatergic NMJ.

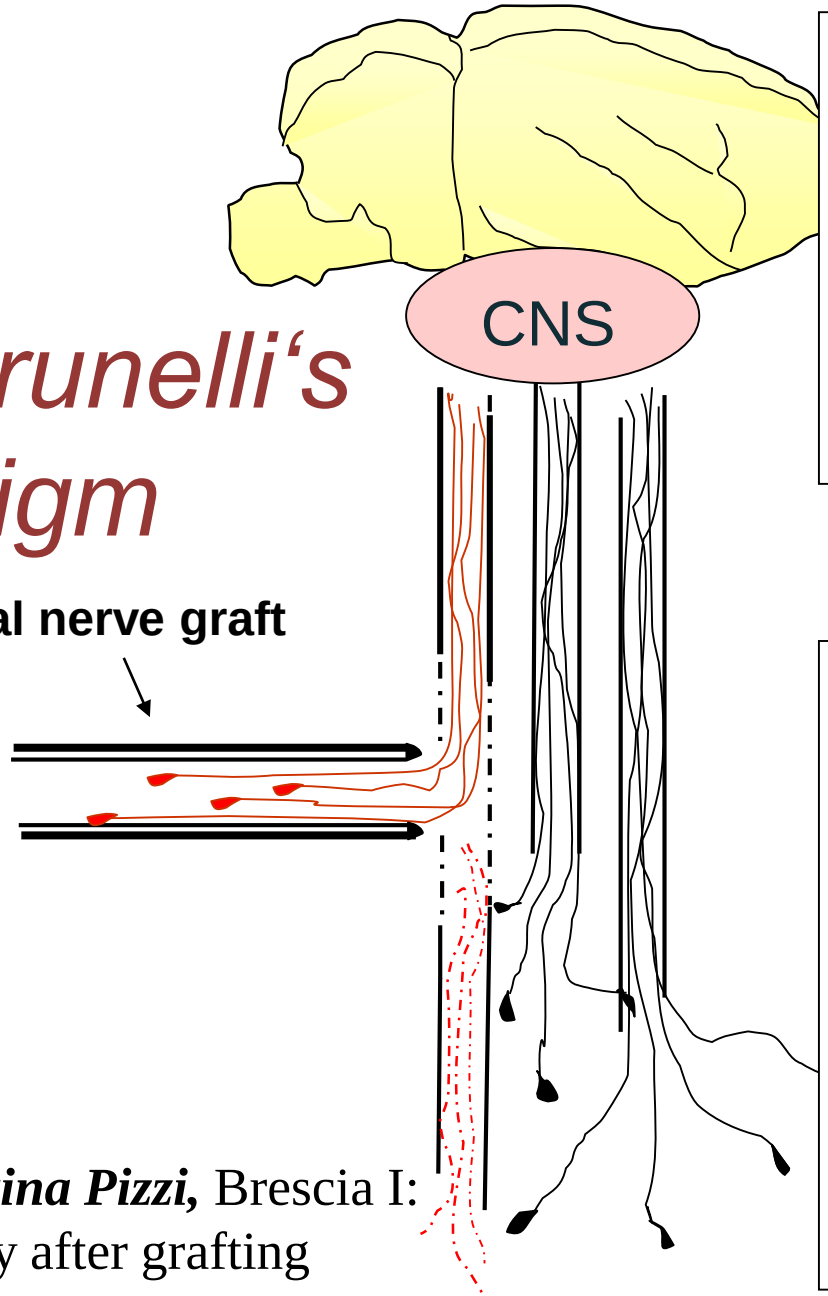
could be responsible for functional muscle reinnervation. Here we tested this hypothesis by connecting the distal stump of a transected rat motor nerve with lateral white matter. An autologous sural nerve graft was implanted into the acutely severed lateral white matter of the spinal cord and connected to the transected nerve of the internal obliquus abdominis muscle. We found the grafting of the motor nerve into the lateral bundle of the spinal cord led to a new glutamatergic innervation of skeletal muscle, replacing the original cholinergic one (16). By electrophysiological, molecular, and immunohistochemical analysis, we show that reinnervated muscles were reprogrammed by supraspinal neurons to organize functional glutamatergic neuromuscular junctions (NMJ).

Materials and Methods

Surgical Procedure. Experiments were performed on 30 adult male Sprague–Dawley rats (350–400 g). Rats received carprofen (8 mg/kg) and, 10 min later, they were anesthetized with tiletamine (16 mg/kg) and zolazepam (16 mg/kg). All experimental and surgical procedures conformed to the National

8752-8757 I **PNAS** I June 14, 2005 I vol 102 I 21
www.pnas.org/doi/10.1073/pnas 050053102

The *Brunelli's Paradigm*



Central axons are able to regenerate and progress throughout a peripheral nerve graft, suggesting that they can regrow in an appropriate environment. (David & Aguayo, 1981)

Central fibers regrowing into a peripheral nerve graft derive from neurons axotomized during the grafting procedure and not from uninjured neurons spared by graft implantation. (David & Aguayo, 1985)

Courtesy *Marina Pizzi,* Brescia I:
Motor recovery after grafting
May 2011

G. Brunelli, K. von Wild, Luisa Monini-B.

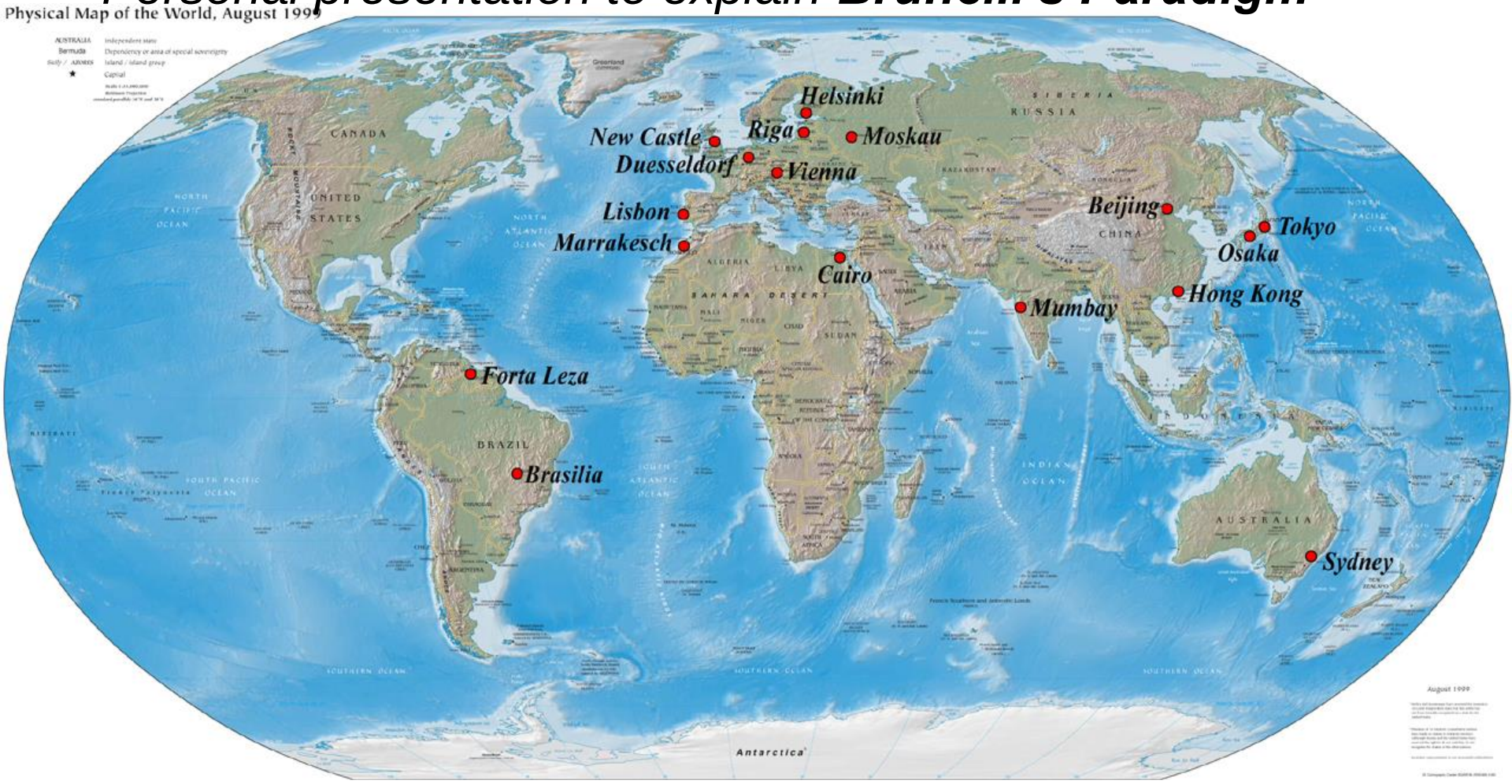
Results after CNS- PNS grafting July 2000

1. After 12 months, well in advance on the expected time (1mm/day), some **voluntary, selective contraction of the reinnervated muscles were present.**

Walking after 2 years **till 2018**

Advertising inter-national scientific interest

Personal presentation to explain ***Brunelli's Paradigm***



Controversial discussions 2001-2008 international /national Congresses of Neurosurgery, Neurology, Neuro-rehabilitation:at WFNS, EANS, ISRN, AANS, ACNS WFNR, EFNS, PANS, **EMN**,German DANC, RoSNC. **Consequence**: **World-AMN**

AMN Founding & Honorary Member

On May 19, 2003 *Giorgio A. Brunelli*, **It**, Anwar El Etribi, **EGY**, Tetsuo Kanno, **JP,** Mario Prosiegel, **DE**, Wai S Poon, Hongkong,**HK**, Motoi Shoda, Klaus and Monika von Wild ,**DE** ***established The AMN*** in Munich, registered in Münster 2004.

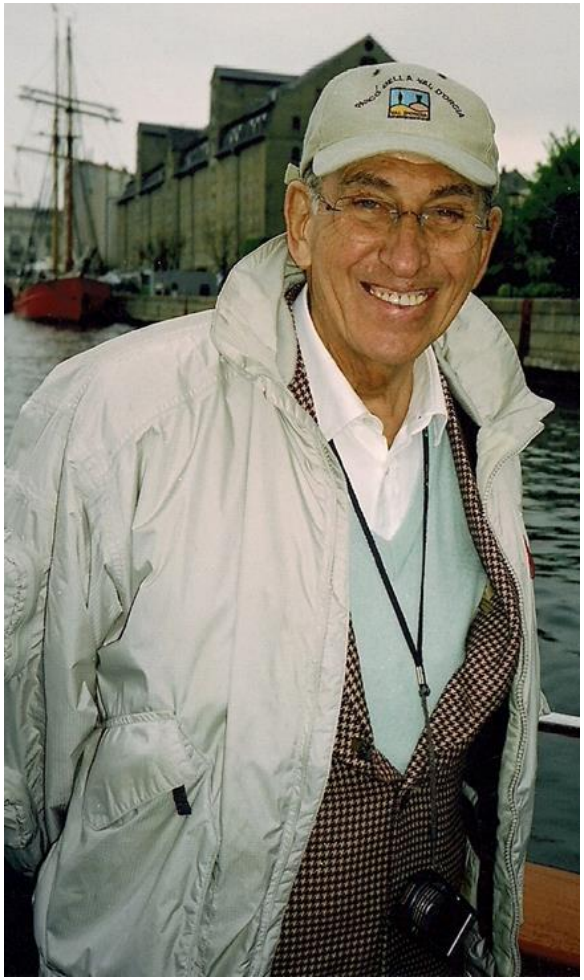
Giorgio became 1st AMN congress president, Brescia,IT

Giorgio & Tetsuo check at dinner the dates for 1st AMN 2004 :29-30, 03.

1st AMN Brescia March 29-30, **2004**

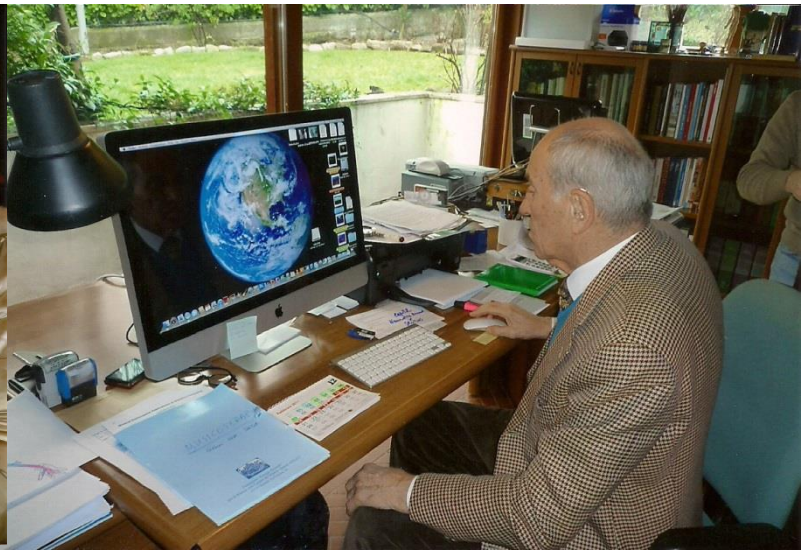
Prof. Rita Levi Montalcini, Italian Nobel laureate, Brescia Univ., Luisa Monini-Brunelli, and Brunelli, Italian Nobel Prize candidate 2007

4th AMN Copenhagen, 2006,
Congress President A.-L.Christensen



Giorgio Brunelli Hon. Member

From left:W.S.Poon,G.Barlati,G.Brunelli,AL.Christensen, D. Stein,Th.W.Teasdale, K.v Wild, G.Prigatano President F. Humle Center BI Rehab.A.W.Engbert,E.Neugebauer

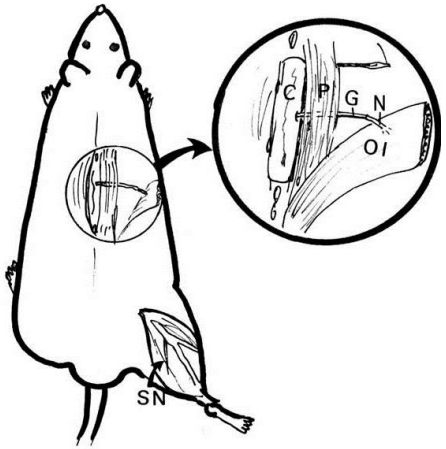


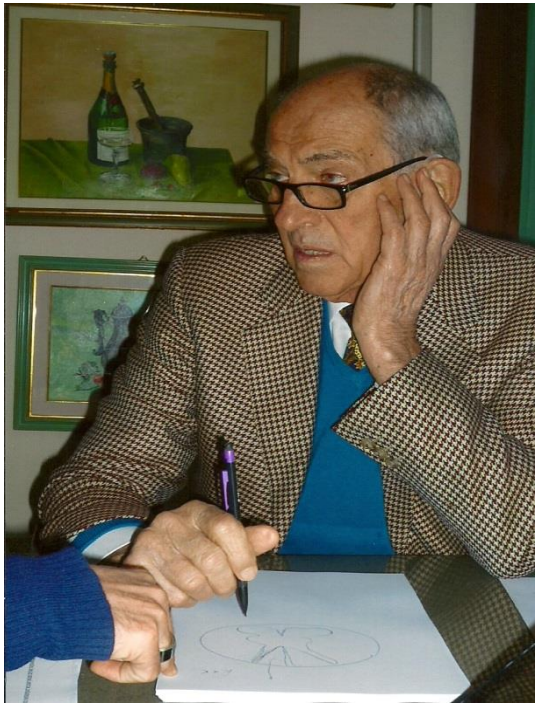
Command Center

Fondazione Giorgio Brunelli per la ricerca sulle lesion del midollo spinale, Cellatica, IT

2008 till now!

Prof. Luisa Monini- Brunelli, MD, PhD Director of the Foundation



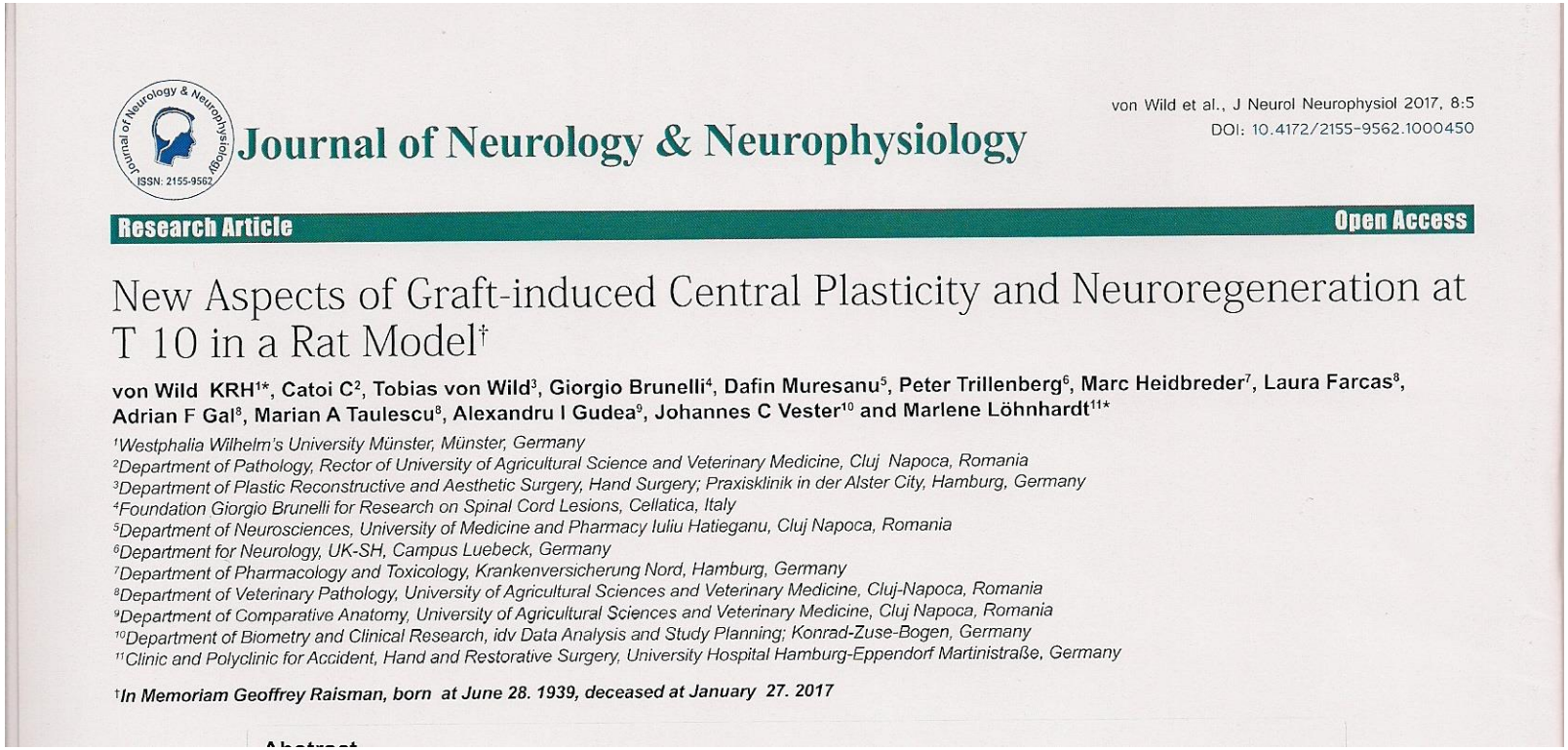


G Brunelli explained his Paradigma for replication to Tobias and Klaus von Wild

New Aspects on graft induced central plasticity and neuroregeneration at T 10 in rat model. **2017 J Neurol Neurophysiol 8:5** DOI: 10.4172/2155-9562.1000450

Replication of Brunelli's Paradigm

Transdisciplinary cooperative RCT 2008- 2018



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Research Article
Open Access

New Aspects of Graft-induced Central Plasticity and Neuroregeneration at T 10 in a Rat Model†

von Wild KRH[1*], Catoi C[2], Tobias von Wild[3], Giorgio Brunelli[4], Dafin Muresanu[5], Peter Trillenberg[6], Marc Heidbreder[7], Laura Farcas[8], Adrian F Gal[8], Marian A Taulescu[8], Alexandru I Gudea[9], Johannes C Vester[10] and Marlene Löhnhardt[11*]

[1]*Westphalia Wilhelm's University Münster, Münster, Germany*
[2]*Department of Pathology, Rector of University of Agricultural Science and Veterinary Medicine, Cluj Napoca, Romania*
[3]*Department of Plastic Reconstructive and Aesthetic Surgery, Hand Surgery; Praxisklinik in der Alster City, Hamburg, Germany*
[4]*Foundation Giorgio Brunelli for Research on Spinal Cord Lesions, Cellatica, Italy*
[5]*Department of Neurosciences, University of Medicine and Pharmacy Iuliu Hatieganu, Cluj Napoca, Romania*
[6]*Department for Neurology, UK-SH, Campus Luebeck, Germany*
[7]*Department of Pharmacology and Toxicology, Krankenversicherung Nord, Hamburg, Germany*
[8]*Department of Veterinary Pathology, University of Agricultural Sciences and Veterinary Medicine, Cluj-Napoca, Romania*
[9]*Department of Comparative Anatomy, University of Agricultural Sciences and Veterinary Medicine, Cluj Napoca, Romania*
[10]*Department of Biometry and Clinical Research, idv Data Analysis and Study Planning; Konrad-Zuse-Bogen, Germany*
[11]*Clinic and Polyclinic for Accident, Hand and Restorative Surgery, University Hospital Hamburg-Eppendorf Martinistraße, Germany*

†***In Memoriam Geoffrey Raisman, born at June 28. 1939, deceased at January 27. 2017***

Giorgio **Brunelli** Prof. of Orthopaedics, CEO Giorgio Brunelli Foundation Ricera sulle lesioni del midollo spinale ESCRI, ONLUS,
Tobias **von Wild** Consultant Dpt. of Plastic-reconstructive-, Hand and Burns Surgery, University Clinic Schleswig-Holstein, **Lubeck, G**
Dafin **Muresanu** Prof. of Neurology, Chairman Dept. of Neuroscience , Univ. of Medicine and Pharmacy **Cluj Napoca,, RO**
Cornel **Catoi** Head Dpt. of Pathology, Dean of Faculty Veterinary Medicine, Univ. of Agricultural Sc. & Veterinary. Med., **Cluj Napoca, RO**

Giorgio- The *Rounder*

Giorgio was not only an exceptional surgeon, he was also both athletic, cultured and aesthete. As talented **novelist** he described inter alia the Etruscans life by their antique language. As a passionate **painter** he had his own lovely collection at home. Giorgio manufactured all his anatomical **sketches,** demonstrated before! His bright eyes as an outstanding **photographer** are shown by his books**.** The **sportsman** loved to swim 1000 m every day from 6.10- 6.30; when with Luisa in holiday in *Forte dei Marmi in Ligurian Sea* ! His **precious old-timers** were used successfully for racing at *Mille Millia* competitions with Luisa, his ingenious co-pilot! His charity meant operating with Luisa nil paid lepers et al.
We will remember Giorgio Brunelli in gratitude by expressing our deep sympathy to Luisa Monini-Brunelli and the families.