



MEDICAL RESEARCH IN POLAND: OPPORTUNITIES FOR COOPERATION



Wojciech Maksymowicz
Professor of neurosurgery
Head of Department of Neurosurgery
Dean of Medical Faculty
University of Warmia and Mazury in
Olsztyn



12 Polish Medical Schools



Polish Governmental Research Medical Institutes

Cancer and ...

Cardio-vascular+rheumatology



Children and mother health



Psychiatry+
Neurology+
Audiology



Public health, food and drug and occupational
medicine





Polish Academy of Sciences Division VI Medical Sciences



Warsaw

Institute for Medical Biology Centre of Excellence in Medical
Polish Academy of Sciences Biology
BIOLMED

Łódź

Institute of Pharmacology

Polish Academy of Sciences

Center of Excellence in Neuropsychopharmacology - FRAM

Kraków

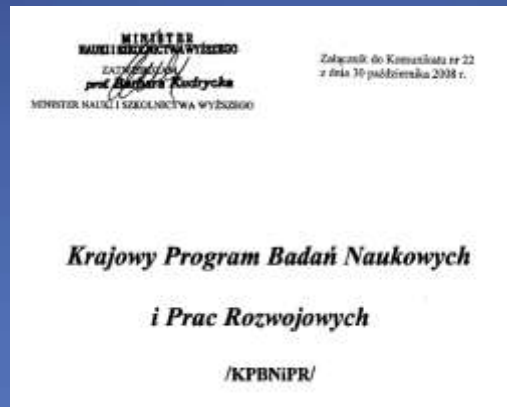


Poznań

**Ludwik Hirszfild Institute of Immunology
and Experimental Therapy**

Wrocław

GOVERNEMENTAL PRIORITIES



Health

1. **Epidemiology of lifestyle diseases.**
2. **Molecular basis of the diseases . The implementation of molecular biology methods in the diagnosis.**
3. **Nervous system function; diagnosis and treatment of psychiatric and neurological diseases.**
4. **Regenerative medicine (stem cells and ...)**
5. **New technologies in pharmacotherapy**

**Restorative neurology.
Improving function without structural
damage.**



Restorative neurosurgery

Electrical stimulation

Stem cells Implantation

Delivery drugs into the CSF
spaces and brain



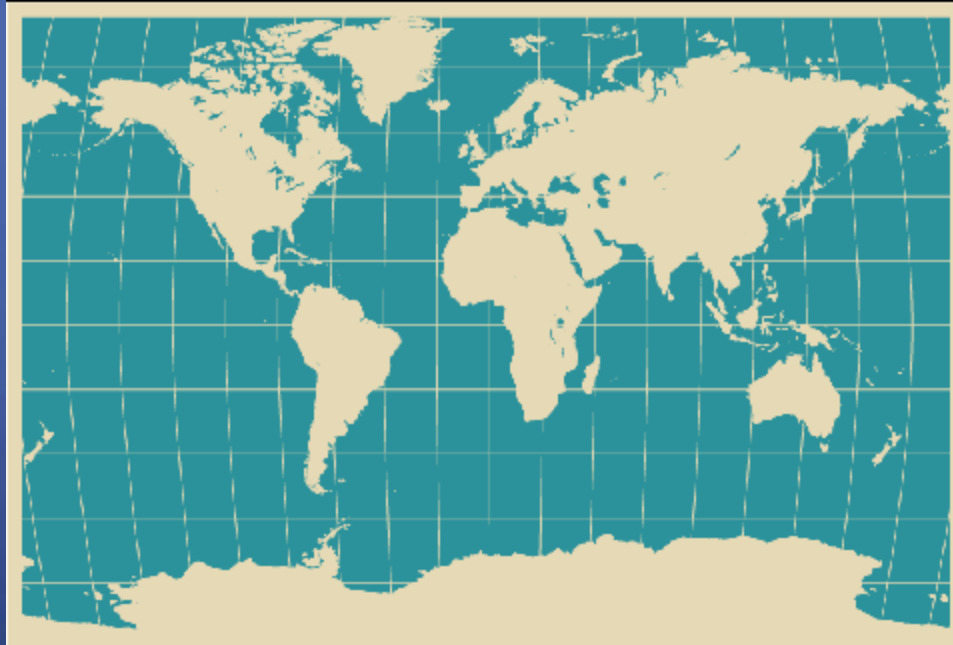
Historic, contemporary and future surgical treatment of refractory epilepsy.



Wojciech S. Maksymowicz

Department of Neurosurgery,
Central Clinical Hospital of Ministry of Internal Affairs and Administration
(MSWiA), Warsaw, Poland

**The begining of the research on epilepsy
was common for eastern and western
world.**



Caton (1875)	Bartley and Newman (1930)
Fleischl von Marxow (1890)	Bartley and Newman (1931)
<u>Beck (1890)</u>	Travis and Herren (1931)
<u>Danilewsky (1891)</u>	Travis and Dorsey (1931)
Gotch and Horsley (1891)	Davis and Saul (1931)
<u>Beck and Cybulski (1892)</u>	Adrian (1931)
<u>Larinow (1898)</u>	Adrian and Buytendijk (1931)
Trivus (1900)	Bishop and Bartley (1932)
<u>Tchiriev (1904)</u>	Travis and Dorsey (1932)
<u>Kaufman (1912)</u>	Fischer (1932)
<u>Prawdicz-Neminski (1913)</u>	Kornmüller (1932)
<u>Cybulski and Macieszyna (1919)</u>	Perkins (1933)
<u>Prawdicz-Neminski (1925)</u>	Bartley (1933)
<u>Berger (1929)</u>	Gerard, Marshall, and Saul (1933)

——— Polish
——— Russian
——— Ukrainian

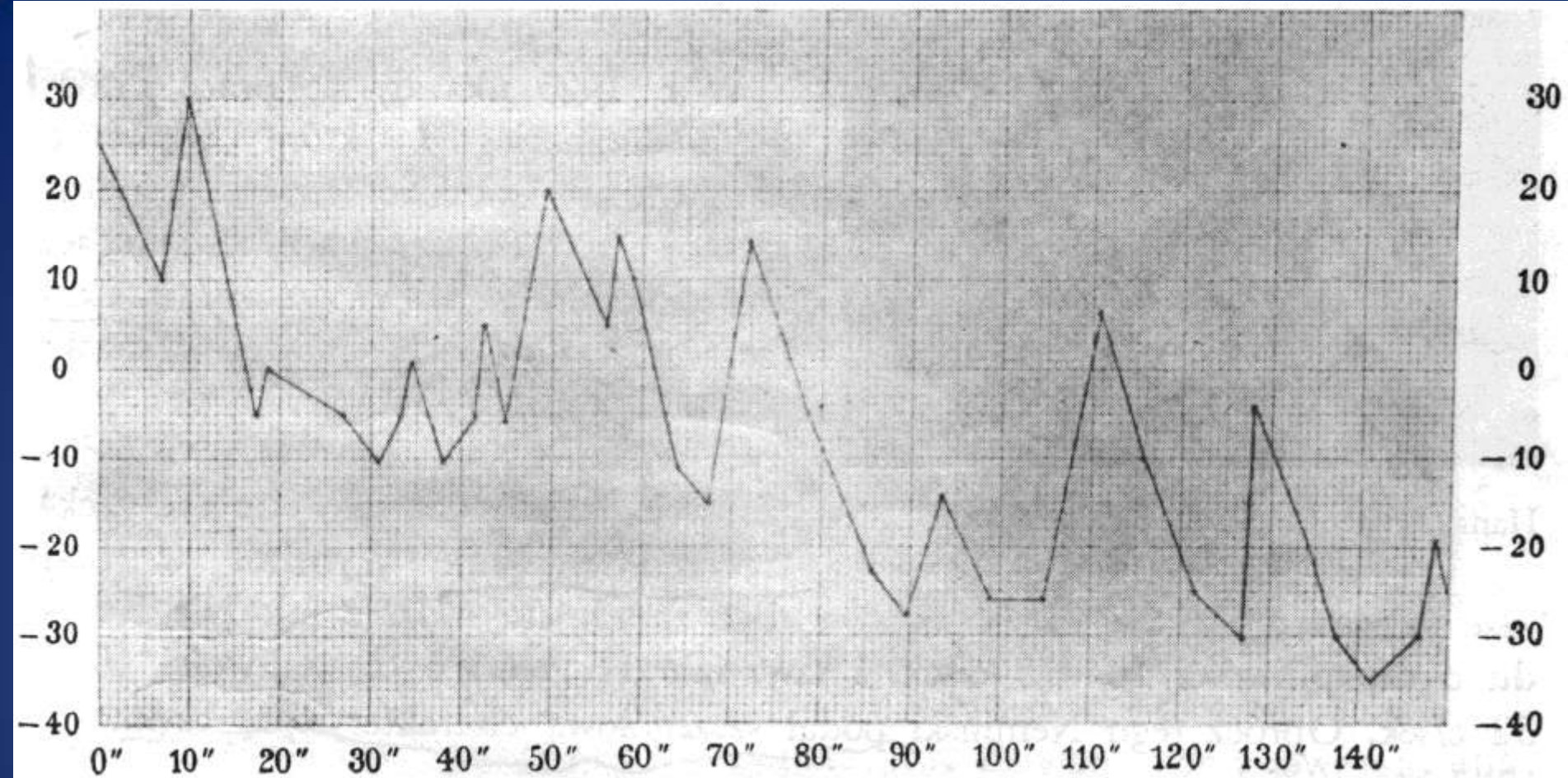
Who discovered and developed EEG before Lord Edgar Douglas Adrian
 (by Donald B. Lindsley)



Adolf Beck (1863-1942)

Polish neurophysiologist of Jewish origine, professor and rector of Jan Kazimierz University in Lwów. He did not know about Caton`s works and undependently discovered the spontaneous electric activity of brain (later known as electroencephalography). Main topics of his scientifical activity: the use of neurophysiology for the localization of brain functions (mainly sensoric). *Die Ströme der Nervencentren. Centerblatt für Physiologie*, 4:572-573, 1890.

He dramatically decided to suicide in German nazi camp for Jewish people in Janowiec in 1942.



Galvanometric record of brain cortex activity. A. Beck and N. Cybulski (published in Polish journal in 1896r. „Dalsze badania zjawisk elektrycznych w korze mózgowej”)



Napoleon Cybulski

Napoleon Nikodem Cybulski (1854- 1919)

He established the Polish School of Neurophysiology, together with Adolf Beck .

He published the first recording of experimental epileptic seizure in dog provoked by cortex stimulation (1914).

The first photographic records of bioelectric epileptic seizure caused by electric stimulation of dog's brain cortex.

Written from right to left.

Curve IV- EKG

Curve III -cortex

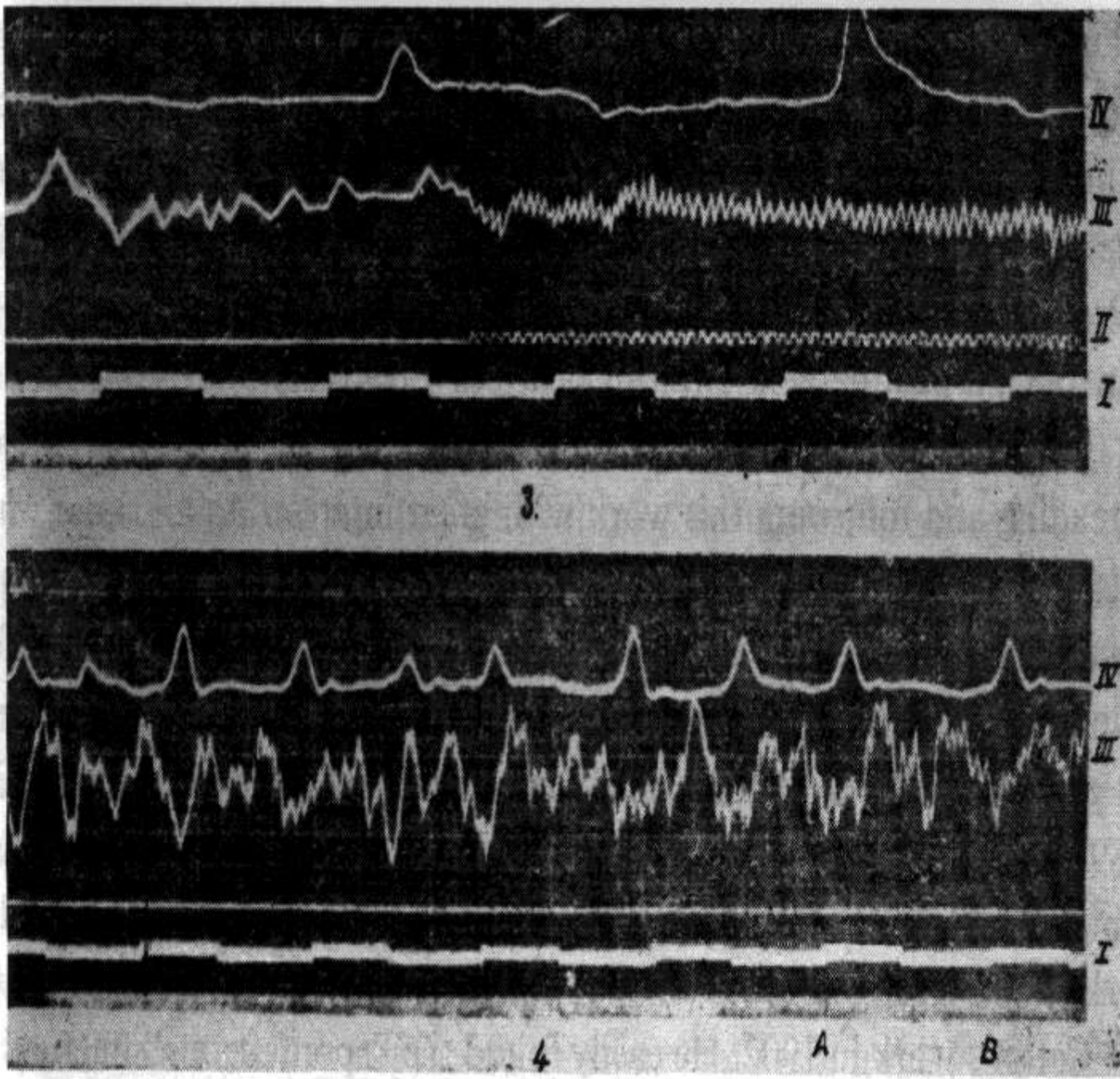
Curve II - stimulus

Curve I -time

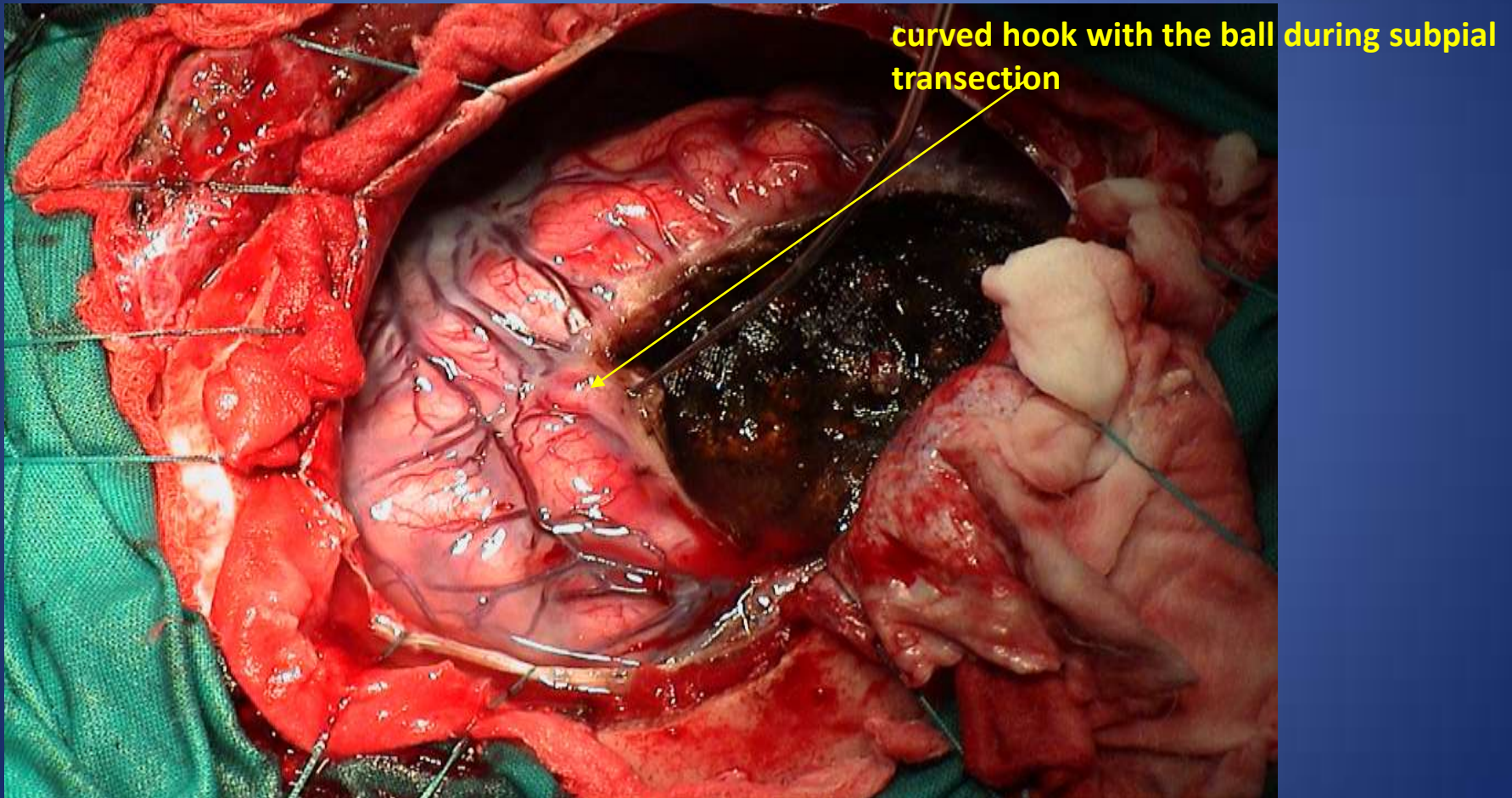
N. Cybulski and

S. Jeleńska

Macieszyna 1914.



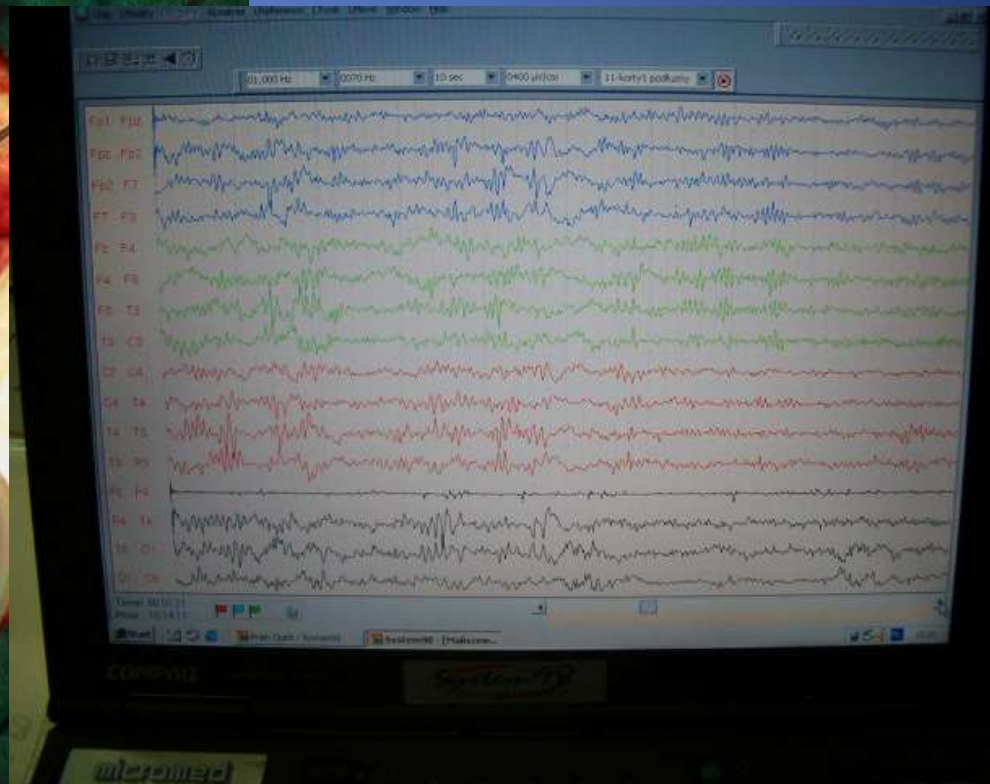
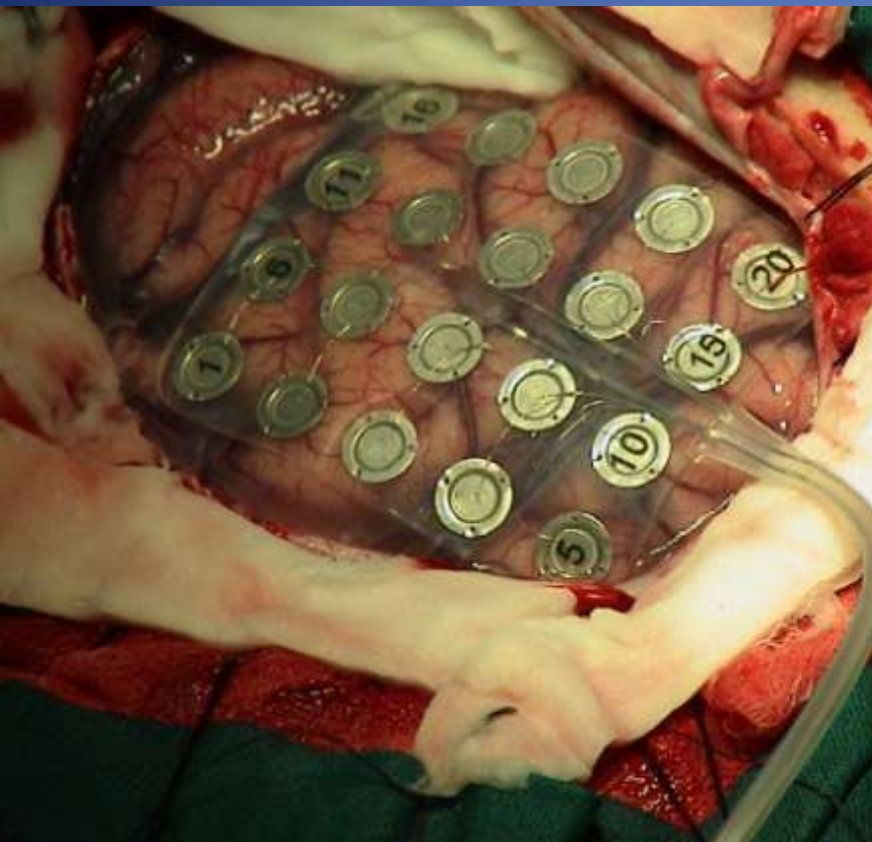
Intraoperative picture. Subpial transection following the brain resection.



Multiple Subpial Transections in the Dep. of Neurosurgery,

Central Clinical Hospital MSWiA, Warsaw

Intraoperative ECoG recording.



Multiple Subpial Transections in the Dep. of Neurosurgery,
Central Clinical Hospital MSWiA, Warsaw
Intraoperative ECoG recording.



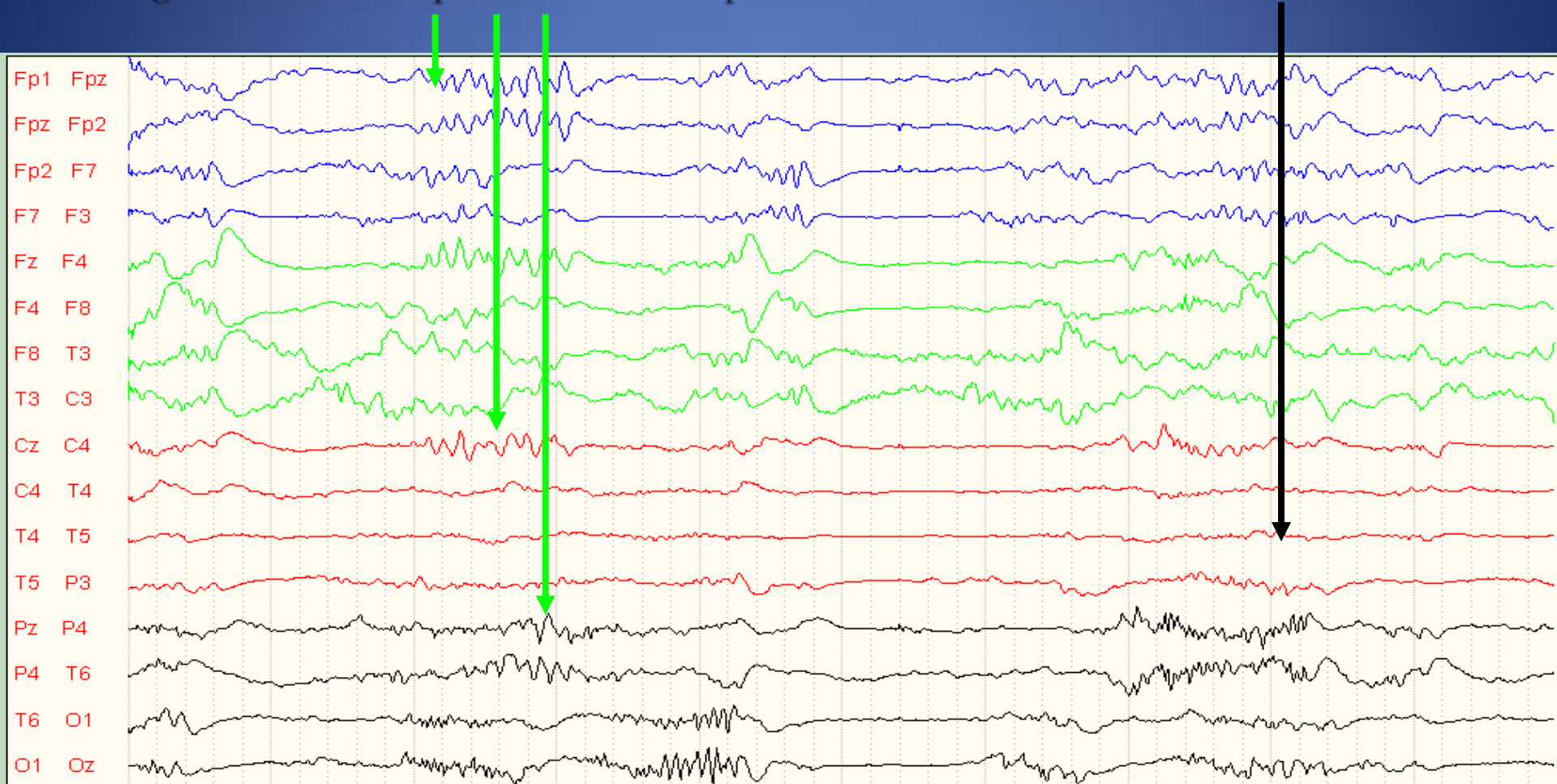
Monitoring of the ECoG following every MST

36 years old patient (R.G.) left temporal epilepsy

Stage O (beginig):

Changes in the anterior part of the left temporal lobe

Depression with the signs of the damage under the 13-th and 14-th electrode

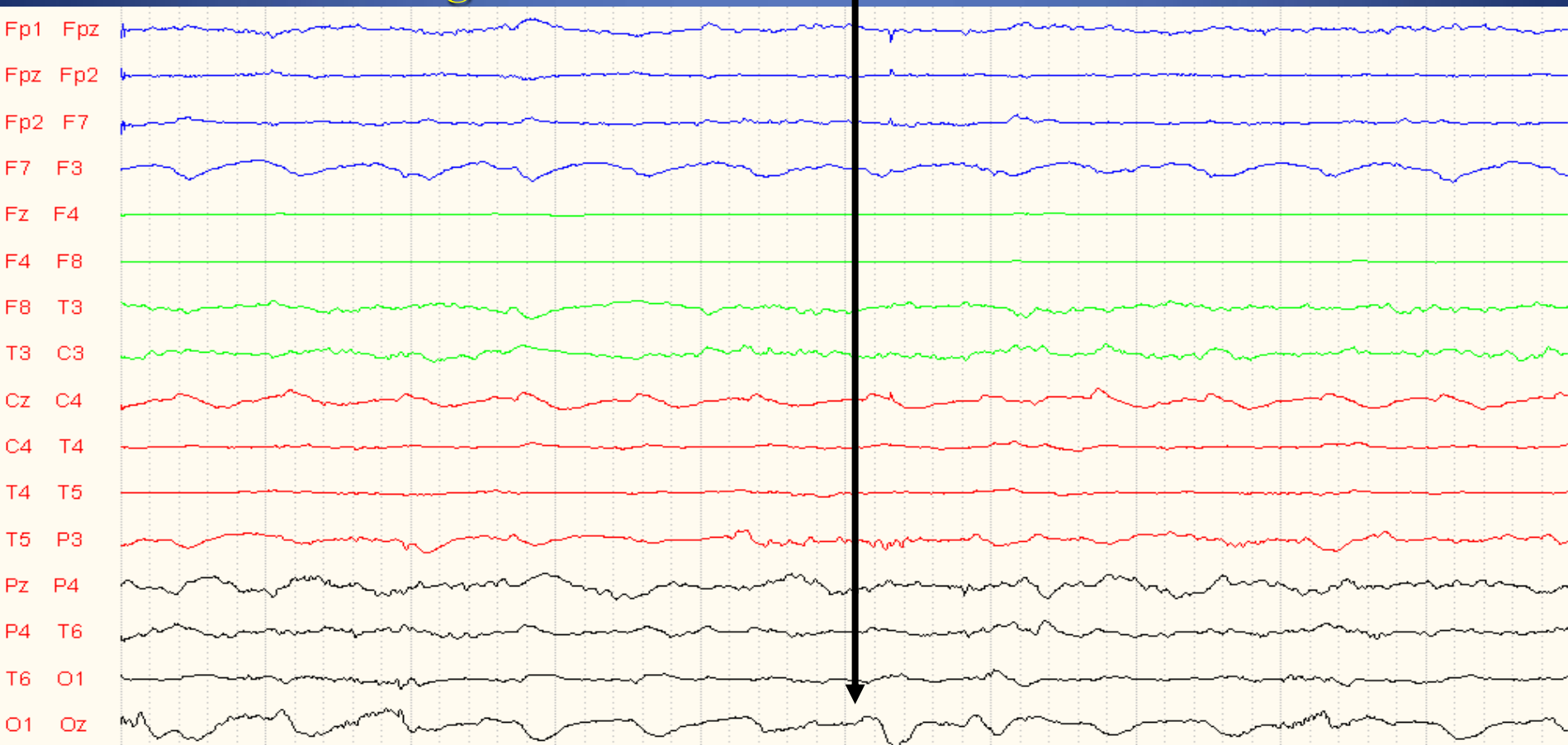


Monitoring of the ECoG following every MST

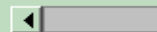
Patient R.G.

Stage 3

Final recording after the MST under the electrode No 20



Timer: 00:00:00
Hour : 11:22:38



Electrical Brain Stimulation to Reduce Epileptic Seizures

This study is currently recruiting patients.

Verified by National Institutes of Health Clinical Center (CC) May 2007



Delivery the antyneoplastic and antyepileptic agents into the brain.



„Therapies under development may result in the delivery of AEDs directly to the regions of the brain involved in seizures. Experimental protocols are underway to allow continuous infusion of potent excitatory amino acid antagonists into the CSF. In experiments with animal models of epilepsy, AEDs have been delivered successfully to seizure foci in the brain by programmed infusion pumps, acting in response to computerised EEG seizure detection.”

Fisher RS, Ho J

What and how to delivery ?



„CONCLUSIONS: This study showed for the first time that epidural AED delivery can prevent, as well as terminate, locally induced neocortical seizures. The findings support the viability of transmeningeal pharmacotherapy for the treatment of intractable neocortical epilepsy.”

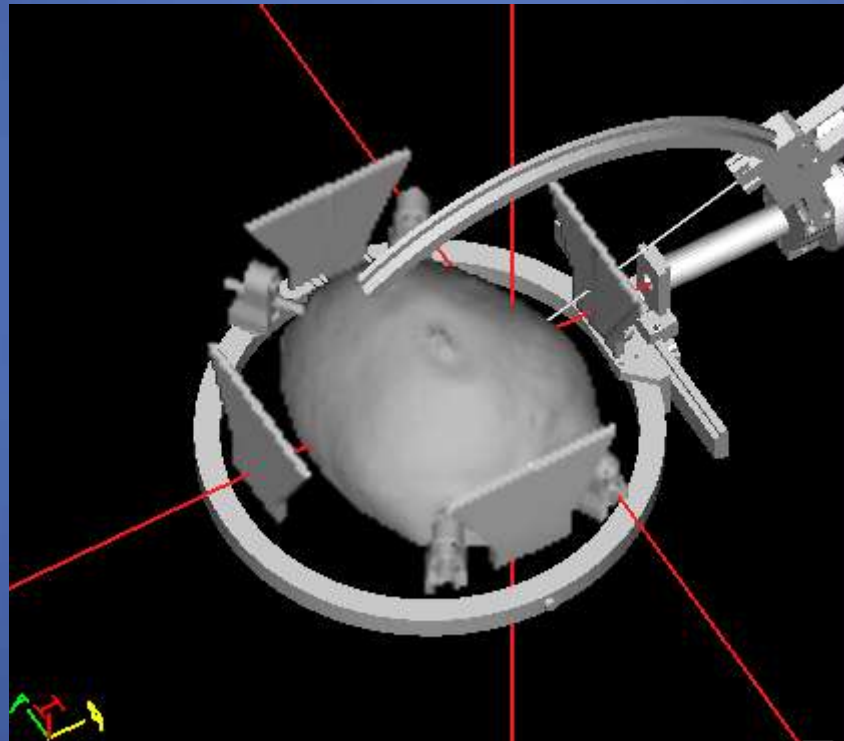


Epidural pentobarbital delivery can prevent locally induced neocortical seizures in rats: the prospect of transmeningeal pharmacotherapy for intractable focal epilepsy.

[Ludvig N](#), [Kuzniecky RI](#), [Baptiste SL](#), [John JE](#), [von Gizycki H](#), [Doyle WK](#), [Devinsky O](#).

Comprehensive Epilepsy Center, Department of Neurology, New York University School of Medicine, New York Epilepsia. 2006 Nov;47(11):1792-802.

Deep brain stimulation for the treatment of Parkinson disease, pain and Epilepsy



Restorative neurosurgery

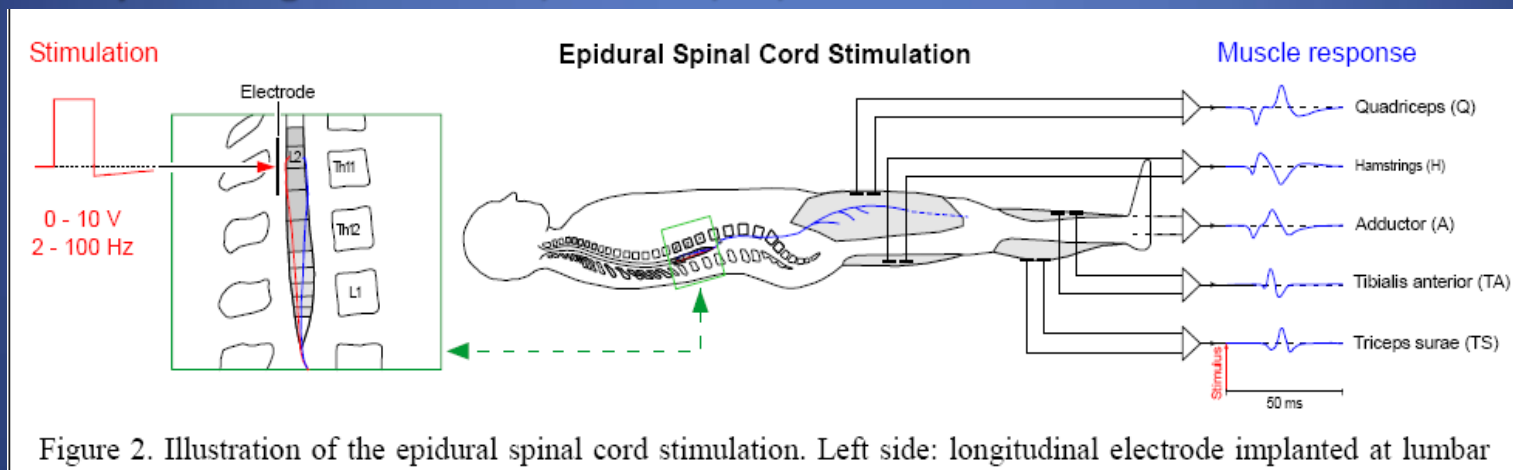
EPIDURAL SPINAL CORD STIMULATION



Restorative neurosurgery

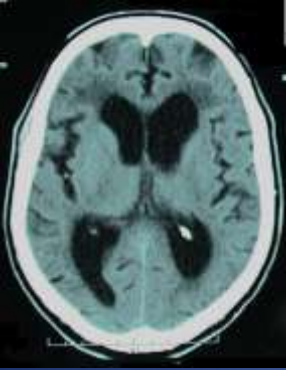
EPIDURAL SPINAL CORD STIMULATION

- **E**ffective spinal cord stimulation (SCS) for evoking stepping movement of paralyzed human lower limbs: study of posterior root muscle reflex responses.
- K. Minassian¹, B. Jilge¹, F. Rattay¹, M.M. Pinter², F. Gerstenbrand³, H. Binder³, M.R. Dimitrijevic⁴
- **4. Baylor College of Medicine, Houston, TX,**



- **Maksymowicz W.**, Bidziński J, Koziarski A., Rakowicz M., Bacia T. : Epidural spinal electric stimulation in spasticity, pain syndromes and peripheral vascular diseases. Proceedings of International Congress on Epidural Spinal Cord Stimulation – Groningen 1989

Cooperation with Neurosurgical Dep. of Cambridge University (U.K.)

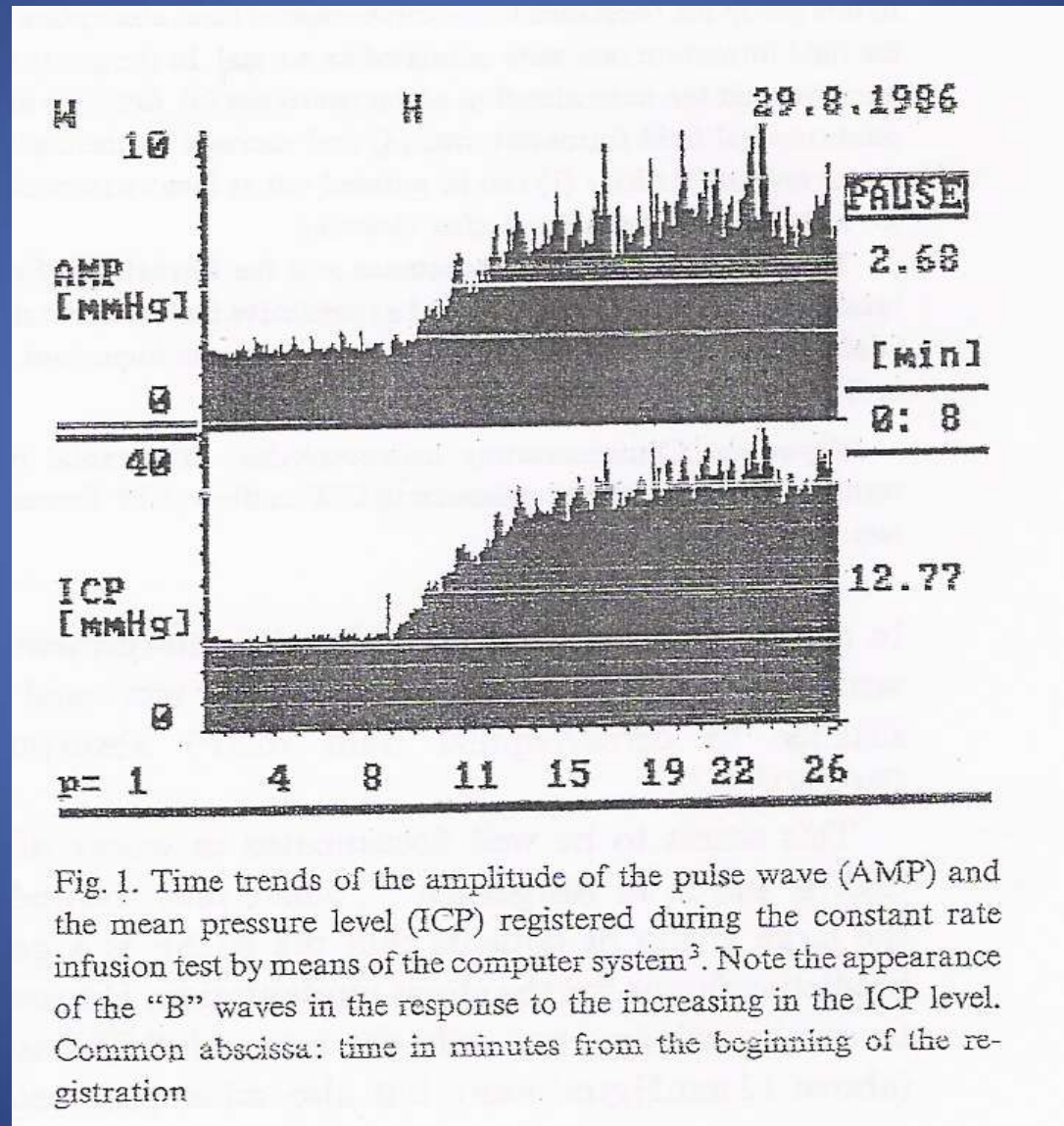


- **Maksymowicz W., Czosnyka M., Koszewski W., Szymańska A., Traczewski W.:** The role of cerebrospinal parameters in the estimation of implanted shunt system in patients with communicating hydrocephalus: preliminary report. W: Matsumoto S., Sato K., Tamaki N., Oi S. (edit.): Annual Review of Hydrocephalus, 1990, 8: 33
- **Nelson R., Czosnyka M., Pickard J.D., Maksymowicz W., Perry S., Lovick A.H.:** Experimental aspects of cerebrospinal hemodynamics: the relationship between blood flow velocity waveform and cerebral autoregulation. **Neurosurgery 1992, 31, 4: 705**

ICP analysis in hydrocephalus diagnosis



ICP analysis in hydrocephalus diagnosis



INFUSION TEST

*It is necessary to begin from the delivery
the new ideas to our neurosurgical
brain.*



Stem cells for neurology and neurosurgery ???

1. Is possible the neuronal differentiation of the stem cells?
2. Could SC be used for the treatment of **injured spinal cord or brain**?
3. Could SC be used for the treatment of **other brain or spine degeneration**?
4. Could SC be used for the treatment of **peripheral nerves injury**?
5. Could SC be used for the treatment of **brain tumors**?
6. Could SC be used for the treatment of **degenerated intervertebral discs** ?

Restorative neurosurgery

Warsaw research.

Stem cells for neurosurgery

- Habich A., Jurga M., Markiewicz I., Lukomska B., Bany-Laszewicz U., Domanska-Janik K. (2006) Early appearance of stem/progenitor cells with neural-like characteristics in human cord blood mononuclear fraction cultured in vitro. *Exp Hematol* 34:914-925
- Jurga M., Markiewicz I., Sarnowska A., Habich A., Kozłowska H., Lukomska B., Buzanska L., Domanska-Janik K. (2006) Neurogenic potential of human umbilical cord blood - neural-like stem cells depends on their previous long-term culture conditions. *J Neuros Res* 83:627-637
- Jurga M., Buzanska L., Malecki M., Habich A., Domanska Janik K. (2006) Function of ID1 protein in human cord blood-derived neural stem-like cells. *J Neurosc Res* 84(5):993-1002
- Buzanska L., Jurga M., Stachowiak E. K., Stachowiak M. K., Domanska Janik K. (2006) Neural stem like cell line derived from nonhematopoietic population of human umbilical cord blood. *Stem Cell and Development* 15(3):391-406
- Buzanska L., Jurga M., Domanska Janik K. (2006) Neuronal differentiation of human umbilical cord blood neural stem cell line. *Neurodegenerative Diseases* 3:19-26

Restorative neurosurgery

Stem cells for neurosurgery



STEM CELLS®

Voltage-Sensitive and Ligand-Gated Channels in Differentiating Neural Stem-Like Cells Derived from the Nonhematopoietic Fraction of Human Umbilical Cord Blood

Wei Sun, Leonora Buzanska, Krystyna Domanska-Janik, Richard J. Salvi and Michal K. Stachowiak

Stem Cells 2005;23:931-945
DOI: 10.1634/stemcells.2004-0316

This information is current as of August 21, 2007

Restorative neurosurgery

Stem cells for neurosurgery

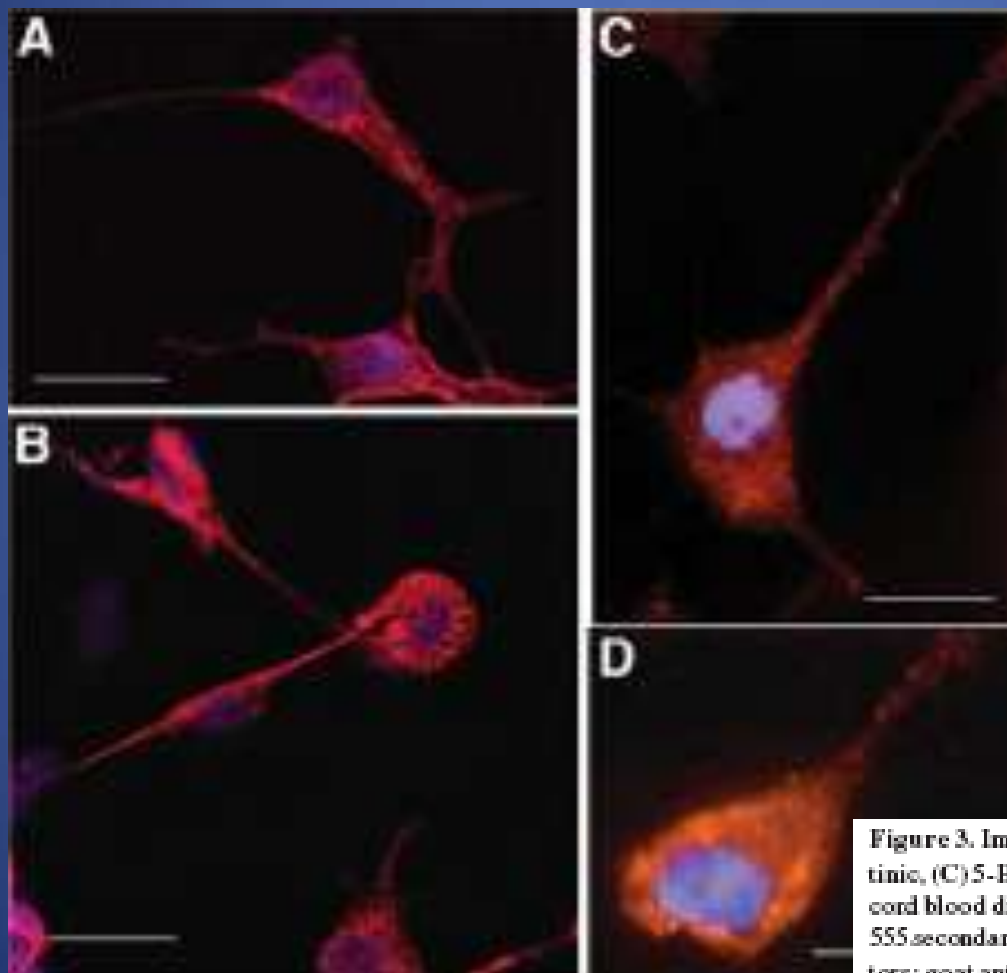
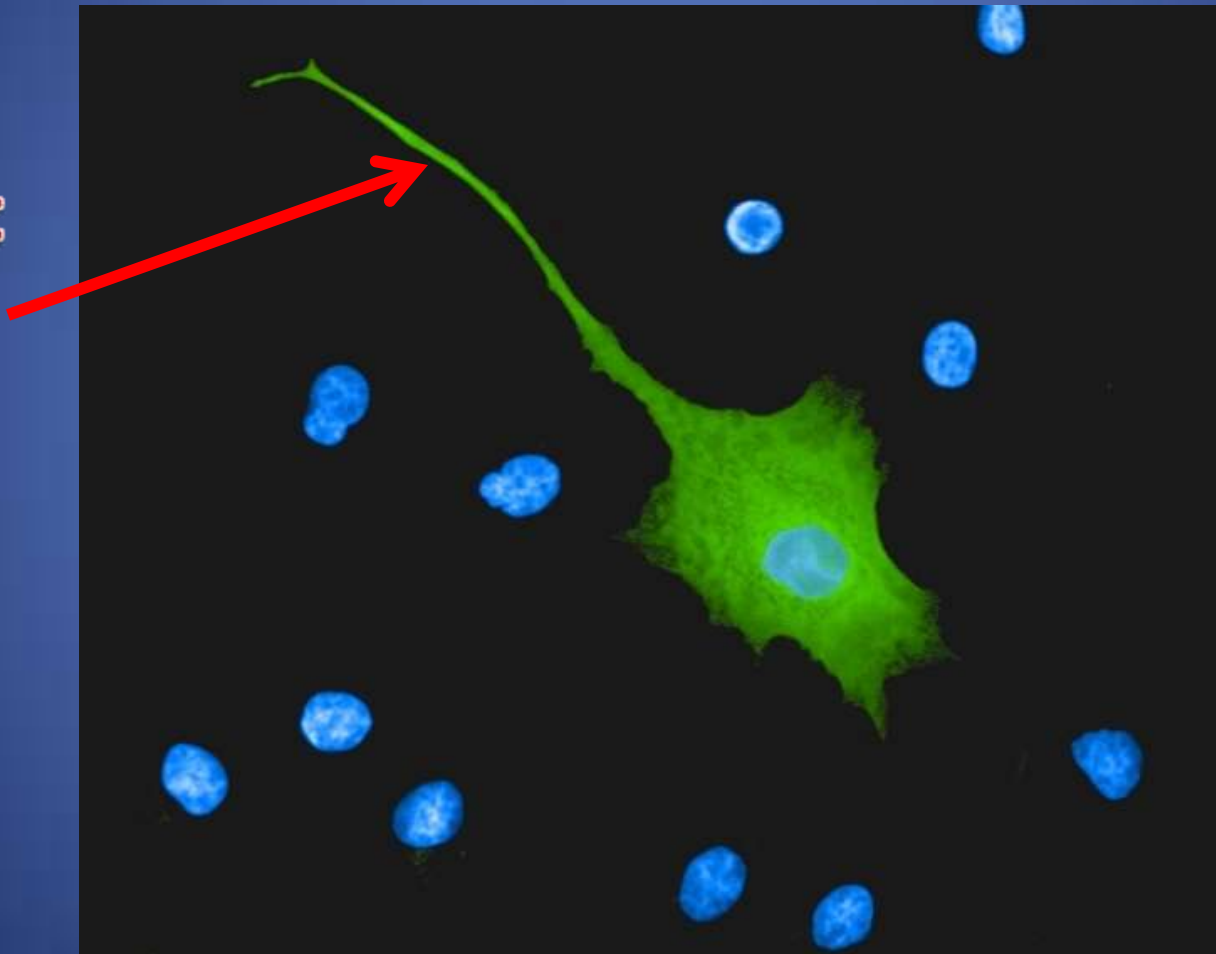


Figure 3. Immunolabeling of (A) glycine, (B) acetylcholine-nicotinic, (C) 5-HT, and (D) D2 dopamine receptors in human umbilical cord blood differentiated neural stem cells. Goat anti-mouse Alexa 555 secondary antibody used to detect acetylcholine and 5-HT receptors; goat anti-rabbit Cy3 used to detect glycine and D2 receptors. Nuclei stained with ToPro-1. Scale bar: 50 μ M. Abbreviation: 5-HT, 5-hydroxytryptamine.

Restorative neurosurgery

Stem cells for neurosurgery

Neurit



Could SC be used for the treatment of injured spinal cord or brain?

Norman Ende MD Capt. MC USNR (ret)
Professor of Pathology and Laboratory Medicine

Kenneth G. Swan, MD Col. MC USAR (ret)
Professor of Surgery/ Trauma

Human Umbilical Cord Blood Treatment of United States Soldiers following Neurological Injury

- I. TBI and Iraq and Afghanistan: the need for treatment
- II. Infant and fetus display increased ability to heal neurological damage

Could SC be used for the treatment of injured spinal cord or brain?

III. Evidence that cord blood can produce neurological cells

a. InVitro

Buzanska and Jurga have developed a body of literature describing in vitro neuronal differentiation of human umbilical cord blood (Buzanska et al., 2005; Buzanska et al., 2006a; Buzanska et al., 2006b; Jurga et al., 2006a; Jurga et al., 2006b). Mononuclear cells isolated from whole human umbilical cord have been able to develop neural precursors in vitro (Kogler et al., 2004). Interestingly, Sun reports that he can develop neural cells by invitro culture of the nonhematopoietic fraction of human umbilical blood (Sun et al., 2005).

Could SC be used for the treatment
of injured spinal cord or brain?



Not only „Hardware”

Could SC be used for the treatment of injured spinal cord or brain?

IX. Conclusion

There is solid evidence that cord blood cells can both produce neural cells in vitro and provide protective support following neurological trauma. Furthermore, there is strong evidence that cord blood cell transfusions, frozen or fresh, are safe or safer than blood transfusion from an adult donor.

With the larger number of neurological injured marines and soldier, failure to attempt to improve their recovery via a very safe procedure could be considered a tragedy.

Norman Ende MD Capt. MC USNR (ret)
Professor of Pathology and Laboratory Medicine

Kenneth G. Swan, MD Col. MC USAR (ret)
Professor of Surgery/ Trauma



Could SC be used for the treatment of other brain or spine degeneration?

- Stroke
- Parkinson disease
- Amyotrophic Lateral Sclerosis (ALS)

Could SC be used for the treatment of other brain or spine degeneration?

Stroke

H. Kozłowska, J. Jabłonka, M. Janowski, M. Jurga, M. Kossut, K. Domańska-Janik:

„Transplantation of Novel Human Cord Blood-Derived Neural-Like Stem Cell Line in a Rat Model of Cortical Infarct.” Stem Cells and Development. 2007, 16(3): 481-488. doi:10.1089/scd.2007.9993.

Could SC be used for the treatment of brain tumors?



Could SC be used for the treatment of malignant brain tumors?

Molecular Cancer

BioMed Central

Review

Open Access

Mismatch repair deficiencies transforming stem cells into cancer stem cells and therapeutic implications

Minal Vaish*

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Published: 2 April 2007

Received: 20 March 2007

Molecular Cancer 2007, 6:26 doi:10.1186/1476-4598-6-26

Accepted: 2 April 2007

For the exceptional self-renewal capacity, regulated cell proliferation and differential potential to a wide variety of cell types, the stem cells must maintain the intact genome. The cells under continuous exogenous and endogenous genotoxic stress accumulate DNA errors, drive proliferative expansion and transform into cancer stem cells with a heterogeneous population of tumor cells. These cells are a common phenomenon for the hematological malignancies and solid tumors. In response to DNA damage, the complex cellular mechanisms including cell cycle arrest, transcription induction and DNA repair are activated. The cells when exposed to cytotoxic agents, the apoptosis lead to cell death. However, the absence of repair machinery makes the cells resistant to tumor sensitizing agents and result in malignant transformation. Mismatch repair gene defects are recently identified in hematopoietic malignancies, leukemia and lymphoma cell lines. This review emphasizes the importance of MMR systems in maintaining the stem cell functioning and its therapeutic implications in the eradication of cancer stem cells and differentiated tumor cells as well. The understanding of the biological functions of mismatch repair in the stem cells and its malignant counterparts could help in developing an effective novel therapies leaving residual non-tumorigenic population of cells resulting in potential cancer cures.

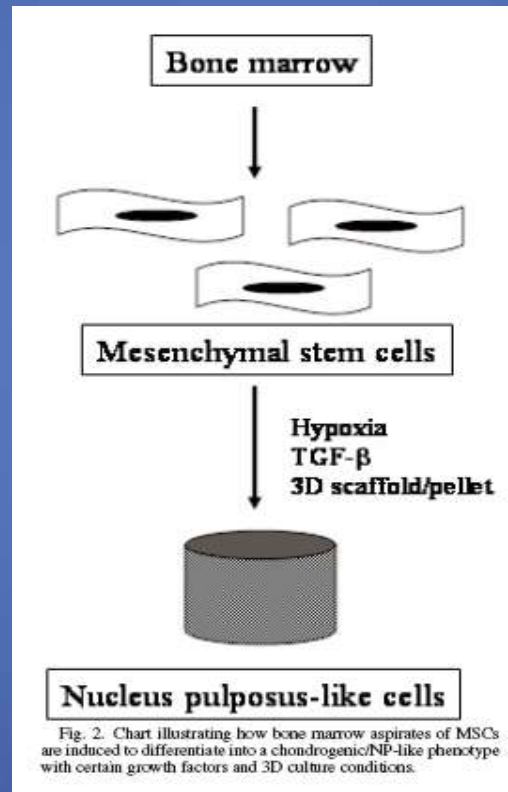
Could SC be used for the treatment of malignant brain tumors?

Neural SCs possess robust tropism for infiltrating tumor cells



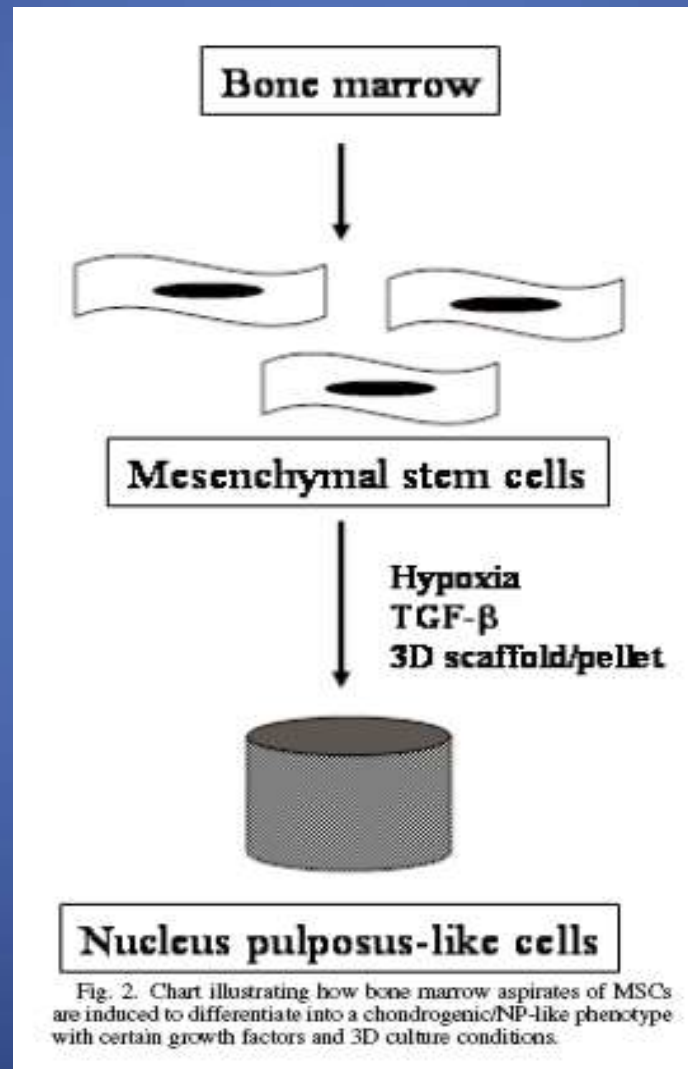
NSCs can be used to deliver therapeutic agents directly to tumor satellites, with significant therapeutic benefit

Could SC be used for the treatment of degenerated intervertebral discs

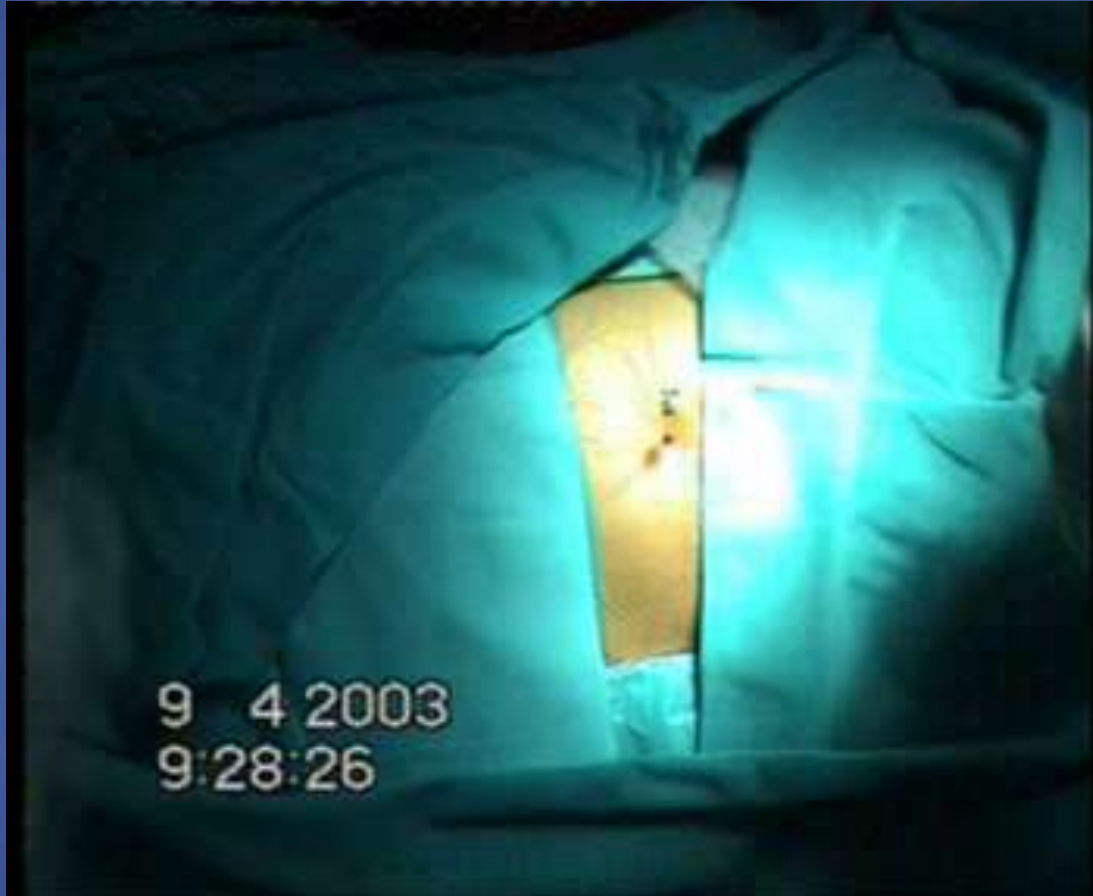


PLDD effect – own material

Could SC be used for the treatment of degenerated intervertebral discs ?

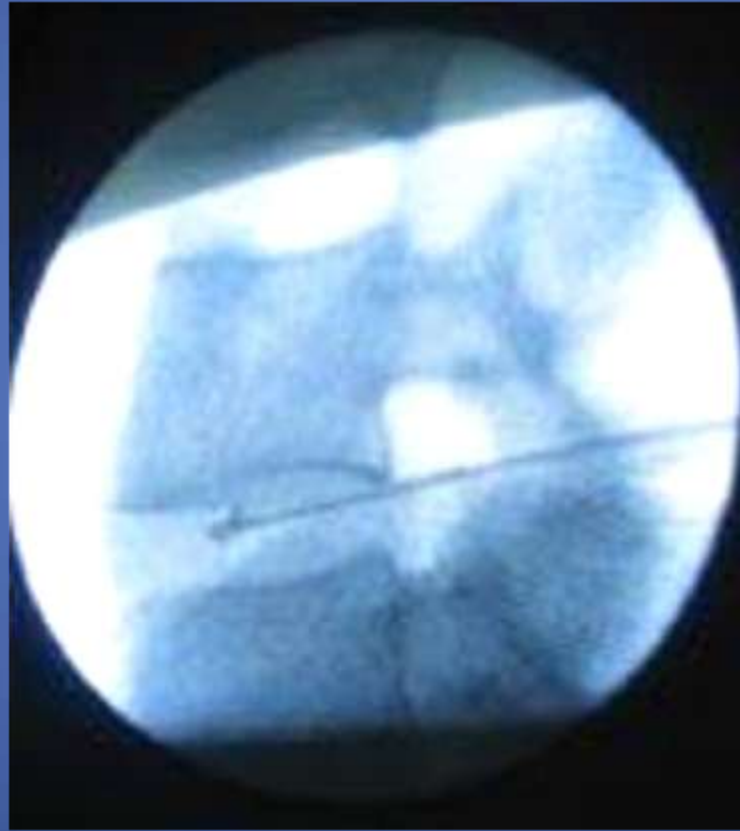


Could SC be used for the treatment of degenerated intervertebral discs ?



Original way of Stem Cells implantation to the
Nucleus Pulposus

Could SC be used for the treatment of degenerated intervertebral discs ?



Discographic image – own material

Cardiovascular diseases

Transvascular or direct application



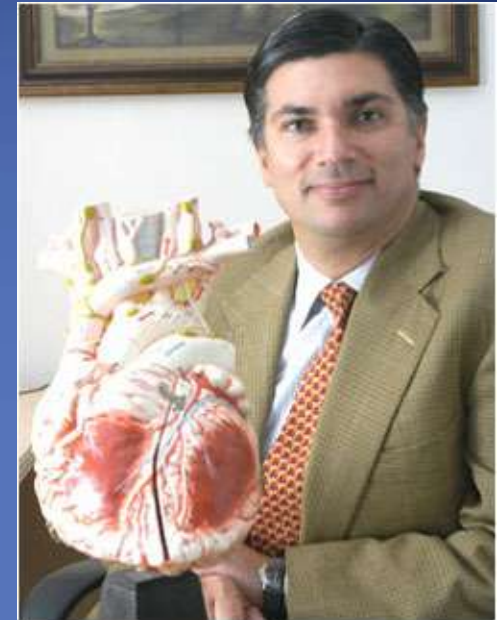
SELECTED HEART CELL-THERAPY TRIALS

Trials of bone-marrow cells dominate the field of heart stem-cell therapy. All except the Osiris trial use patients' own cells.

Sponsor	Cell type	Phase	Expected enrolment
Bioheart, Munich, Germany	Skeletal myoblasts	II/III	390
Osiris Therapeutics, Columbia, Maryland	Mesenchymal stem cells	II	220
Cedars-Sinai Medical Center, Los Angeles, California	Cells from heart biopsies	I	30
Ministry of Health, Brazil	Bone-marrow cells	III	300
Johann Wolfgang Goethe University Hospitals, Frankfurt, Germany	Bone-marrow cells	III	200
Barts and The London NHS Trust, UK	Bone-marrow cells	II/III	165
Seoul National University Hospital, Korea	Circulating blood cells	II/III	116

Source: clinicaltrials.gov

Cardiovascular diseases



Joshua Hare, of the University of Miami in Florida, says his team will soon report results from a phase II trial of mesenchymal stem cells, run by Osiris Therapeutics of Columbia, Maryland, showing that the cells both engraft as new cardiomyocytes and help through the paracrine effect.

SCs for the treatment of skin defects



Dr. Maria Michejda important advices.



- Preparation of Fetal SCs for implantation
- Ethical advices

Dr. M. Michejda (right)
Dr. E. Buda-Określak –
president of PAHA (left)



GEORGETOWN UNIVERSITY MEDICAL CENTER

Center for Interdisciplinary Studies of Immunology

Restorative neurosurgery

Stem cells for neurosurgery

**Is possible the neuronal
differentiation of the stem cells?**



**The Warsaw Research Group
Prof. K. Domanska-Janik and the staff
from Polish Academy of Science,
Department of Neurorepair
Warsaw**

Groundbreaking **research**

It's Happening Here. UofL is shaping the future of health sciences research in Louisville. [FIND OUT HOW](#) ▶



- **Researchers find adult cells that mimic embryonic stem cells**
- December 12th, 2005
- **Researcher Mariusz Ratajczak - director of the stem cell biology program at U of Louisville James Graham Brown Cancer Center, who led the research project.**



Multicenter study on Stem Cells coordinatesd by Medical University in Szczecin (prof. Ratajczak)



2009-08-20 (23:54)

**NATO Anniversary Celebration in Szczecin at Waly Chrobrego,
September 19th–20th Multinational Corps Northeast (MNC NE) with its
Headquarters (HQ) located in the Baltic Barracks in Szczecin is a part of
the NATO Force Structure.**



Hemopoietic Stem Cells
Transplantation Ward

Department
of Transplantology

Stem Cell
Excellence Centre

**KRAKOW
JAGIELLONIAN
UNIVERSITY**



Head - Marcin
Majka MD, PhD

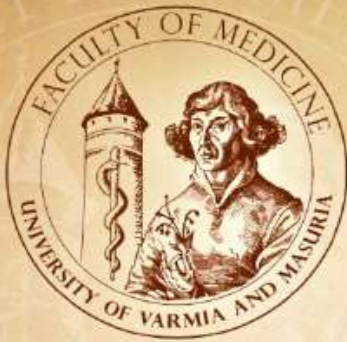


Instytut Kardiologii

im. Prymasa Tysiąclecia Stefana Kardynała Wyszyńskiego



- **Assessing the efficacy and safety of using intracoronary autologous bone marrow transplantations in treating patients with early post-infarction left ventricular dysfunction.**



UNIVERSITY OF WARMIA AND MASURIA IN OLSZTYN

FACULTY OF MEDICINE

ENGLISH DIVISION

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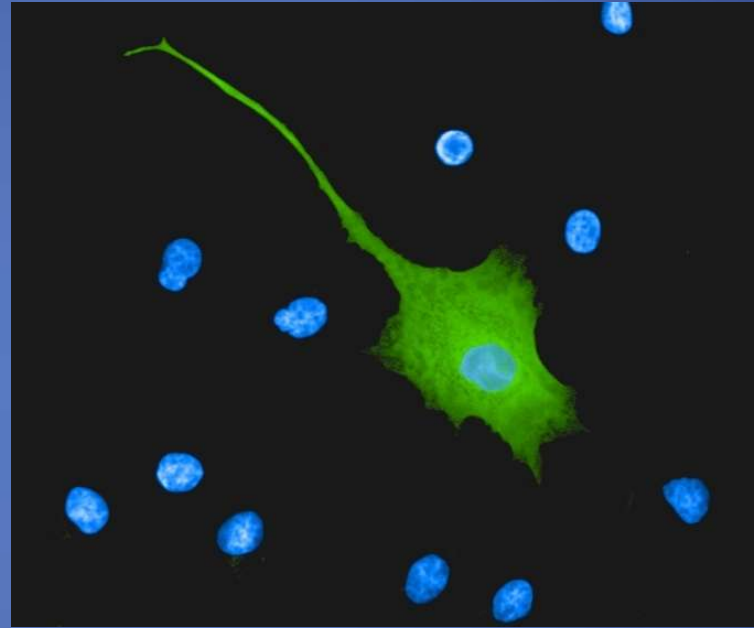
www.uwm.edu.pl/wnm/en



**Establishing of the Stem Cells
Laboratory (the first cost= 6 mln \$)**



To promote the progress of medical sciences



Modern Stem Cells Laboratory

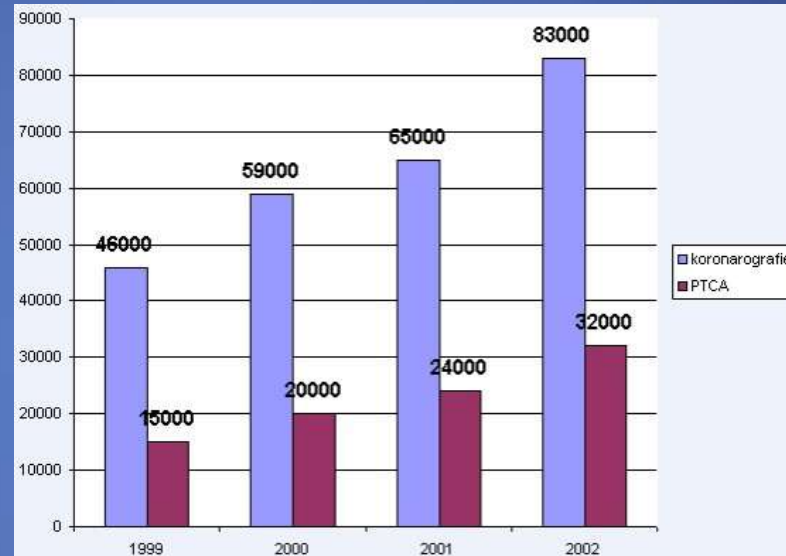
– project partly supported by EU



To promote the progress of medical sciences

Priorities:

- **Cardiology**



- **Neurology (Stroke, Degenerative diseases)**

- **Oncology**



To promote the progress of medical
sciences

Oncology

**Looking for the new
drugs against the
cancer and use of
new technologies in
pharmacotherapy**

Possible cooperation with the
Cancer Centers in Warsaw
and Gliwice



**and with the MD Anderson
Cancer Center in Houston**





promote the progress of medical sciences
**There are only few single
procedures not realised in Poland.**

There is lack of the CYBERKNIFE !



Why the Cyberknife?

- Because it is accurate stereoradiosurgery**
- Because it is stereoradiosurgery dedicated not only for the brain , but also for the treatment of the lung, spine and abdominal tumors**



To promote the progress of medical
sciences

Oncology



Bunker for Cyberknife





To promote the progress of medical sciences



NEW IDEAS CAN BE INTRODUCED IN YOUNG MEDICAL FACULTY OF OUR UNIVERSITY



To promote the progress of medical sciences



Nicolaus Copernicus who lived in Olsztyn Castel invited new medical students

To promote the progress of medical sciences



Why the first Cyberknife could be located in Olsztyn?

BECAUSE NEW IDEAS CAN BE INTRODUCED IN YOUNG MEDICAL FACULTY OF OUR UNIVERSITY AND THAN SPREAD TO OTHER REGIONS OF THE POLAND!

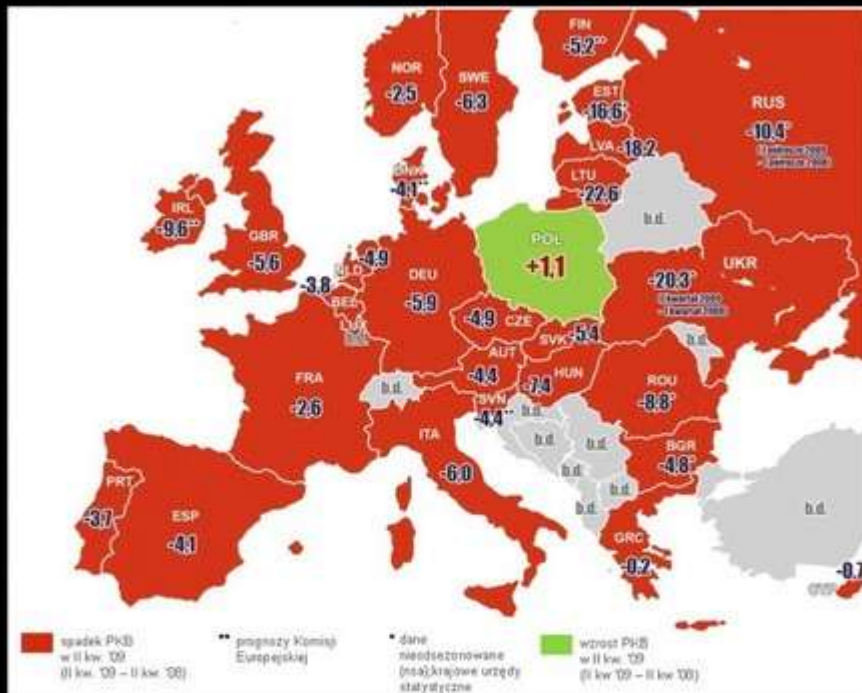
***To promote brain research in Europe
and to improve the quality of life of
those affected by brain diseases***

European Parliament

	Total in FP6	FP7 first 3 calls
Brain	260m	381m
Cancer	485m	265m
Cardiovascular	124m	111m



Poland – growing up (↑ 1,1%)



Polska

tutaj nawet kryzys się nie udał

www.demotywatory.pl

Number of students in tertiary education (in thous.)

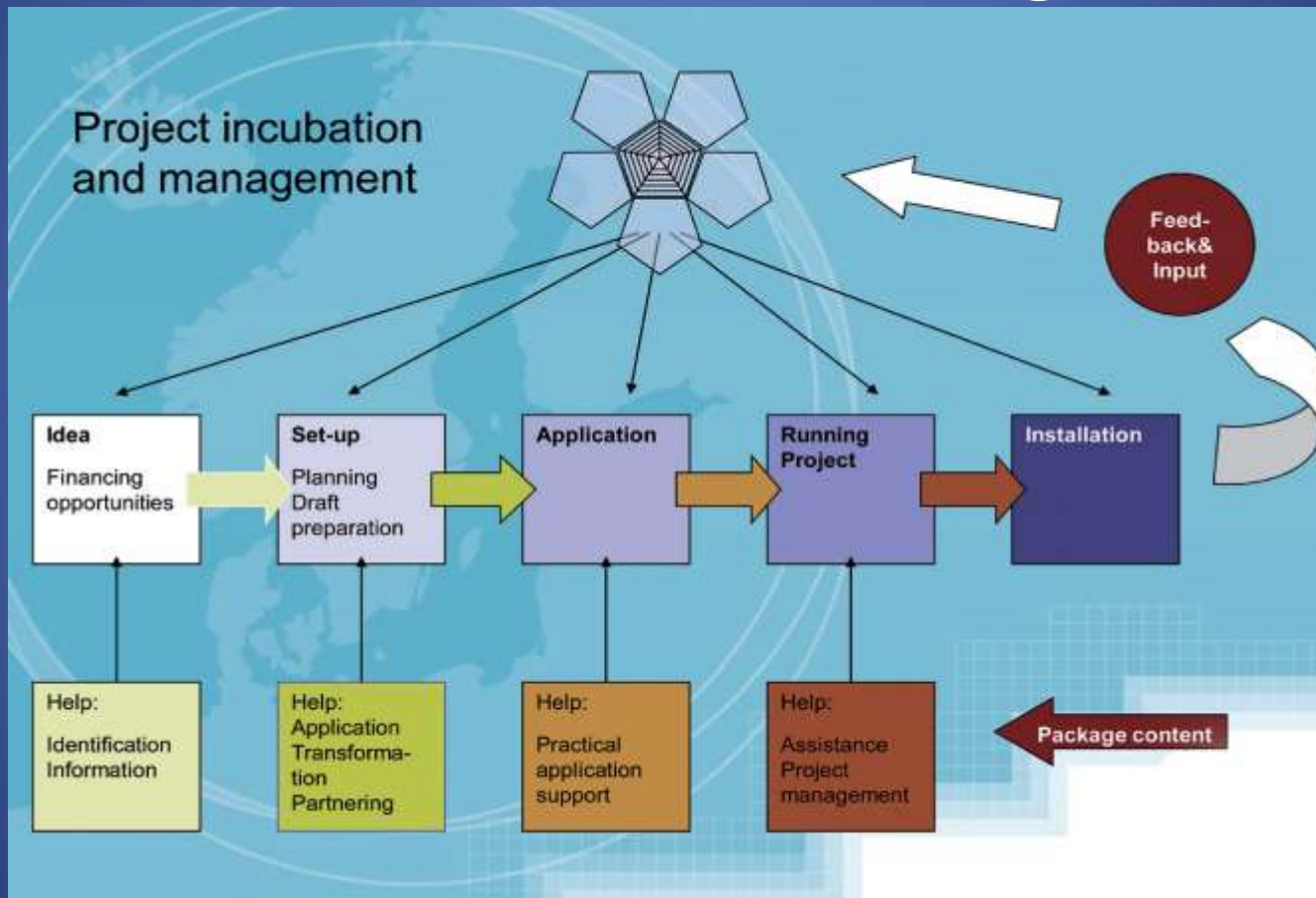




Smart Growth: Bridging Academia and SMEs in the Baltic Sea Region



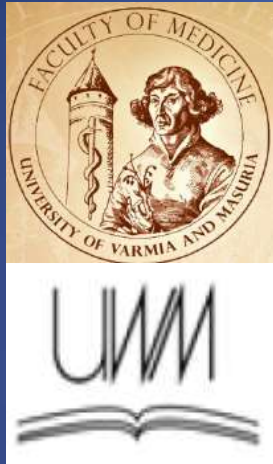
Smart Growth: Bridging Academia and SMEs in the Baltic Sea Region



Organisation of the SMS-BSS module Project
Incubation and Management
(Prepared by Wolfgang Blank, BioCon Valley, June 2009)

BaltNet

International Baltic Biomedical Research Center in Olsztyn



University of
Warmia and
Mazury in
Olsztyn



University
of Turku
(Finland)



University of Greifswald
Germany

**Invitation addressed to MD Anderson
Cancer Center in Houston**

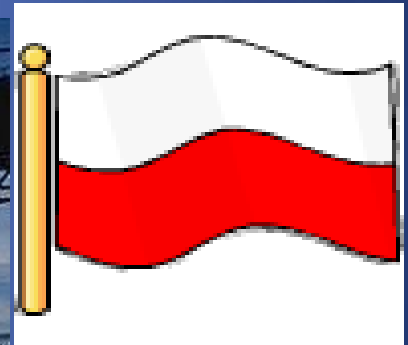
Building the bridges



Ralph Modjeski (1861-1940)
***Polish Immigrant Becomes Famous
Engineer and Bridge Builder***

He was also honored by the Pennsylvania state legislature in 1966 by a resolution citing him as one of America's "greatest inventors".

There are not only symbols



There are
needs of
cooperation

