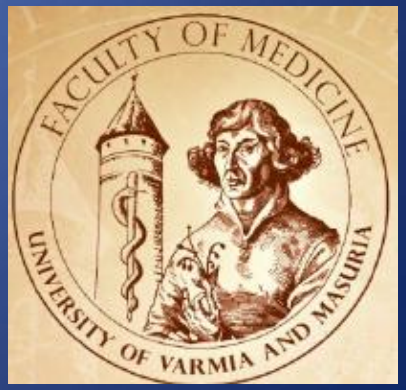
MEDICAL RESEARCH IN POLAND: OPPORUNITIES FOR COOPERATION

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 Governemental Research Medical Institutes

Cancer and …

Cardio-vascular+rheumatology

Children and mother health

Psychiatry+
Neurology+
Audiology

Public health, food and drug and occupational med

Polish Academy of Sciences
Division VI Medical Sciences

Warsaw

Institute for Medical Biology
Polish Academy of Sciences

Centre of Excellence in Medical Biology
BIOLMED

Łódź

Institute of Pharmacology
Polish Academy of Sciences
Center of Excellence in Neuropsychopharmacology - FRAM

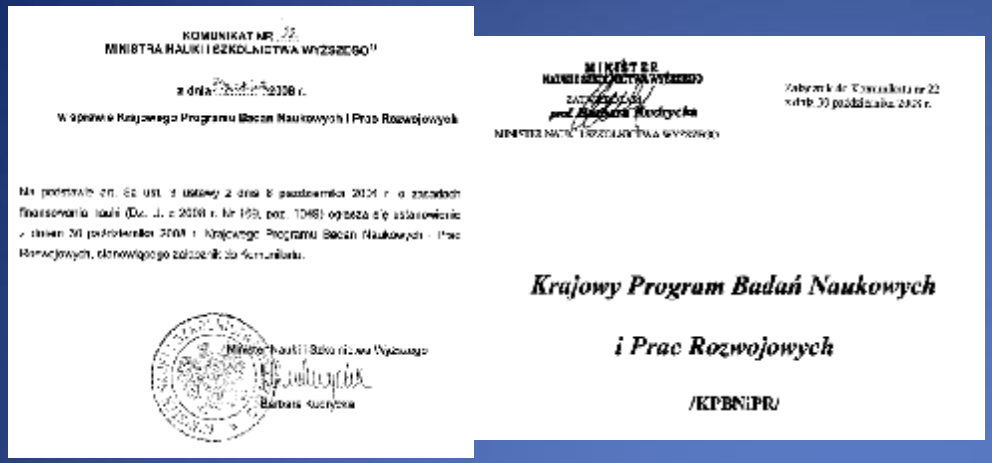
Kraków

Poznań

Ludwik Hirszfeld Institute of Immunology and Experimental Therapy

Wrocław

GOVERNEMENTAL PRIORITIES



KOMUNIKAT NR 33
MINISTRA NAUKI I SZKOLNICTWA WYŻSZEGO

z dnia [redacted] 2024 r.

w sprawie Krajowego Programu Badań Naukowych i Prac Rozwojowych

Na podstawie art. 62 ust. 1 ustawy z dnia 8 października 2024 r. o zasadach finansowania nauki (Dz. U. z 2024 r. Nr 1571, poz. 1948) ogłasza się ustanowienie z dniem 30 października 2024 r. Krajowego Programu Badań Naukowych i Prac Rozwojowych, stanowiącego załącznik do komunikatu.

Minister Nauki i Szkolnictwa Wyższego

Barbara Kudrycka

MINISTER

prof. Barbara Kudrycka

MINISTRA NAUKI I SZKOLNICTWA WYŻSZEGO

Załącznik do Komunikatu nr 33
z dnia 30 października 2024 r.

Krajowy Program Badań Naukowych

i Prac Rozwojowych

/KPBNiPR/

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

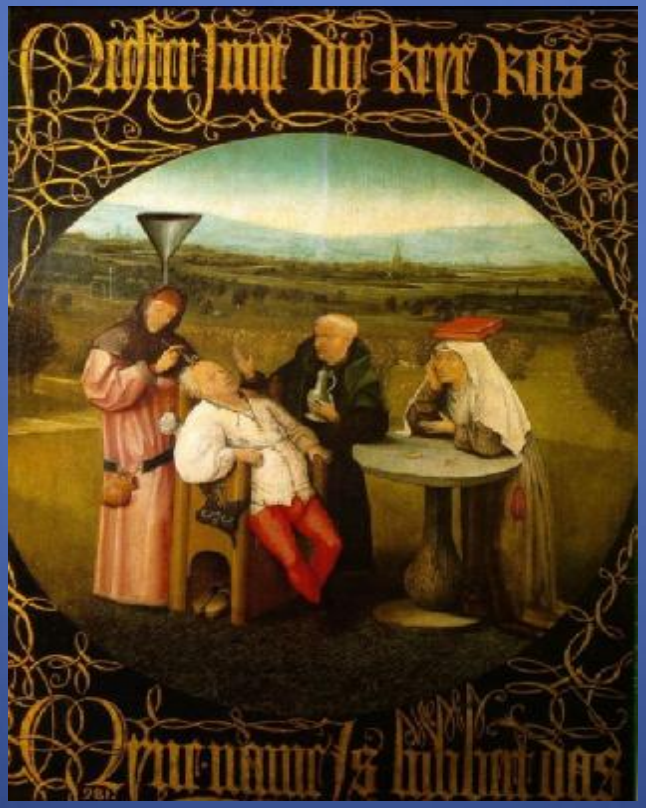
Restorative neurology.
Improving function without structural damage.

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)
Fleischl von Marxow (1890)
Beck (1890)
Danilewsky (1891)
Gotch and Horsley (1891)
Beck and Cybulski (1892)
Larinow (1898)
Trivus (1900)
Tchiriev (1904)
Kaufman (1912)
Prawdicz-Neminski (1913)
Cybulski and Macieszyna (1919)
Prawdicz-Neminski (1925)
Berger (1929)

Bartley and Newman (1930)
Bartley and Newman (1931)
Travis and Herren (1931)
Travis and Dorsey (1931)
Davis and Saul (1931)
Adrian (1931)
Adrian and Buytendijk (1931)
Bishop and Bartley (1932)
Travis and Dorsey (1932)
Fischer (1932)
Kornmüller (1932)
Perkins (1933)
Bartley (1933)
Gerard, Marshall, and Saul (1933)

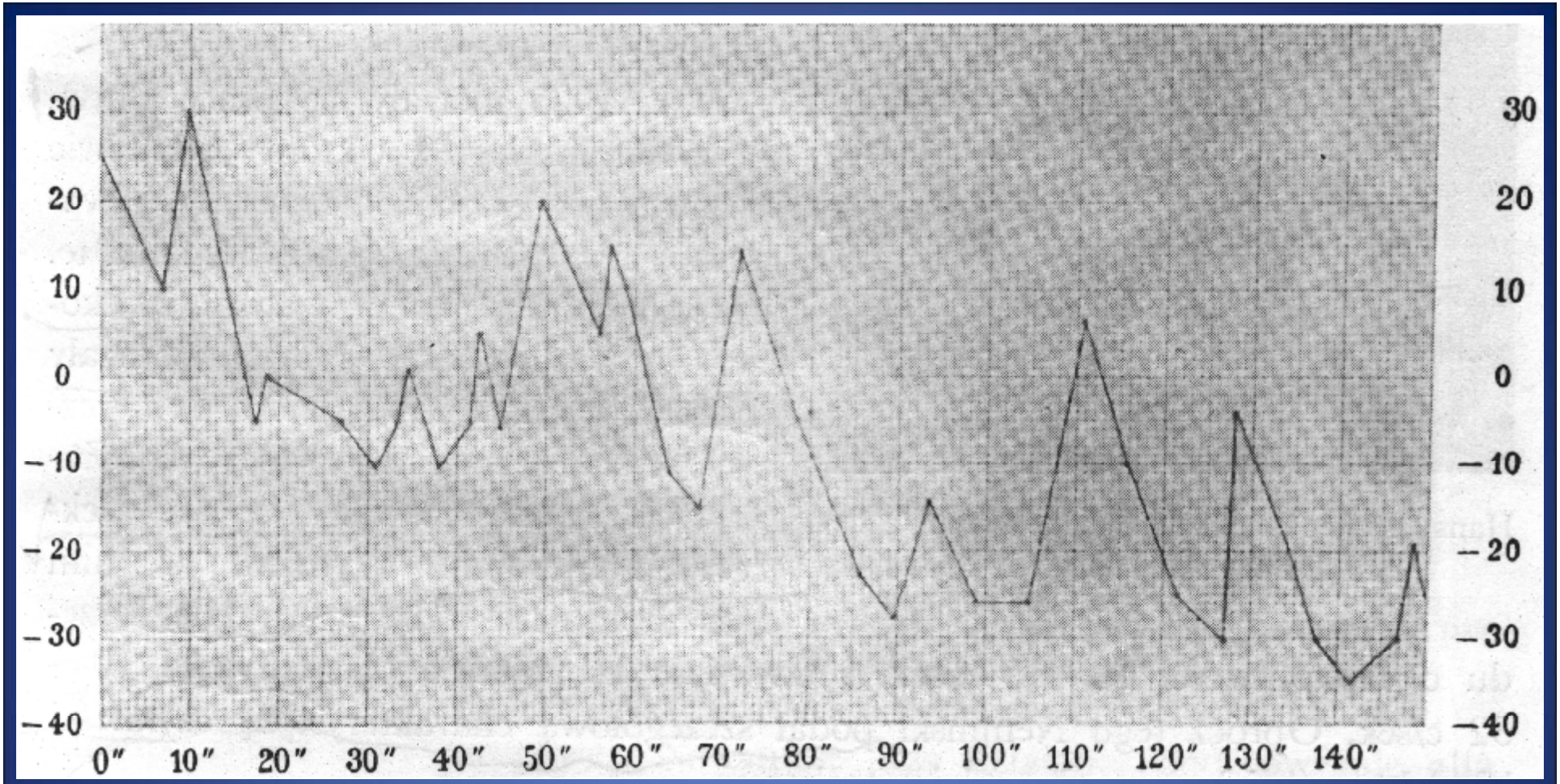
Polish
Russian
Ukrainian

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.

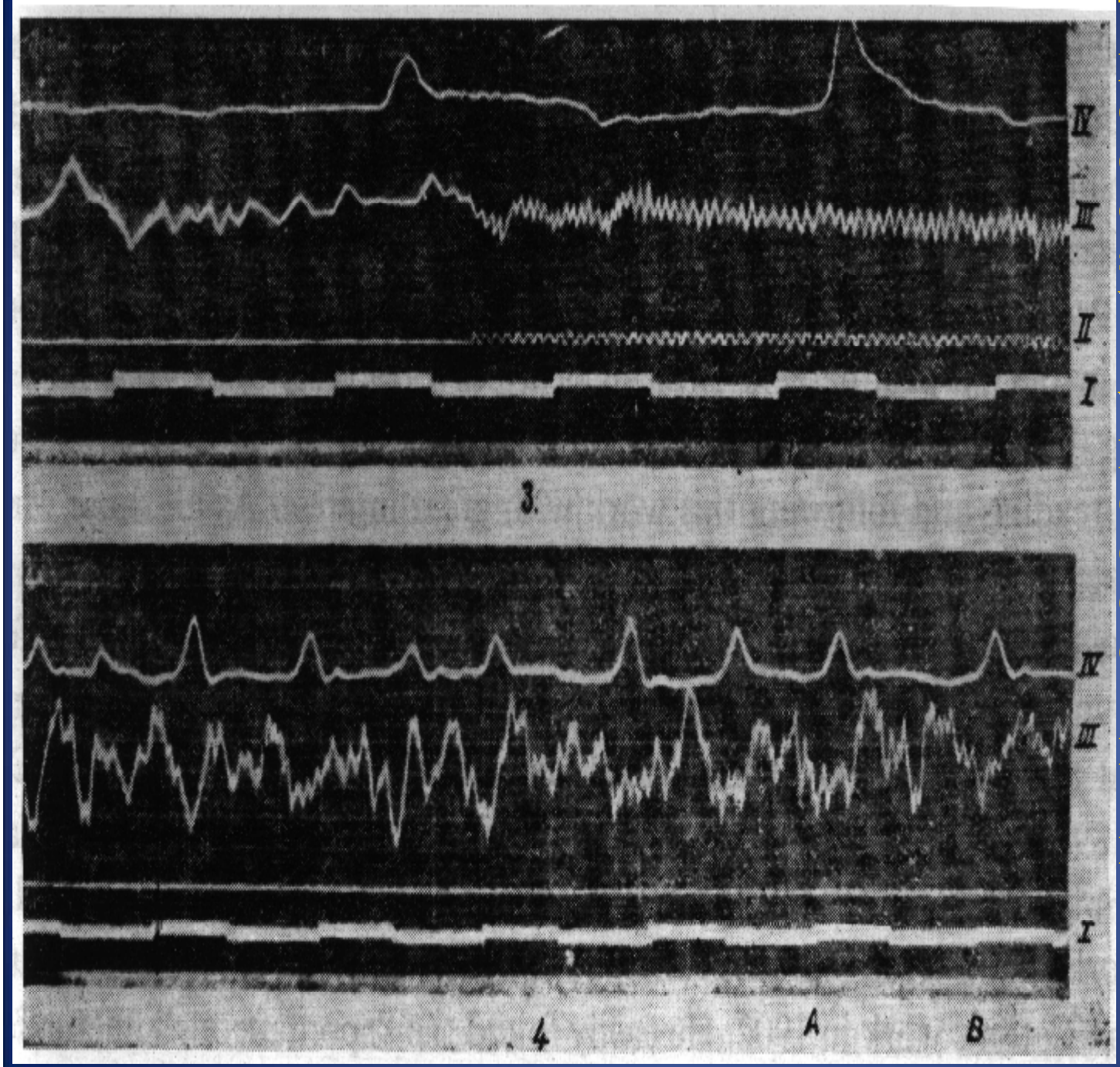
He dramatically decided to suicide in German nazi camp for Jewish people in Janowiec in 1942.



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 Nikodem Cybulski (1854- 1919)

He established the Polish School of Neurophysiology, together with Adolf Beck .
He publicated the first recording of experimental epileptic seizure in dog provocated by cortex stimulation (1914).



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

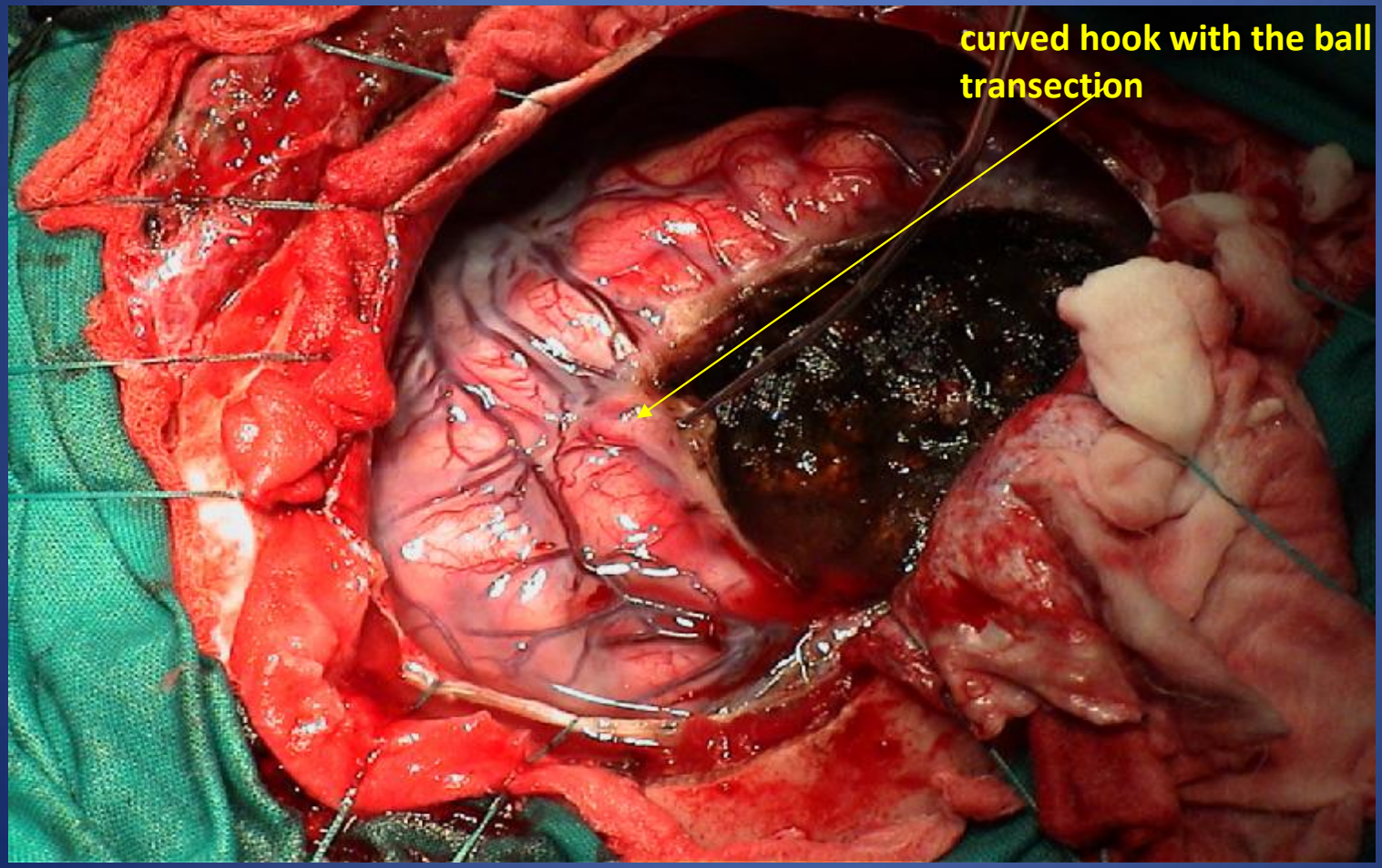
Written from right to left.
Curve IV- EKG
Curve III -cortex
Curve II - stimulus
Curve I -time

N. Cybulski and S. Jeleńska Macieszyna 1914.

Multiple Subpial Transections in the Dep. of Neurosurgery,

Central Clinical Hospital MSWiA, Warsaw

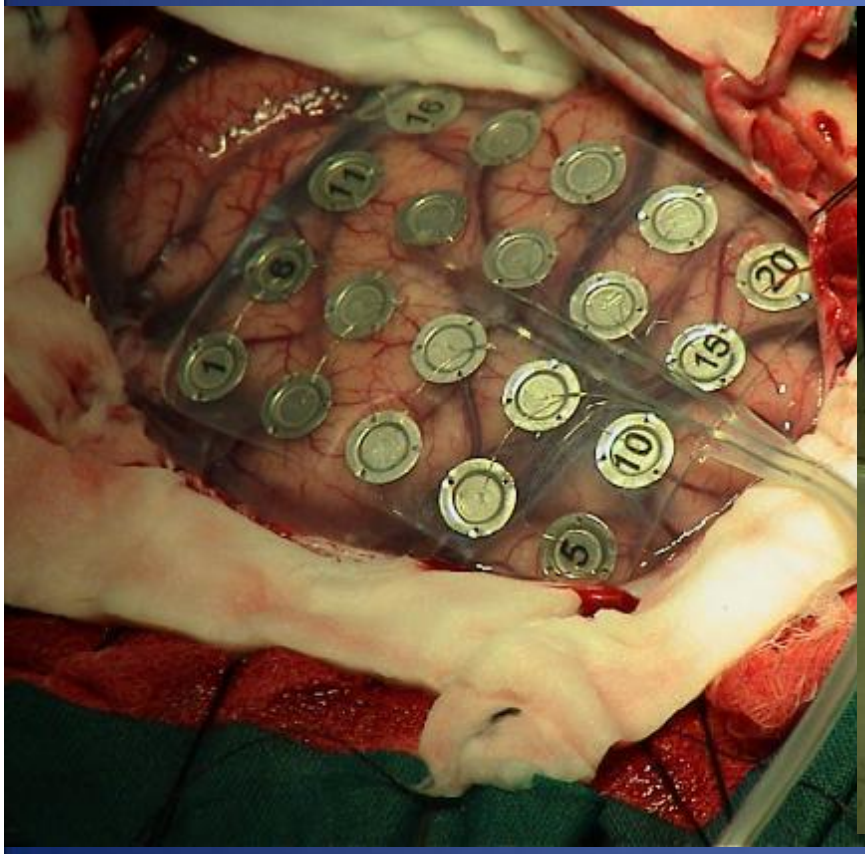
Intraoperative picture. Subpial transection following the brain resection.

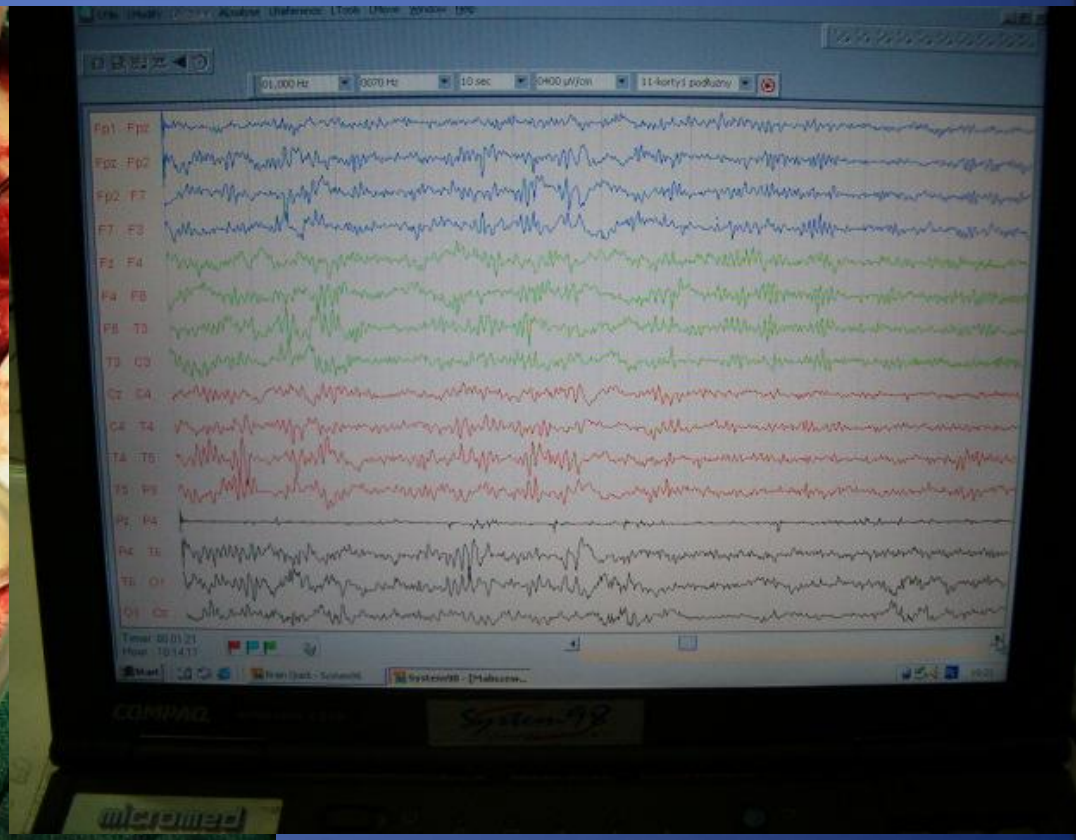


Multiple Subpial Transections in the Dep. of Neurosurgery,

Central Clinical Hospital MSWiA, Warsaw

Intraoperative ECoG recording.





Multiple Subpial Transections in the Dep. of Neurosurgery,

Central Clinical Hospital MSWiA, Warsaw

Intraoperative ECoG recording.

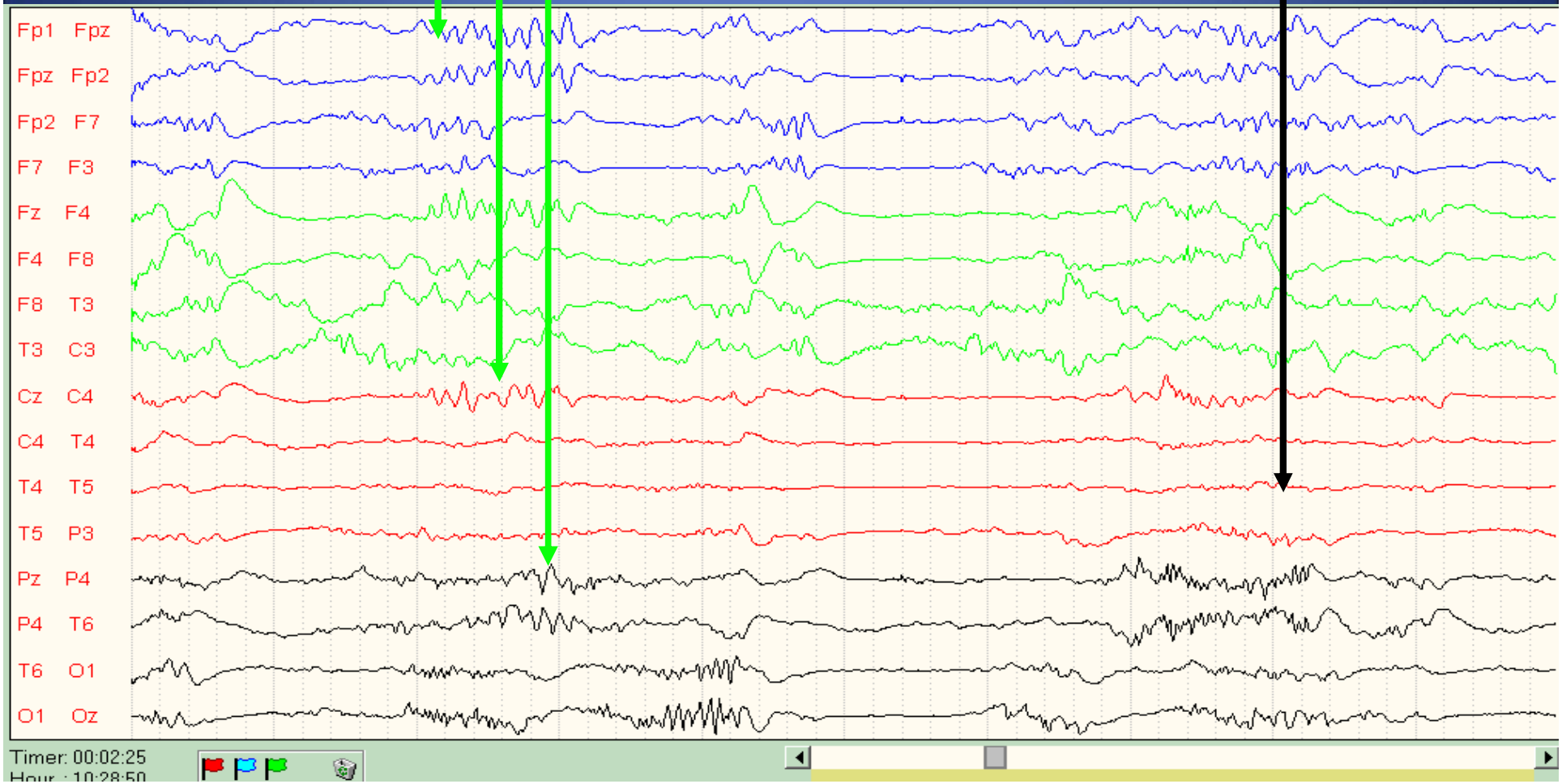
Monitoring of the ECoG following every MST

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

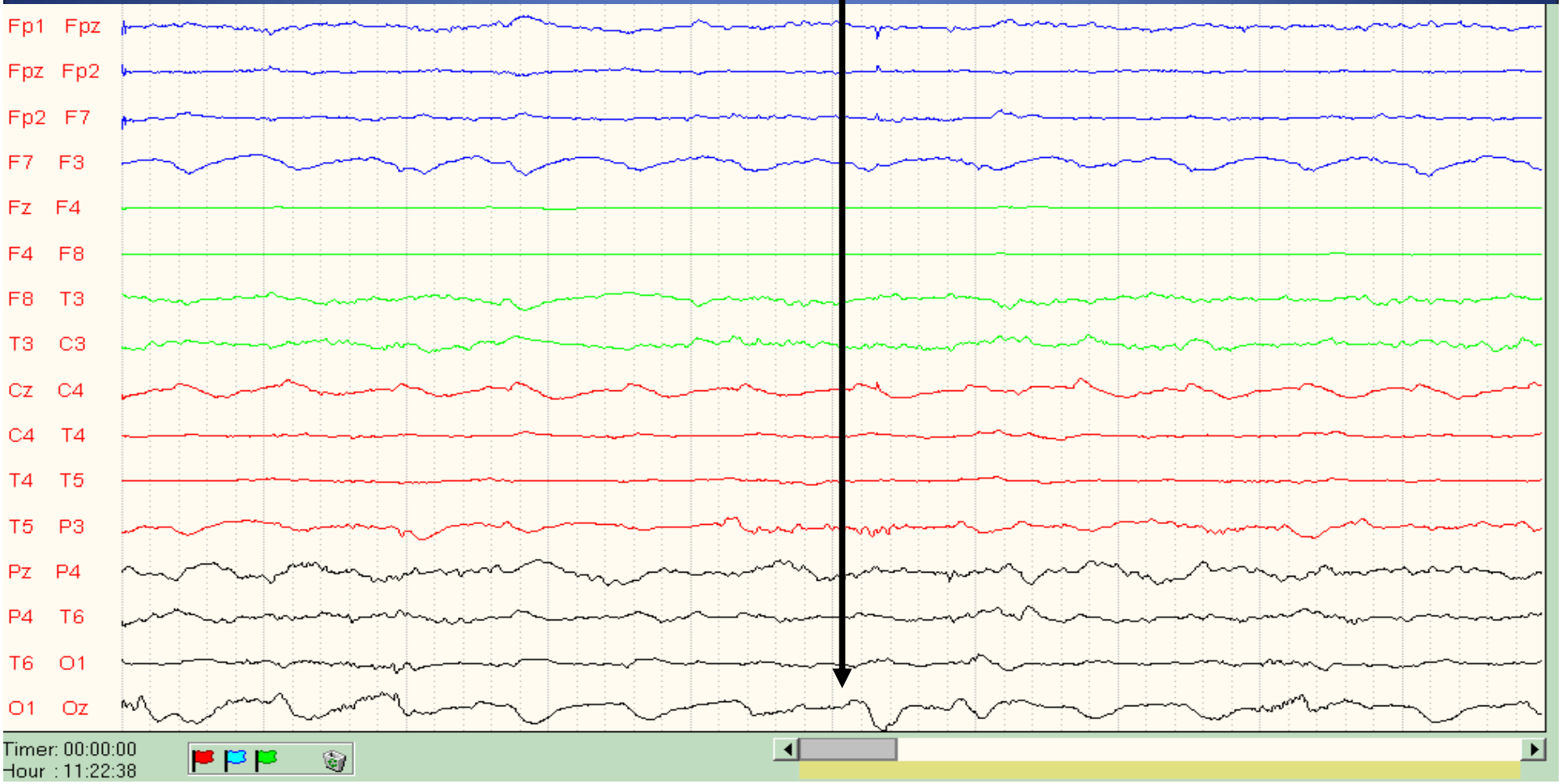


Monitoring of the ECoG following every MST

Patient R.G.

Stage 3

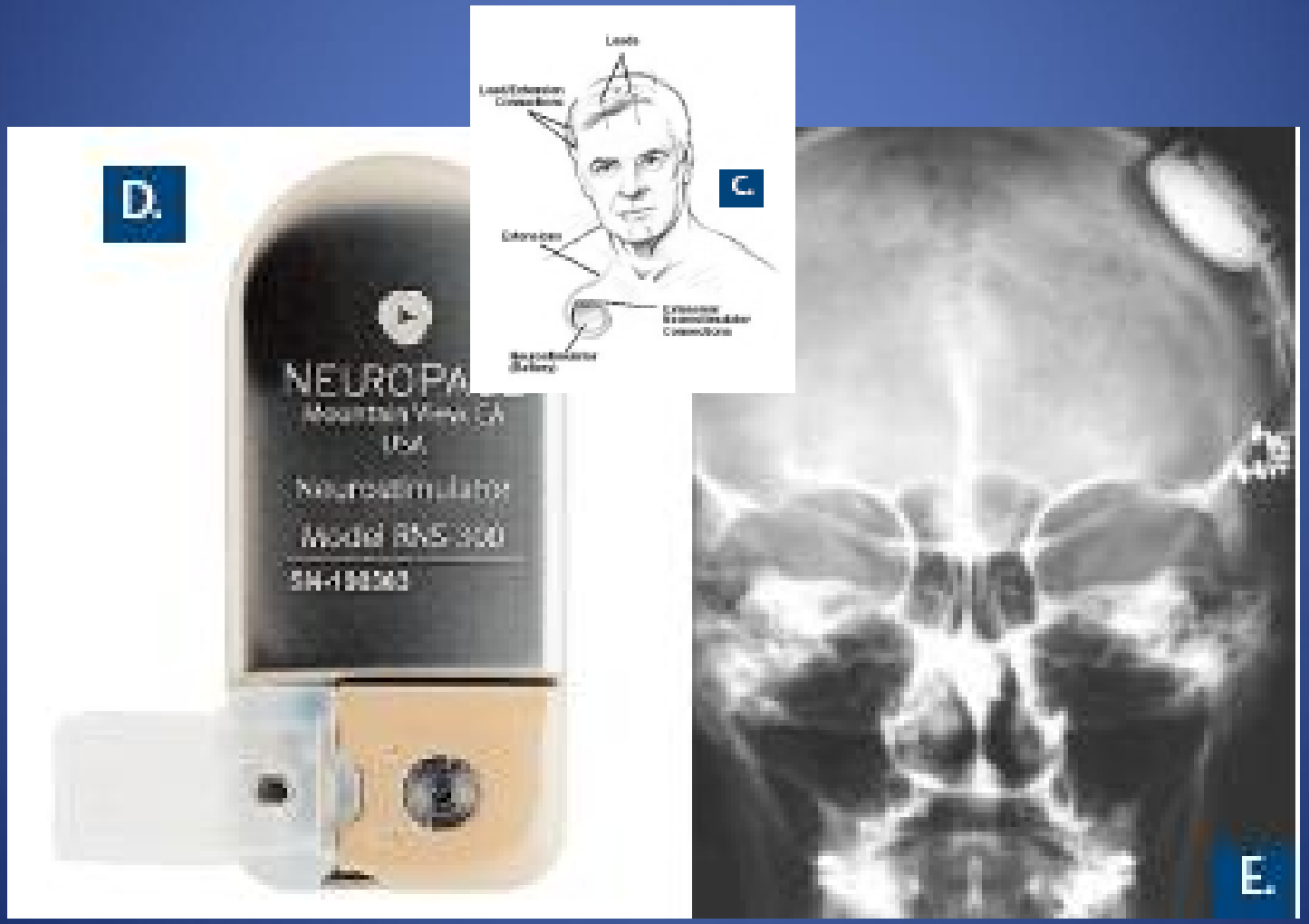
Final recording after the MST under the electrode No 20



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

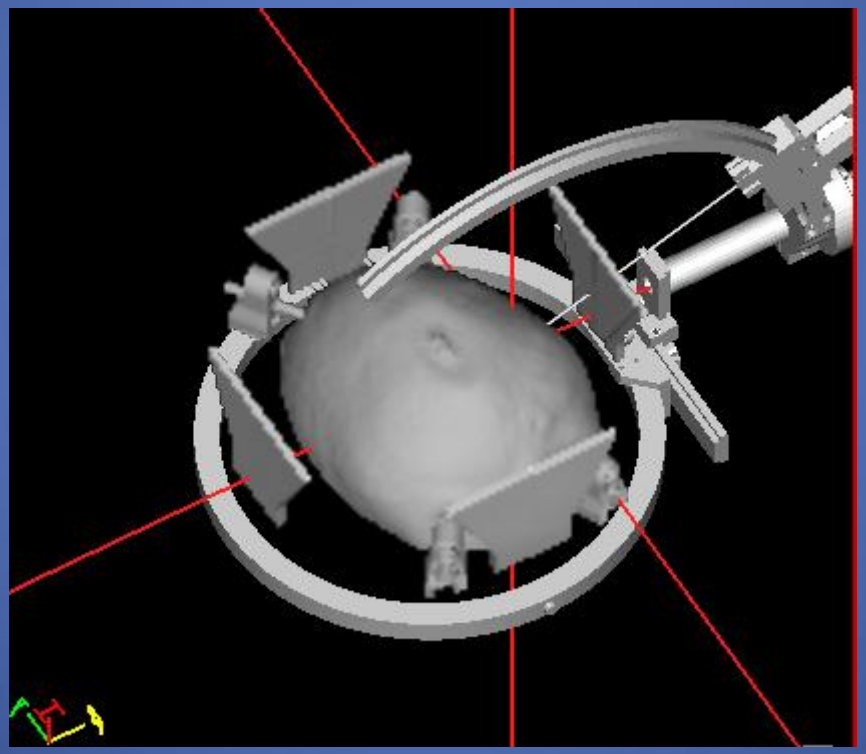
What and how to delivery ?

„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."

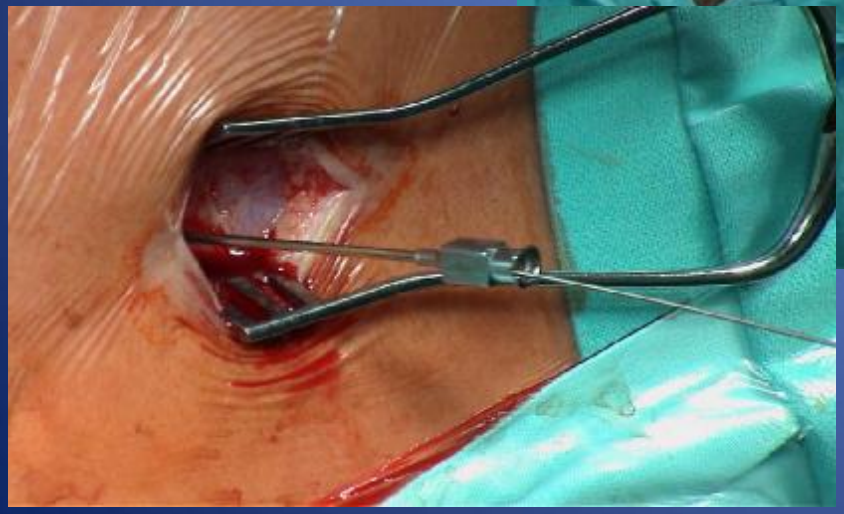
Epidural pentobarbital delivery can prevent locally induced neocortical seizures in rats: the prospect of transmeningeal pharmacotherapy for intractable focal epilepsy.

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

- **Effective 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,**

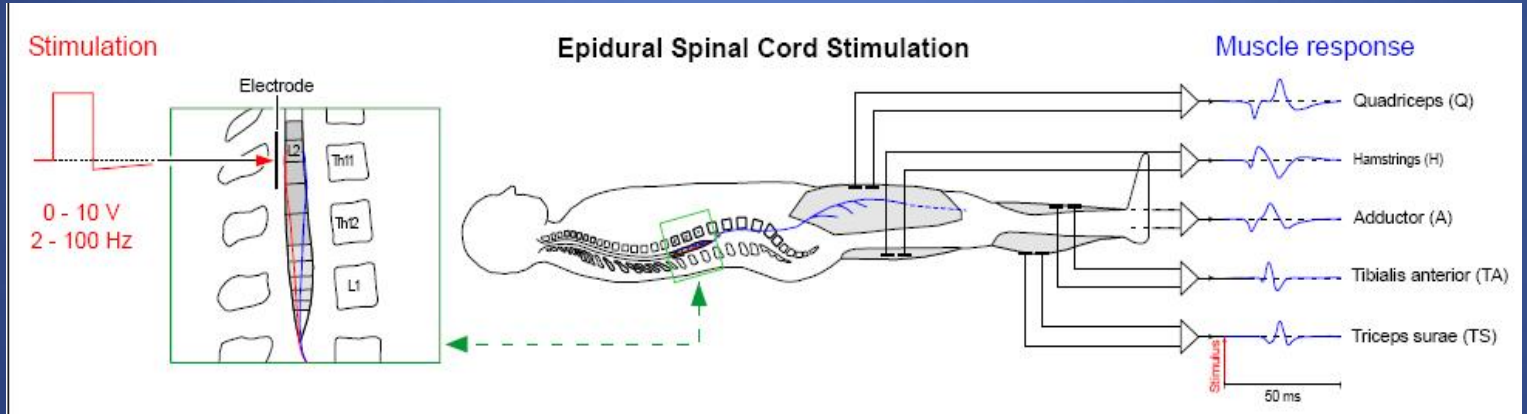
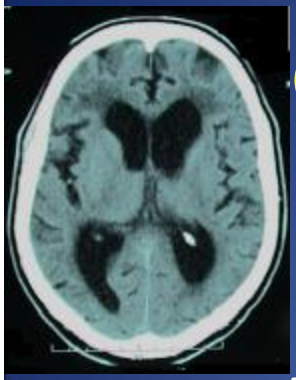


Figure 2. Illustration of the epidural spinal cord stimulation. Left side: longitudinal electrode implanted at lumbar

- **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

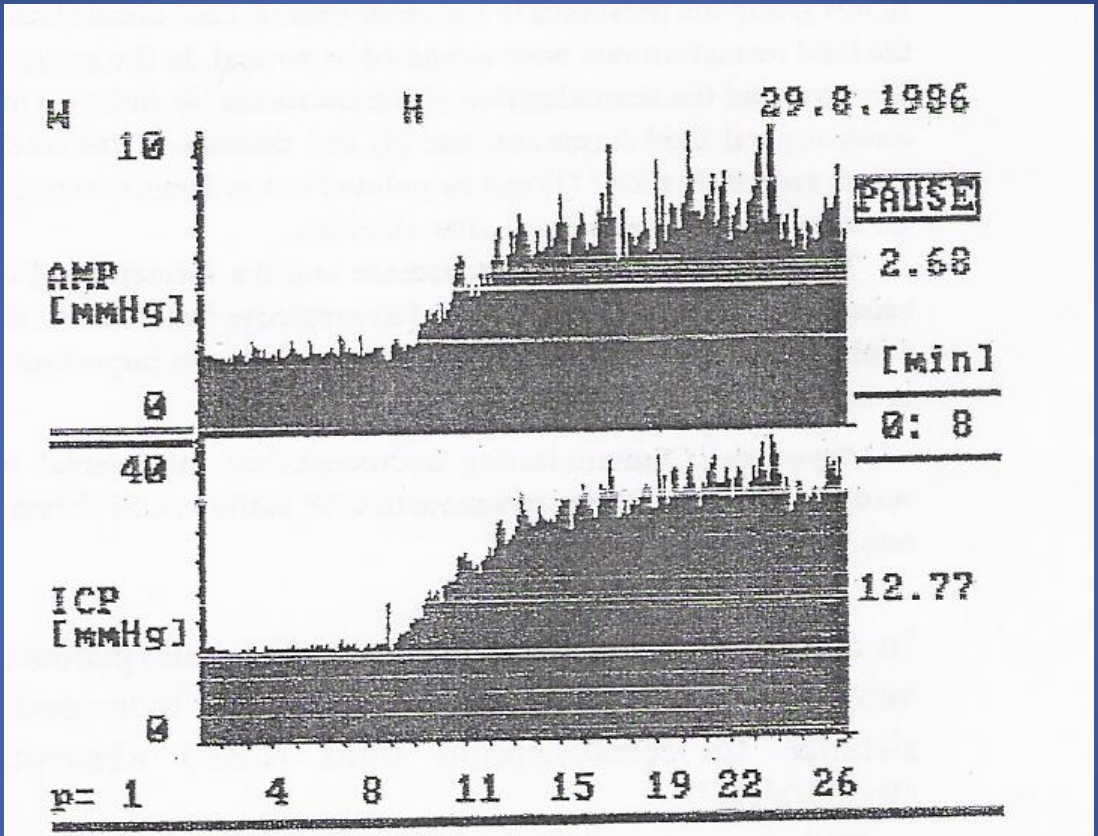
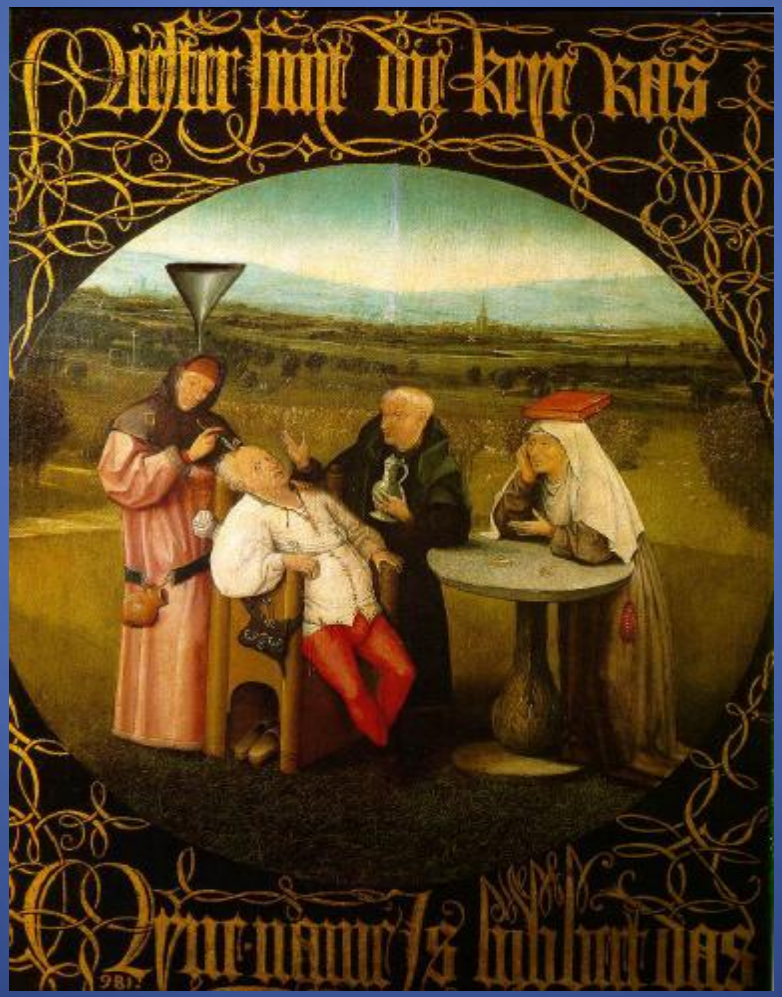


Fig. 1. Time trends of the amplitude of the pulse wave (AMP) and the mean pressure level (ICP) registered during the constant rate infusion test by means of the computer system[3]. Note the appearance of the "B" waves in the response to the increasing in the ICP level. Common abscissa: time in minutes from the beginning of the registration

INFUSION TEST

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



Restorative neurosurgery

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

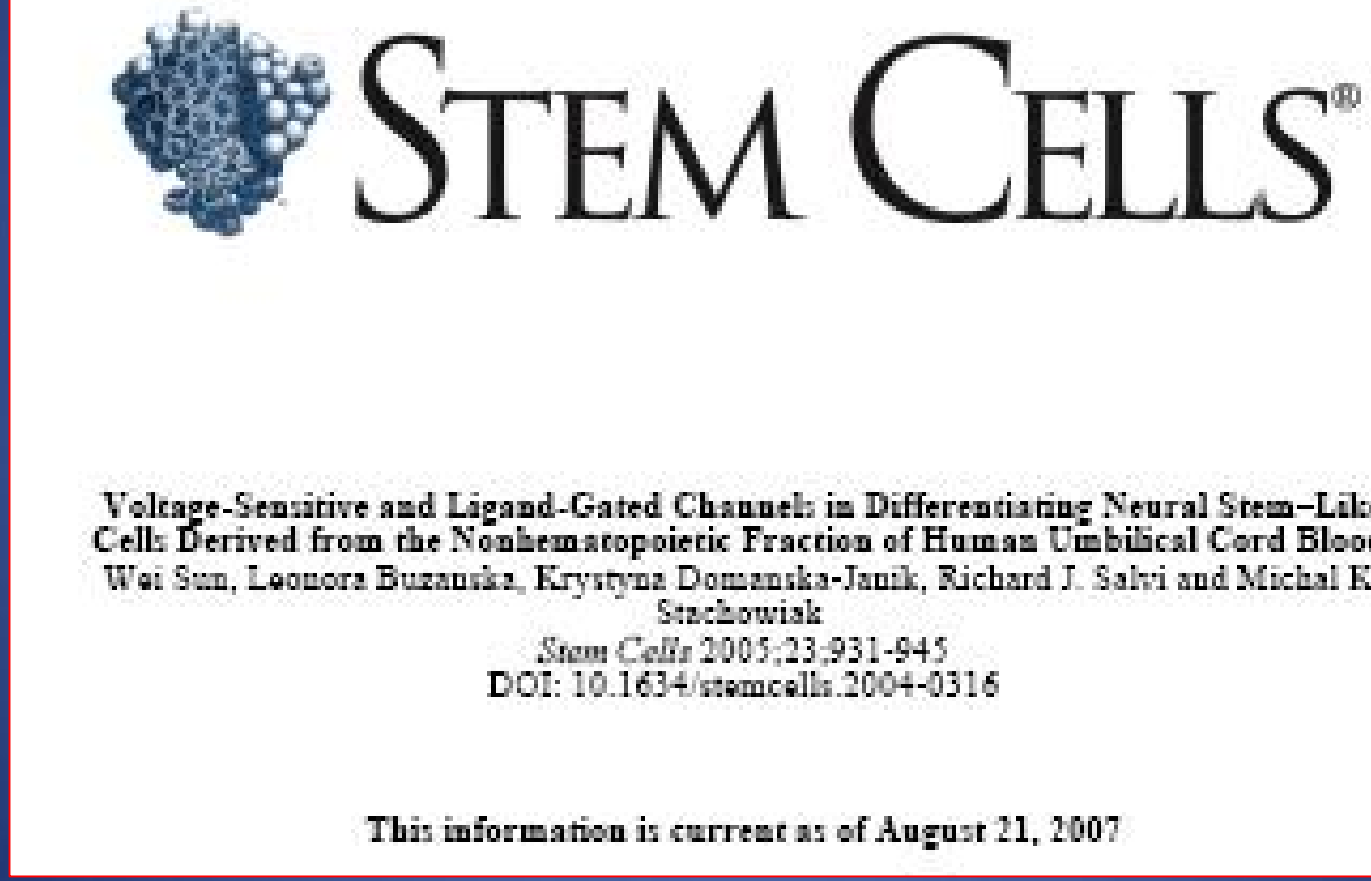
Warsaw research.

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., Kozlowska 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



Restorative neurosurgery

Stem cells for neurosurgery

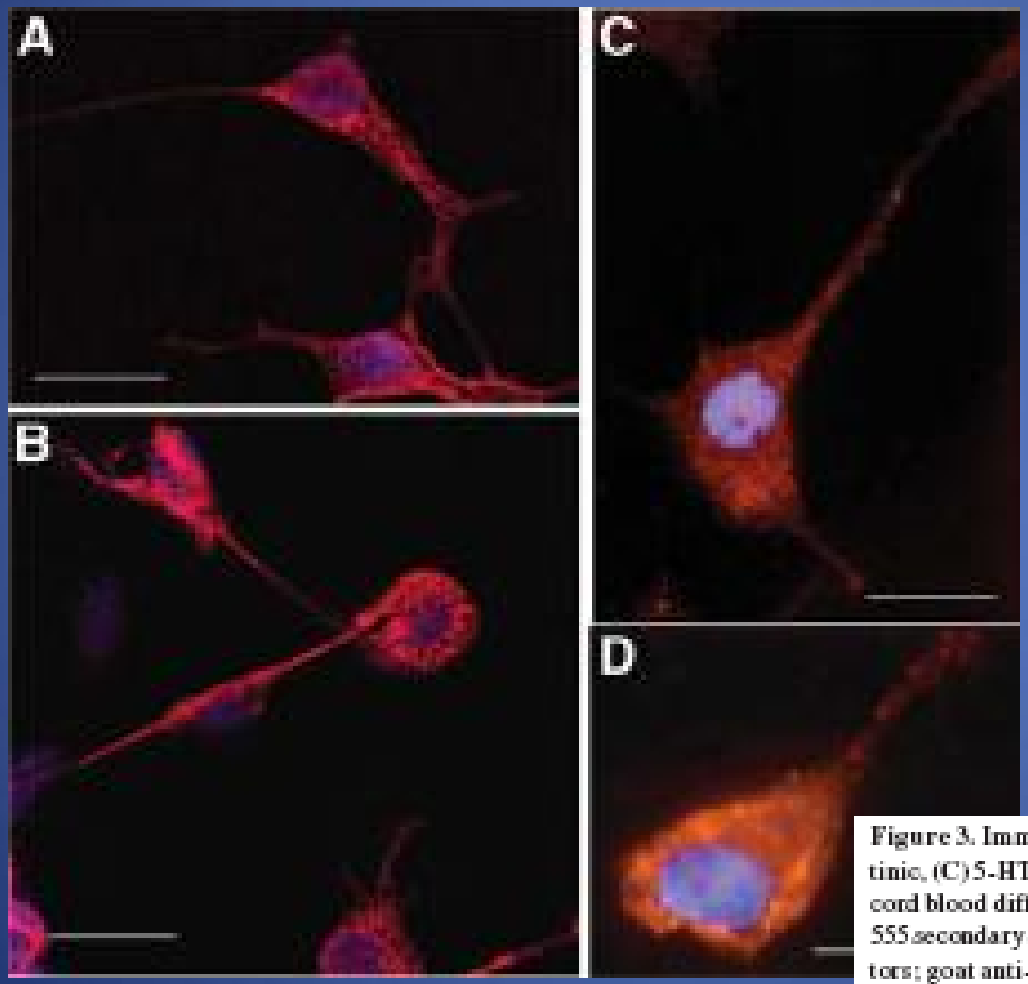
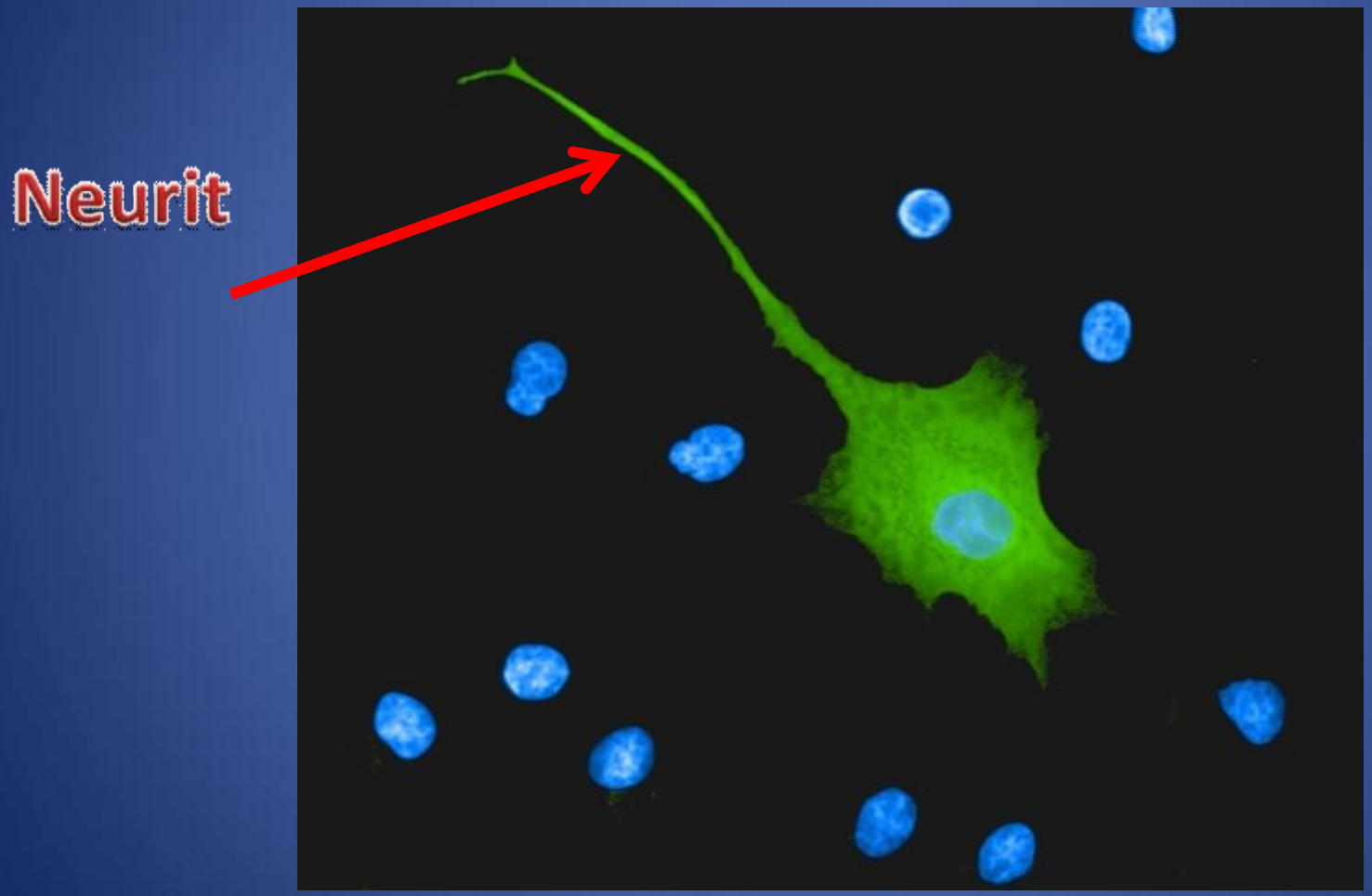


Figure 3. Immunolabeling of (A) glycine, (B) acetylcholine-nicotinic, (C) 5-HT, and (D) D2 dopamine receptors in human umbilical cord blood differentiated neural stem cells. Goat anti-mouse Alexa 555 secondary antibody used to detect acetylcholine and 5-HT receptors; goat anti-rabbit Cy3 used to detect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

Restorative neurosurgery

Stem cells for neurosurgery



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

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Professor of Surgery/ Trauma

?

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

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

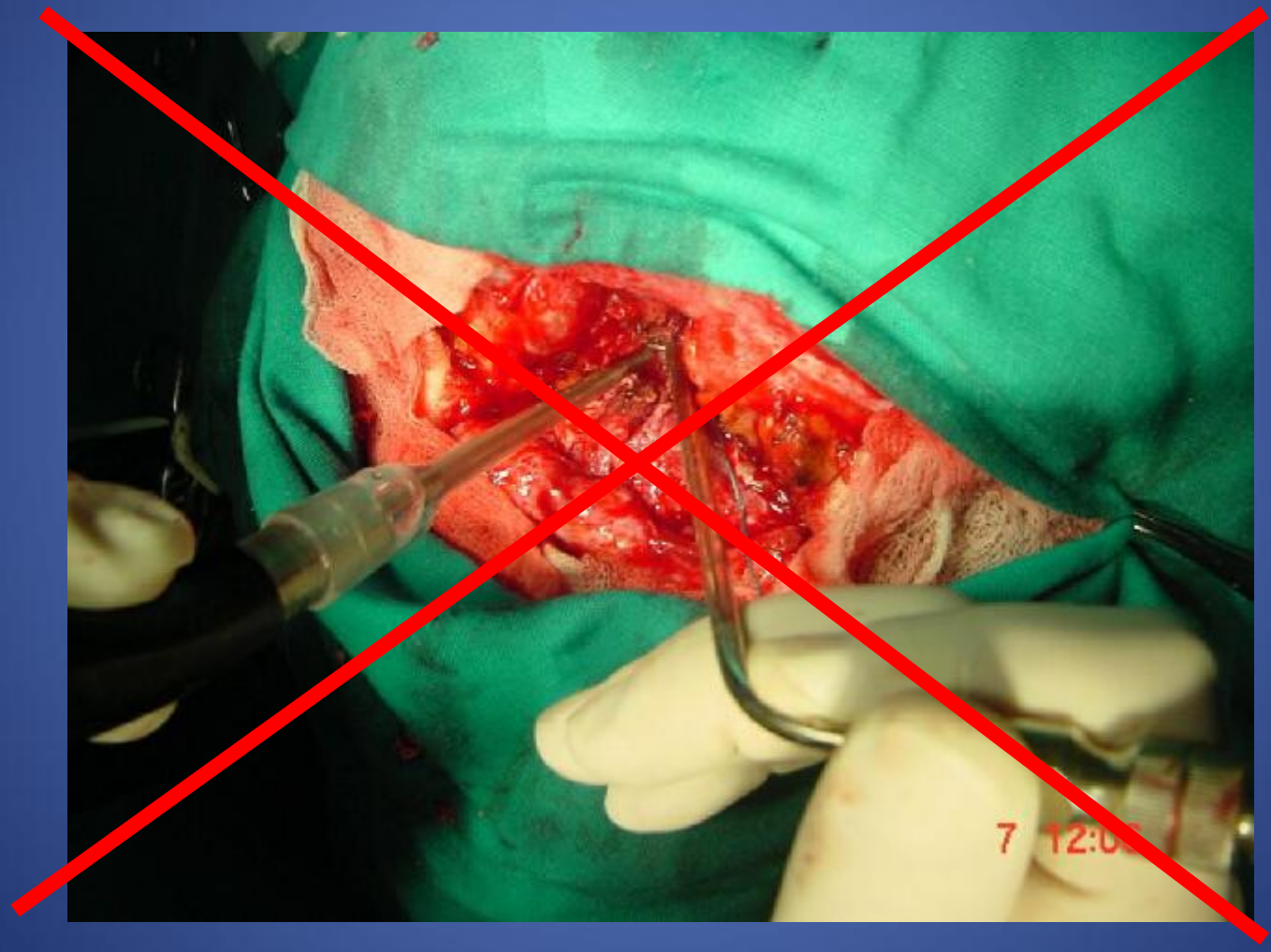
Could SC be used for the treatment of other brain or spine degeneration?

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 Cen

Review

Open Acce

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

Minal Vaish*

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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

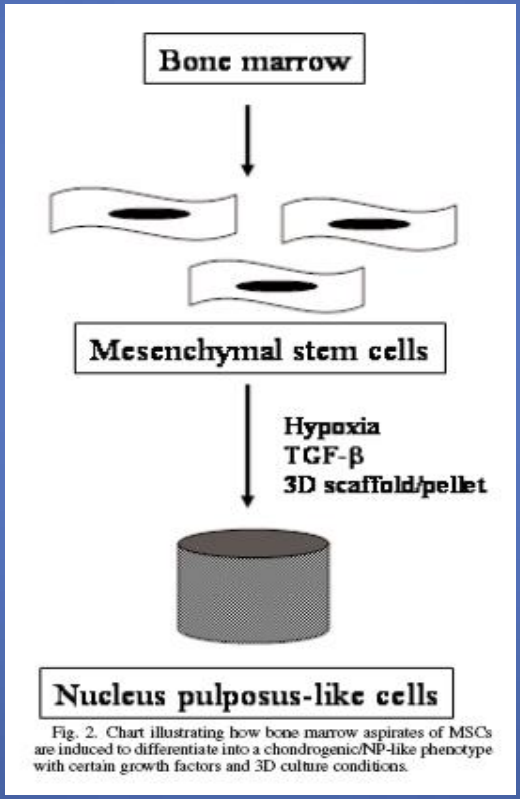


Fig. 2. Chart illustrating how bone marrow aspirates of MSCs are induced to differentiate into a chondrogenic/NP-like phenotype with certain growth factors and 3D culture conditions.

PLDD effect – own material

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

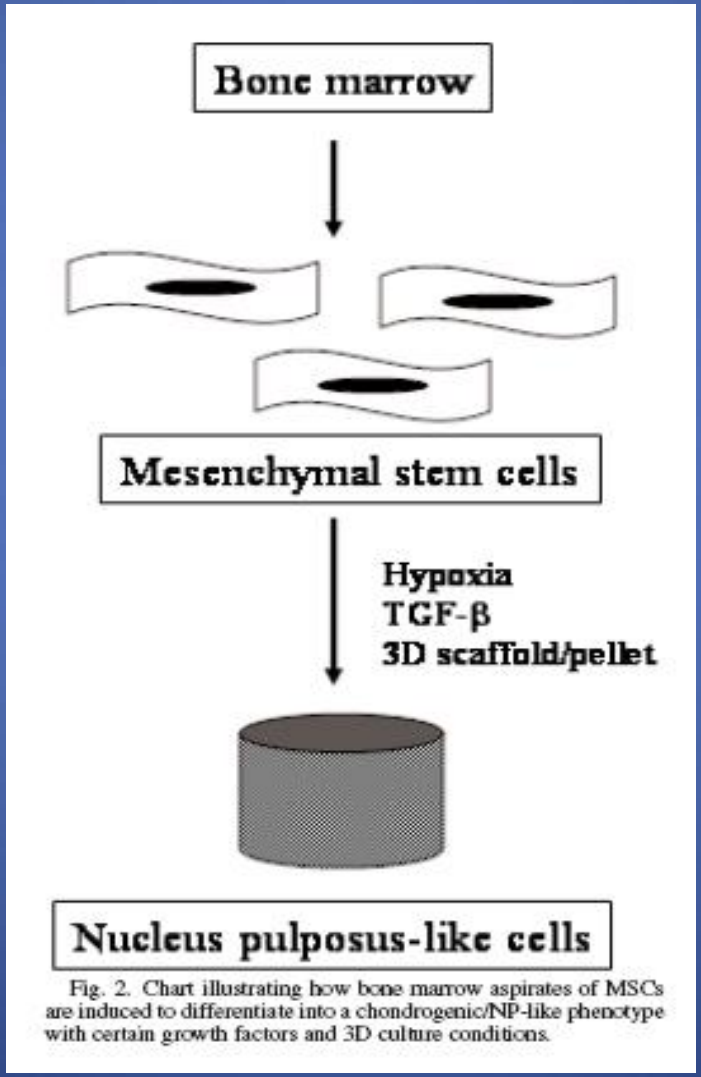


Fig. 2. Chart illustrating how bone marrow aspirates of MSCs are induced to differentiate into a chondrogenic/NP-like phenotype with certain growth factors and 3D culture conditions.

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

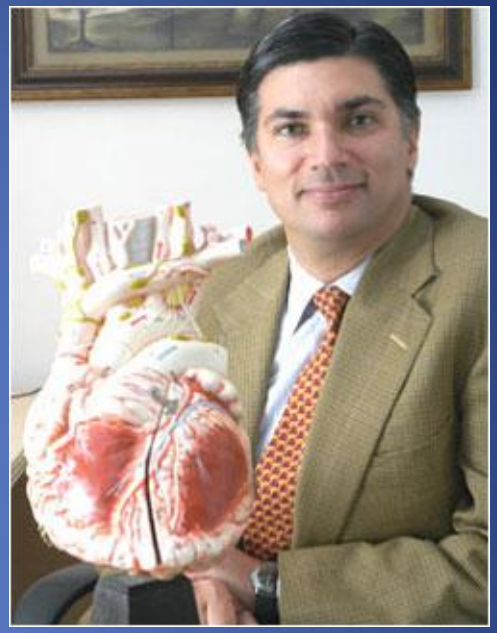
Cardiovascular diseases
Transvascular or direct application

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.

NATURE|Vol 460|2 July 2009

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-Okręglak – 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

- **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

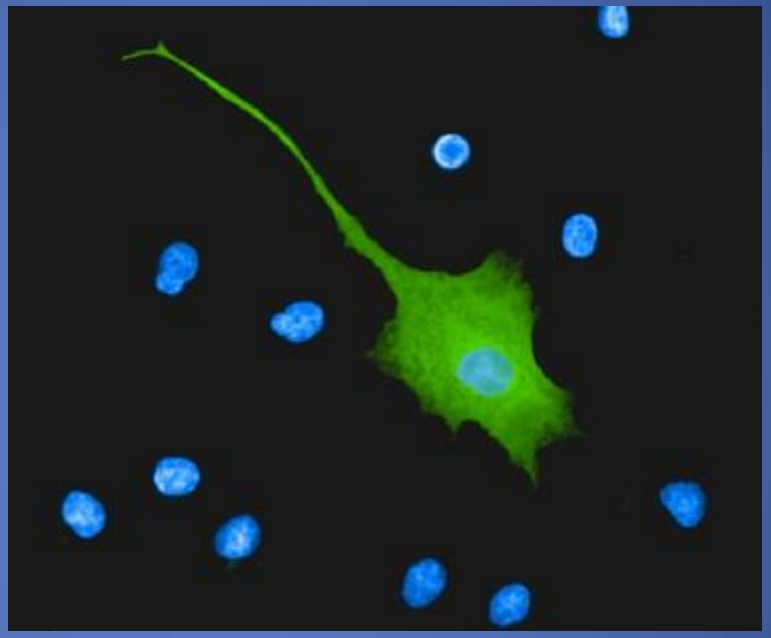
Instytut Kardiologii
im. Prymasa Tysiąclecia Stefana Kardynała Wyszyńskiego

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

UNIVERSITY OF VARMIA AND MASURIA IN OLSZTYN
FACULTY OF MEDICINE
ENGLISH DIVISION
10-082 OLSZTYN, AL. WARSZAWSKA 30, POLAND
TEL. +4889 524-53-01, TEL/FAX. +4889 527-70-04
www.uwm.edu.pl/wnm/en

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

To promote the progress of medical sciences



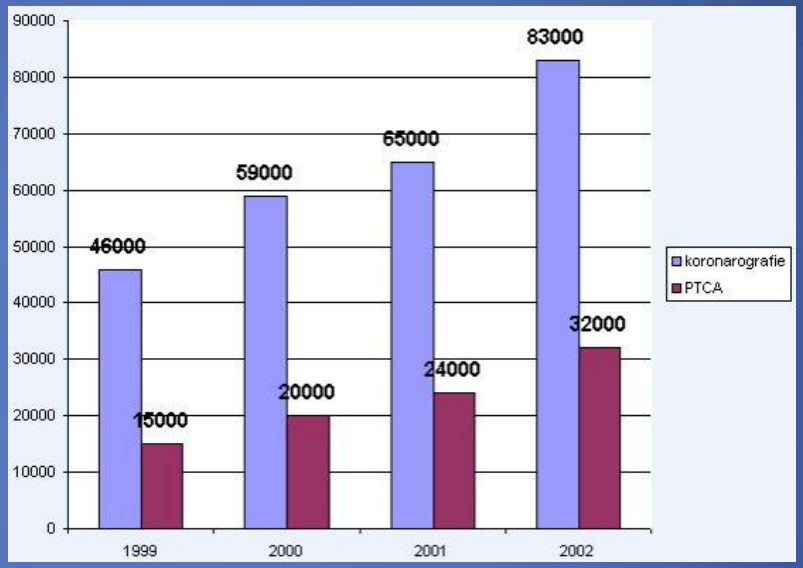
Modern Stem Cells Laboratory

– 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

To 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 Parlament

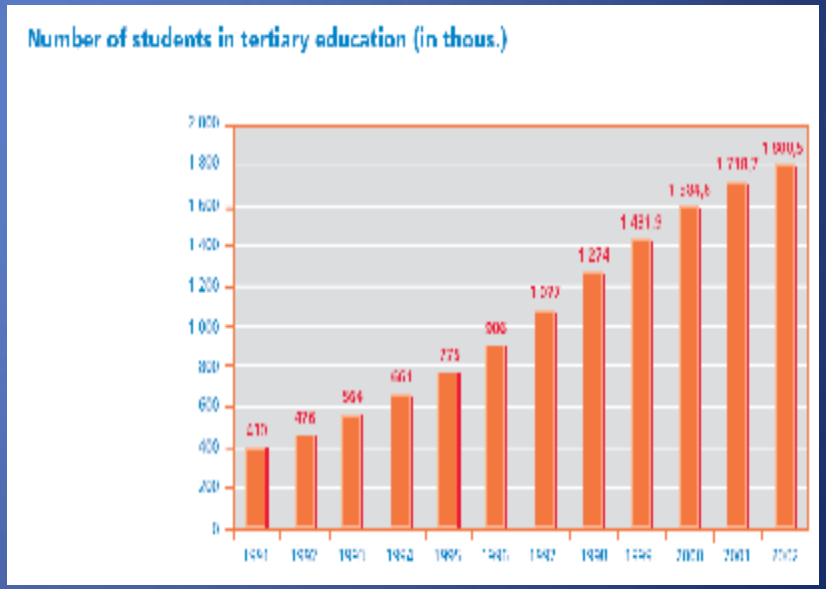
	Total in FP6	FP7 first 3 calls
Brain	260m	381m
Cancer	485m	265m
Cardiovascular	124m	111m

Poland –growing up (↑ 1,7%)

Polska

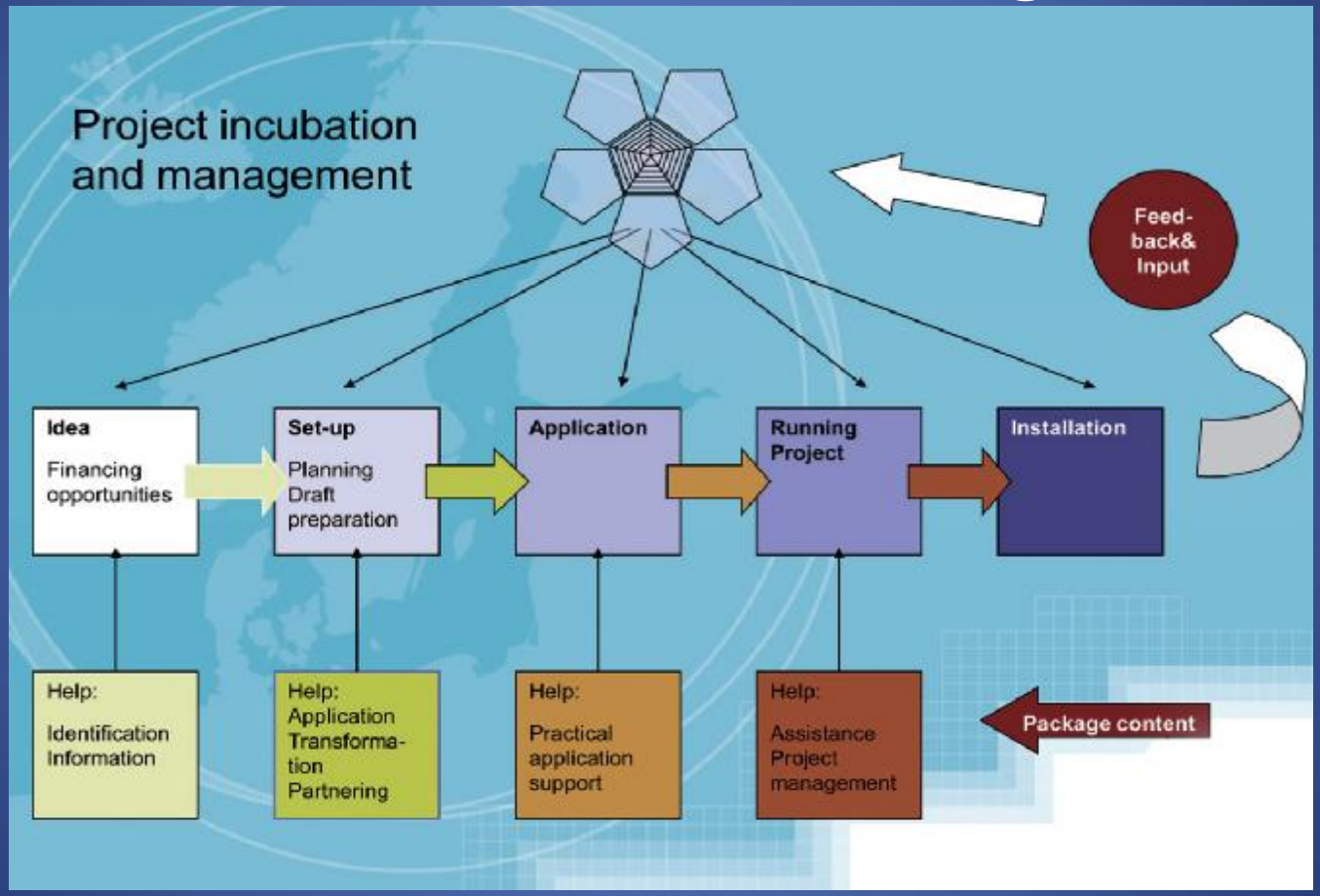
tutaj nawet kryzys się nie udał

www.demotywatory.pl




CAPACITIES
Smart Growth:
Bridging Academia and SMEs
in the Baltic Sea Region
ScanBalt
Bridge-BSR

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

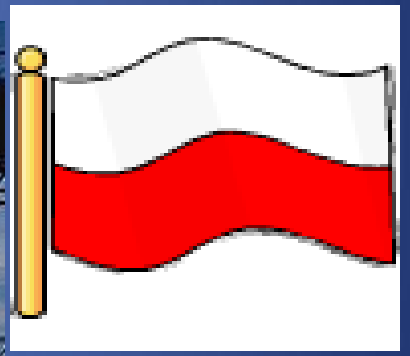
Invitation adressed to MD Anderson Cancer Center in Houston

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