IDROCEFALO NORMOTESO
UNA DEMENZA CURABILE
Latina, 29 Settembre 2012

L'idrocefalo

Passato - Presente - Futuro

Carmelo Anile

Istituto di Neurochirurgia - UCSC - Roma

Idrocefalo normoteso
(idrocefalo cronico dell'adulto)

Insieme di forme patologiche, ad espressione clinica relativamente omogenea, caratterizzate dall'associazione di:

- **Dilatazione degli spazi liquorali ventricolari**
- **Pressione liquorale normale (< 20 cm H_2O)**
- **Andamento evolutivo**
- **Potenzialmente reversibile**

- Algunas observaciones sobre la presion del L.C.R. Sindrome hidrocefalico en el adulto con “presion normal” del L.C.R. Hakim S. *Universidad Javeriana, Tesis 957. Bogota, Colombia, S.A.,* **1964**. Also avalilable in english as: Some observations on CSF pressure. Hydrocephalic Syndrome in adults with “normal” CSF pressure. *(Recognition of a new syndrome)*

- The special clinical problem of symptomatic hydrocephalus with normal cerebrospinal fluid pressure: observations on cerebrospinal fluid hydrodynamics. Hakim S and Adams RD *J Neurol Sci* **2**:307-327, 1965.

Quadro clinico

- ***Disturbi della marcia***
- ***Deterioramento cognitivo***
- ***Incontinenza sfinterica***

"Triade di Hakim e Adams"

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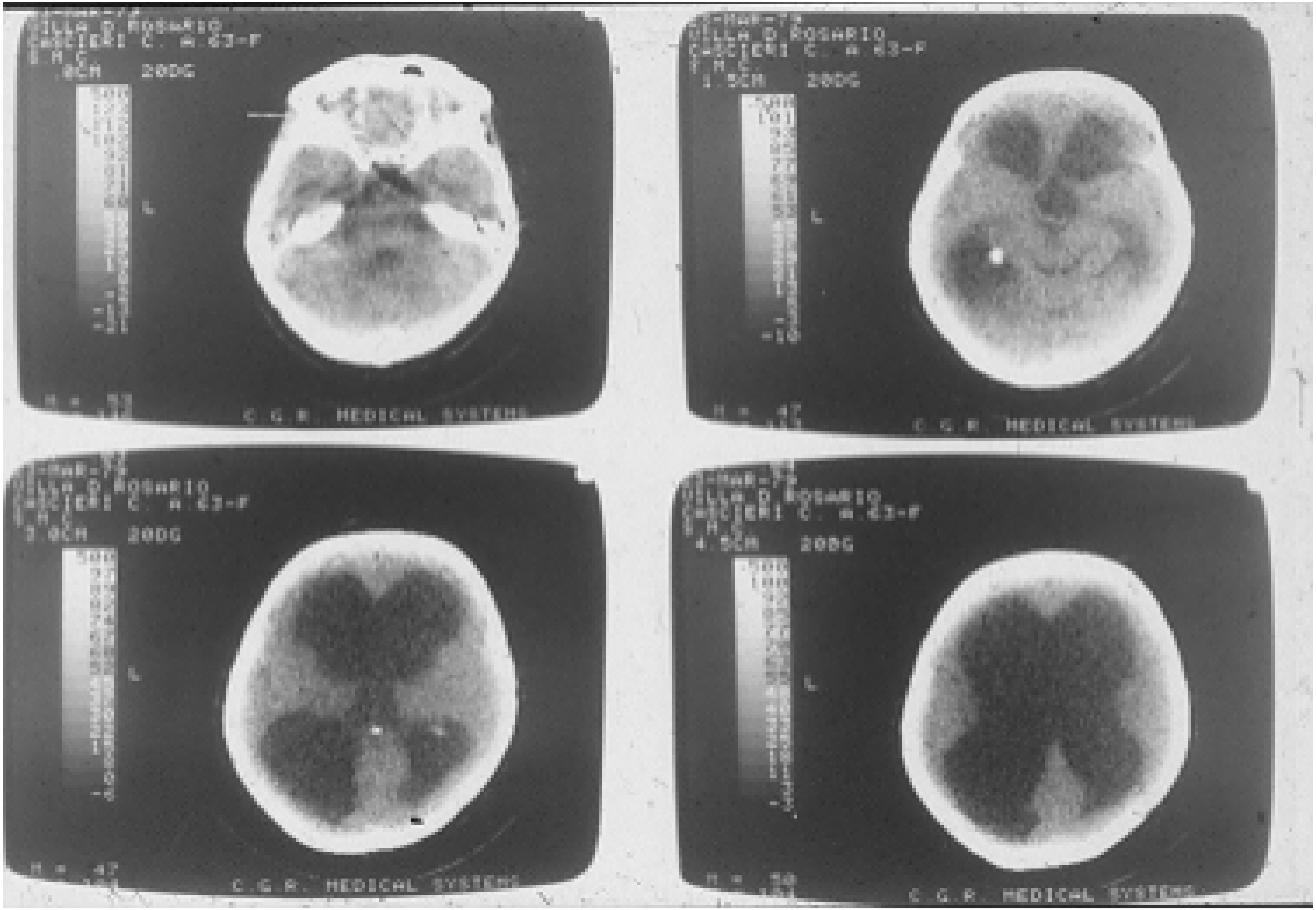
VILLA D.ROSARIO
.0CM 20DG
C.G.R. MEDICAL SYSTEMS
VILLA D.ROSARIO
1.5CM 20DG
C.G.R. MEDICAL SYSTEMS
VILLA D.ROSARIO
3.0CM 20DG
C.G.R. MEDICAL SYSTEMS
VILLA D.ROSARIO
4.5CM 20DG
C.G.R. MEDICAL SYSTEMS

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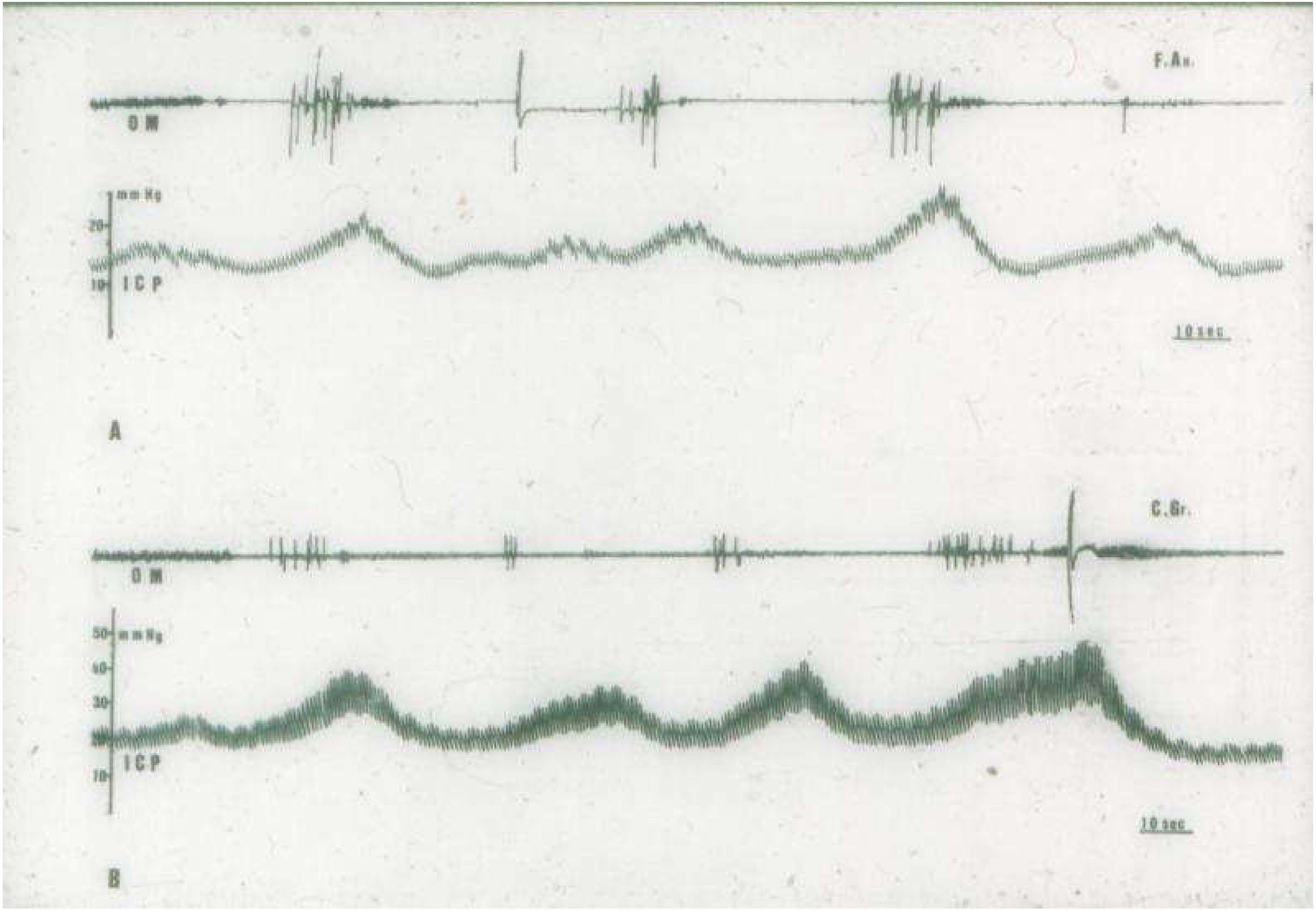
F.An.
OM
mm Hg
20
10
ICP
10 sec
A
C.Gr.
OM
50
mm Hg
40
30
20
10
ICP
10 sec
B

Idrocefalo normoteso
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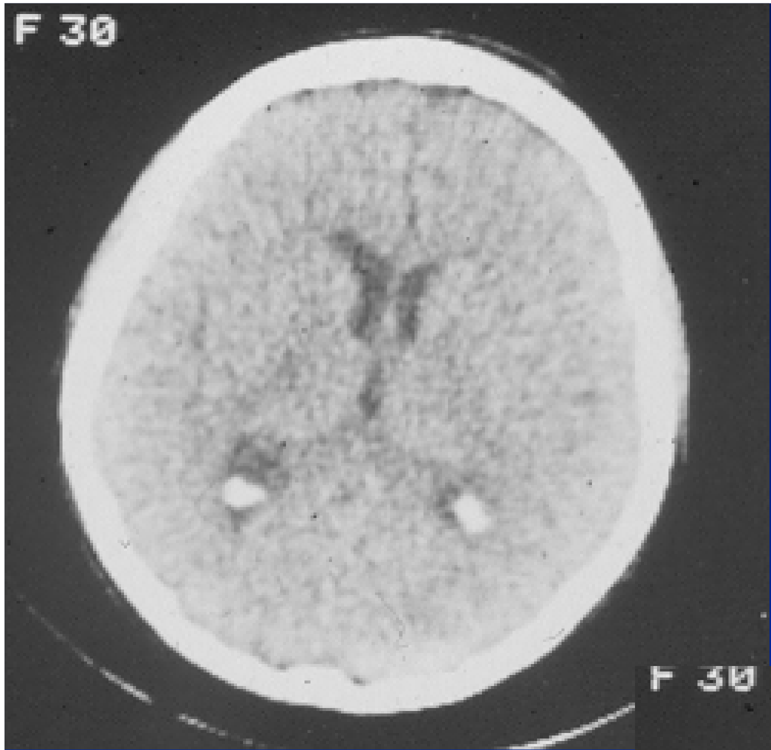
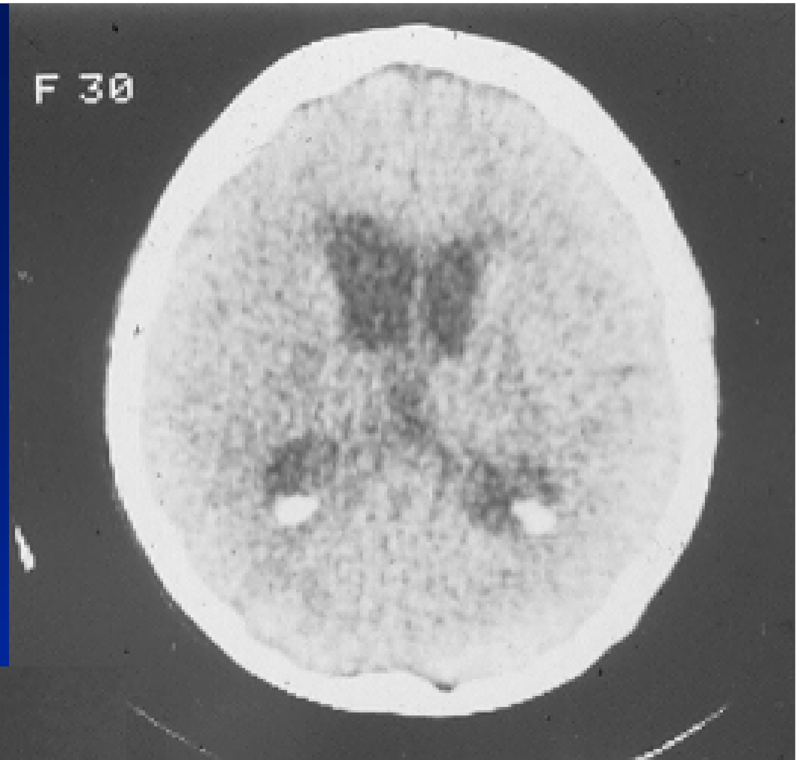

F 30

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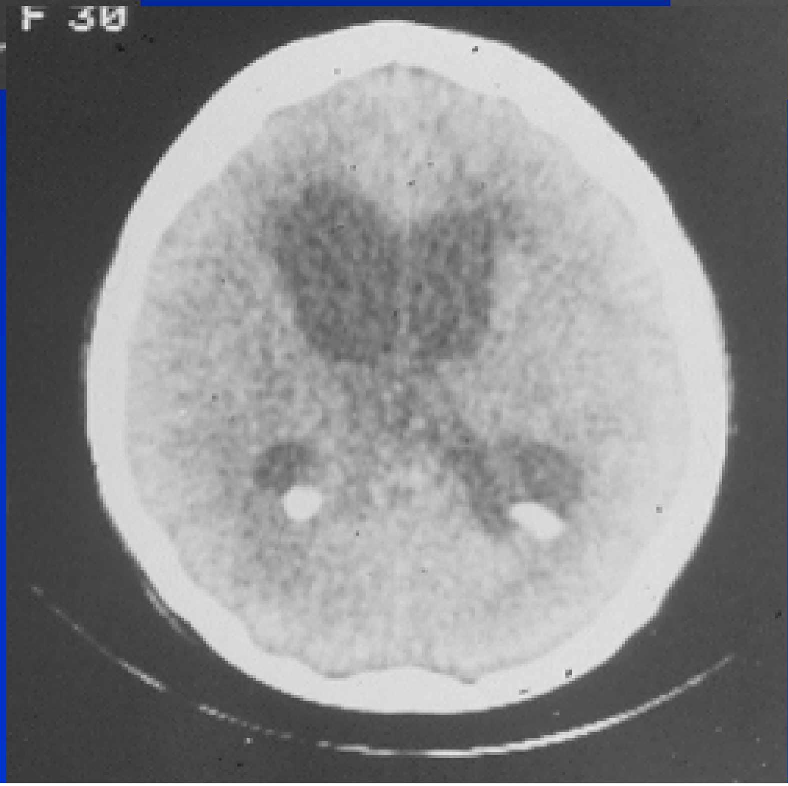
F 30

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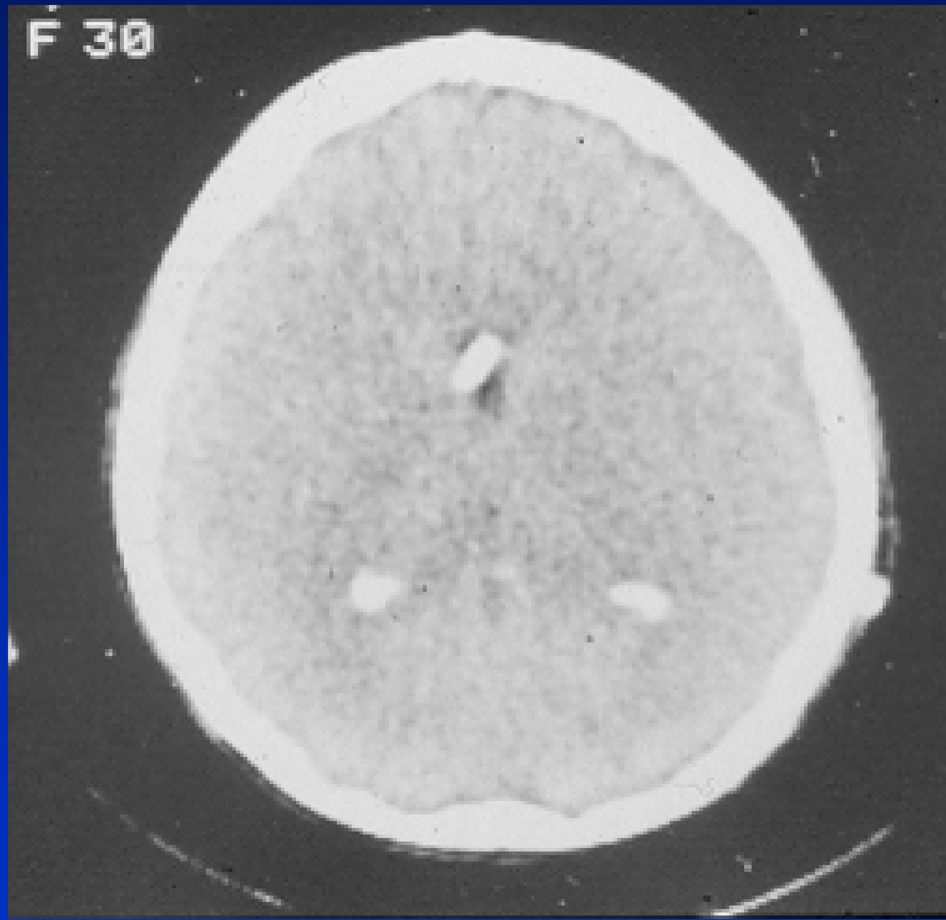
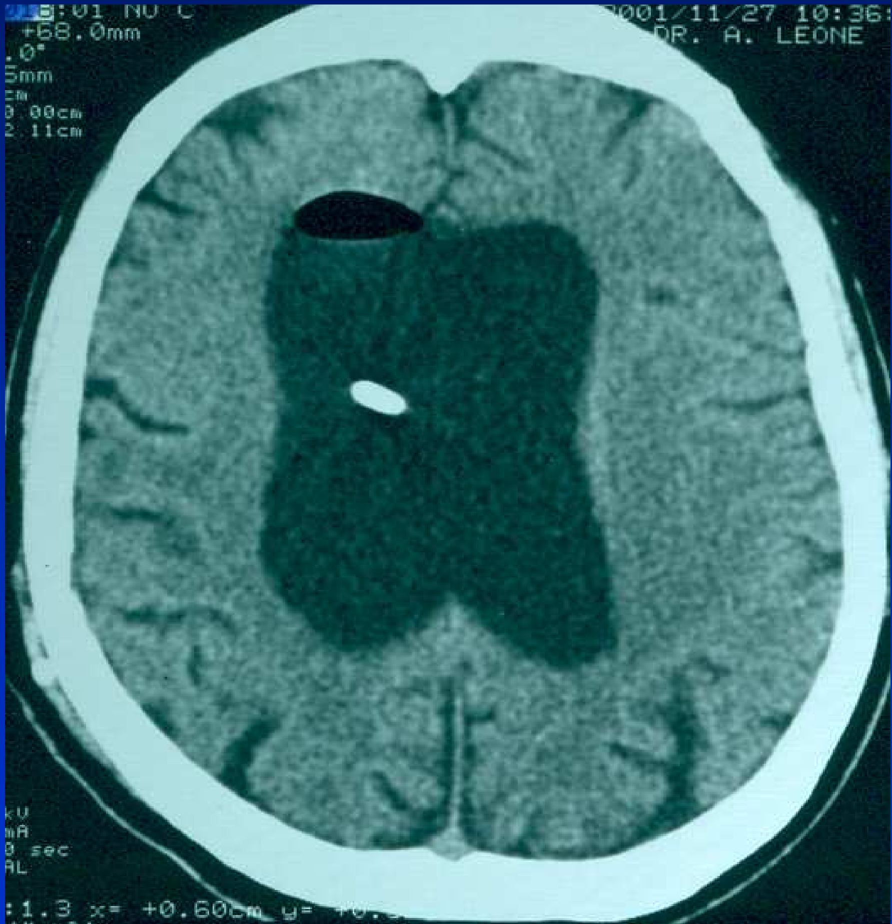
F 30

F 30

27.11.2001 - *16 cm H_2O*



27.12.2001 - *8 cm H_2O*

Diagnostica strumentale nell'Idrocefalo Normoteso

- Criterio *"ex adjuvantibus"*
- Diagnostica fisiopatologica

↓

- Valutazione predittiva
- Efficacia terapeutica

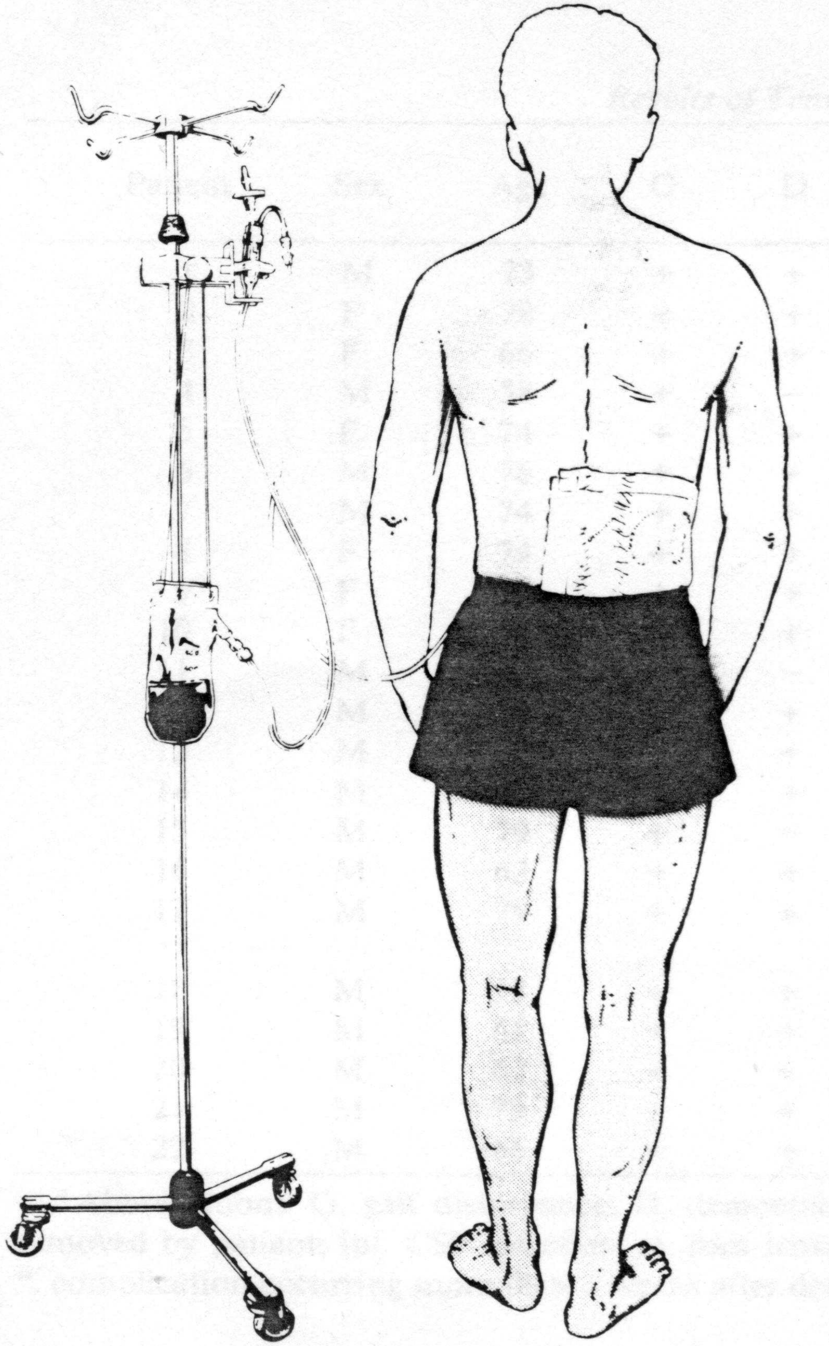
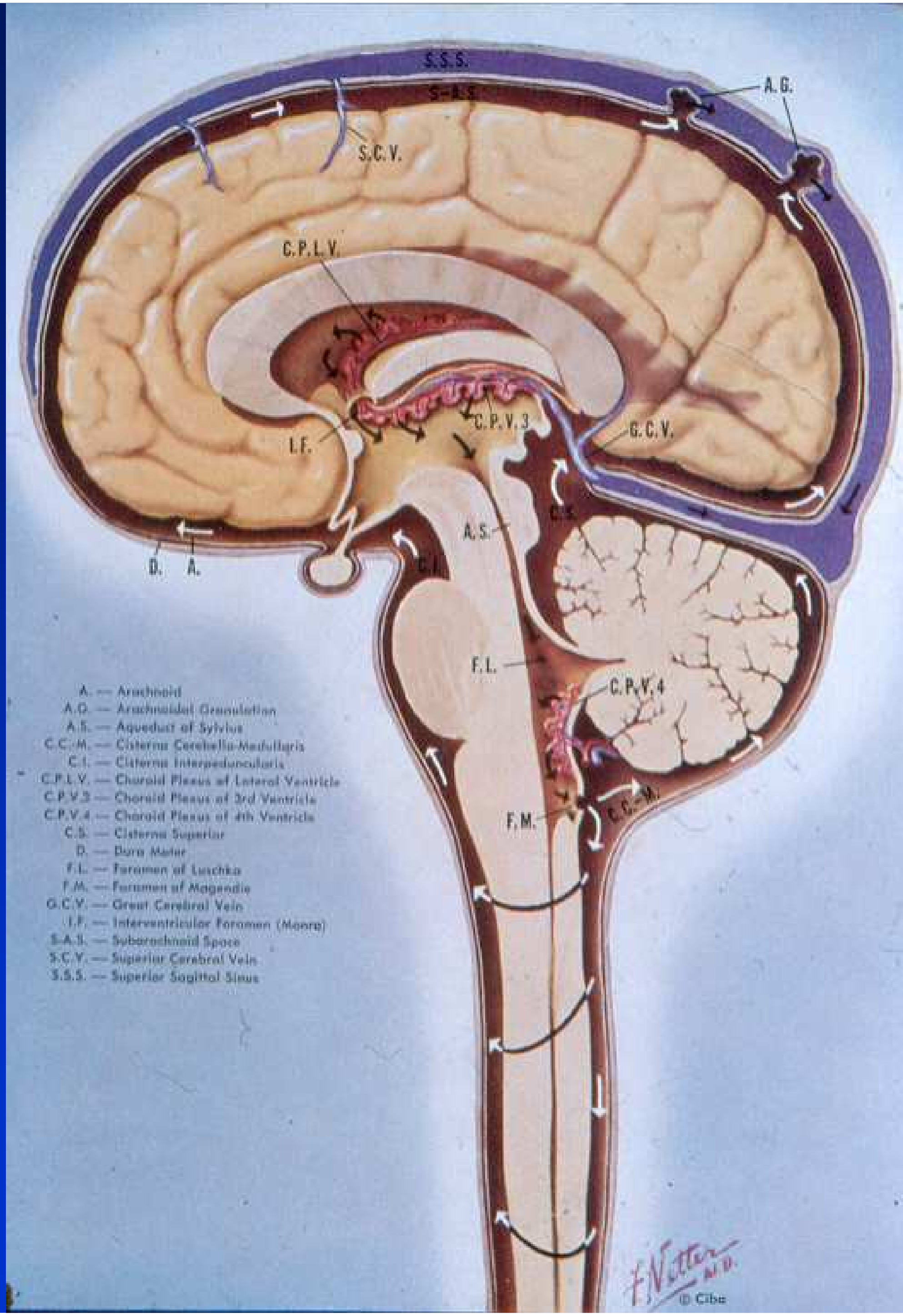


FIG. 2. A patient with an ELD system.


S.S.S.
S-A.S.
A.G.
S.C.V.
C.P.L.V.
C.P.V.3
I.F.
G.C.V.
C.S.
A.S.
D.
A.
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S-A.S. — Subarachnoid Space
S.C.V. — Superior Cerebral Vein
S.S.S. — Superior Sagittal Sinus
F. Netter M.D.
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CSF Outflow Resistance calculation

$$\textbf{R-out:}\ \frac{\text{Plateau Diastolic ICP} - \text{Basal Diastolic ICP}}{\text{Infusion rate}}$$

Normal values ranging from 8 to 12 mmHg/ml/min

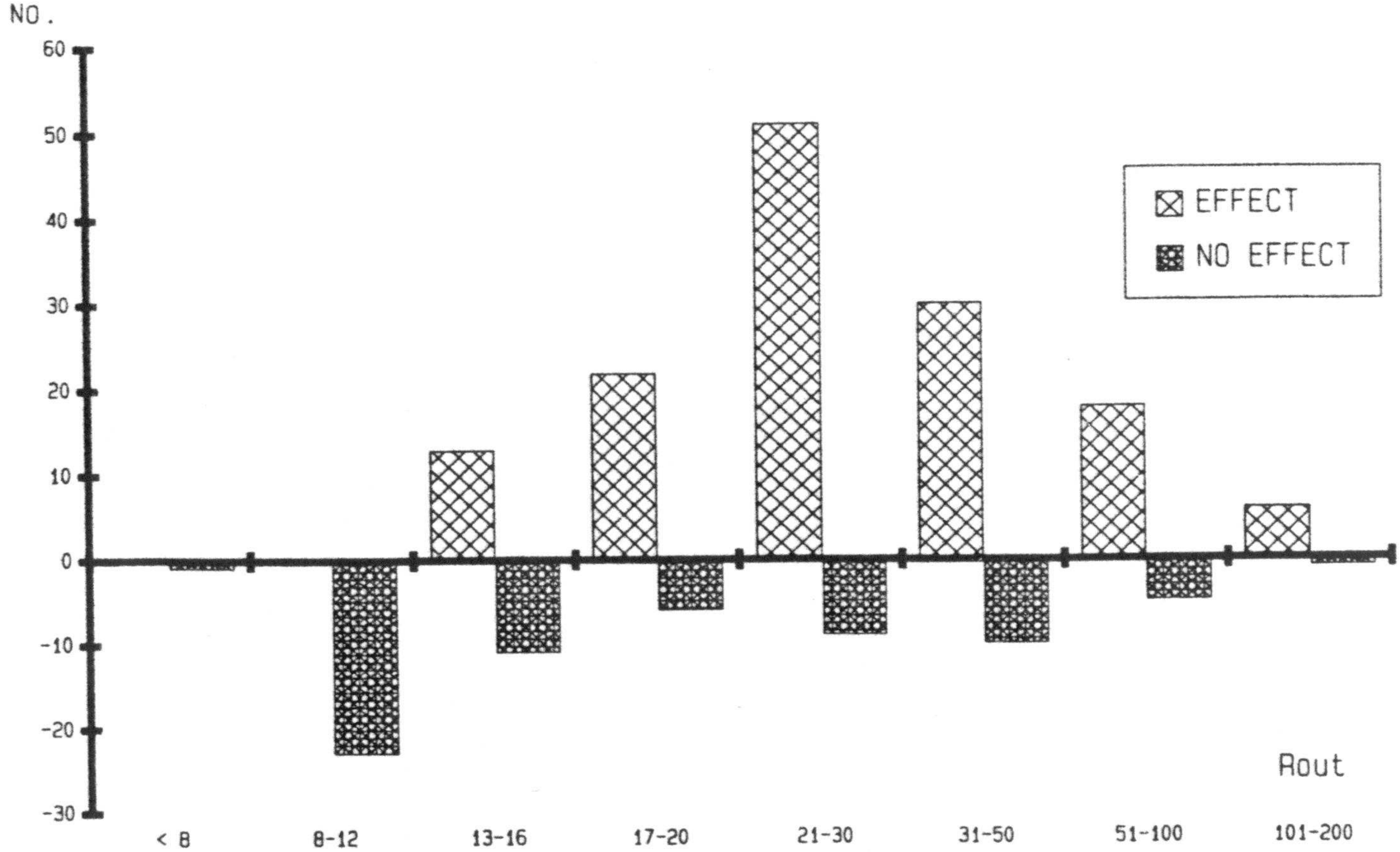

Fig. 15. Effect of shunting correlated to R_{out} in patients with NPH

DOI: 10.3171/2010.1.JNS091296

Selection of patients with idiopathic normal-pressure hydrocephalus for shunt placement: a single-institution experience

Clinical article

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Alessandro Di Chirico, M.D.,[2] Annunziato Mangiola, M.D.,[1]
Gianpaolo Petrella, M.D.,[3] and Pietro Santini[1]

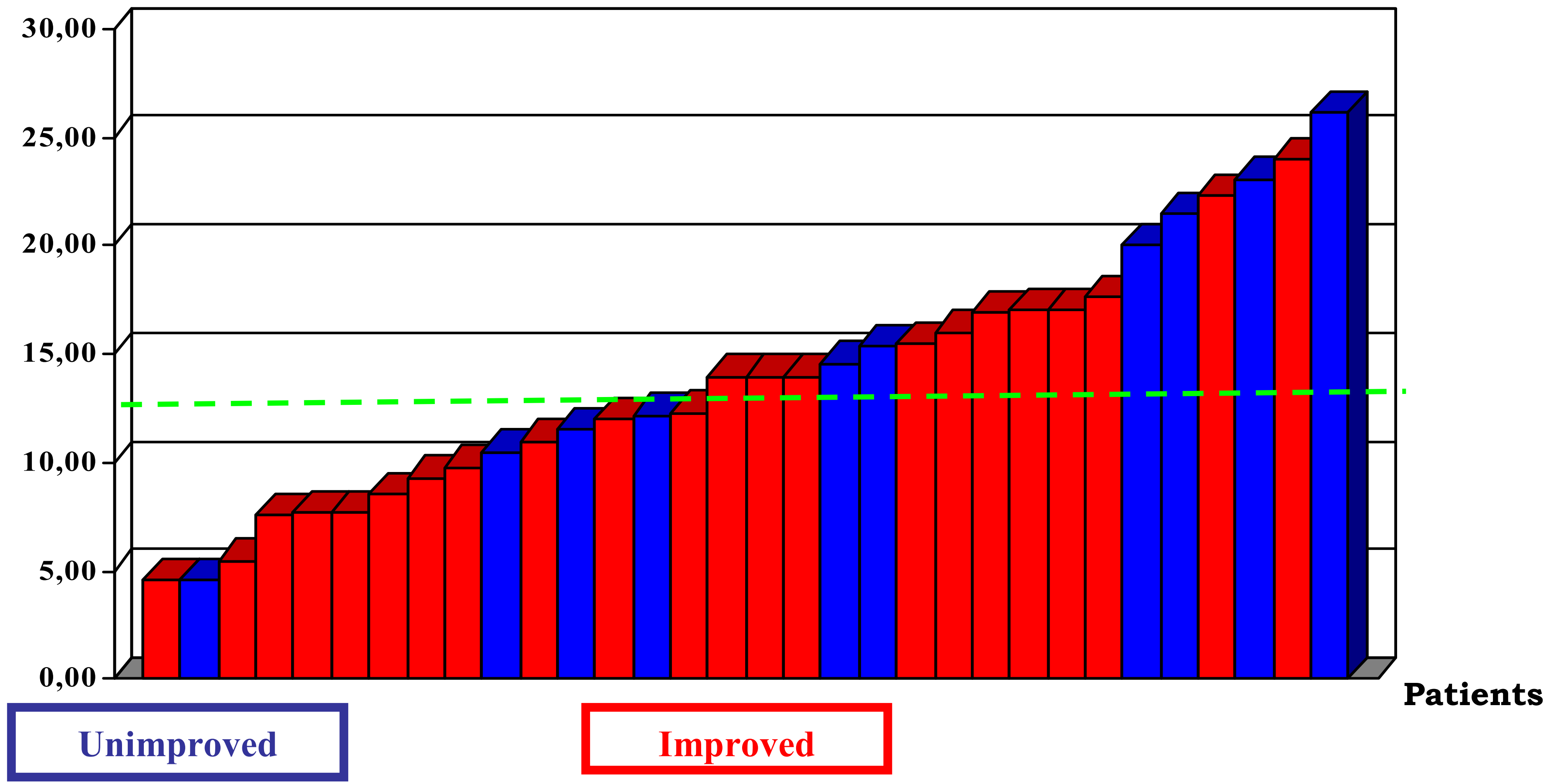
[1]Institute of Neurosurgery, Catholic University School of Medicine, Rome; [2]Neurosurgical Department, Ospedale Santo Spirito, Rome; and [3]Neurosurgical Department, Azienda Ospedaliera S. Maria, Terni, Italy

J Neurosurg 2010

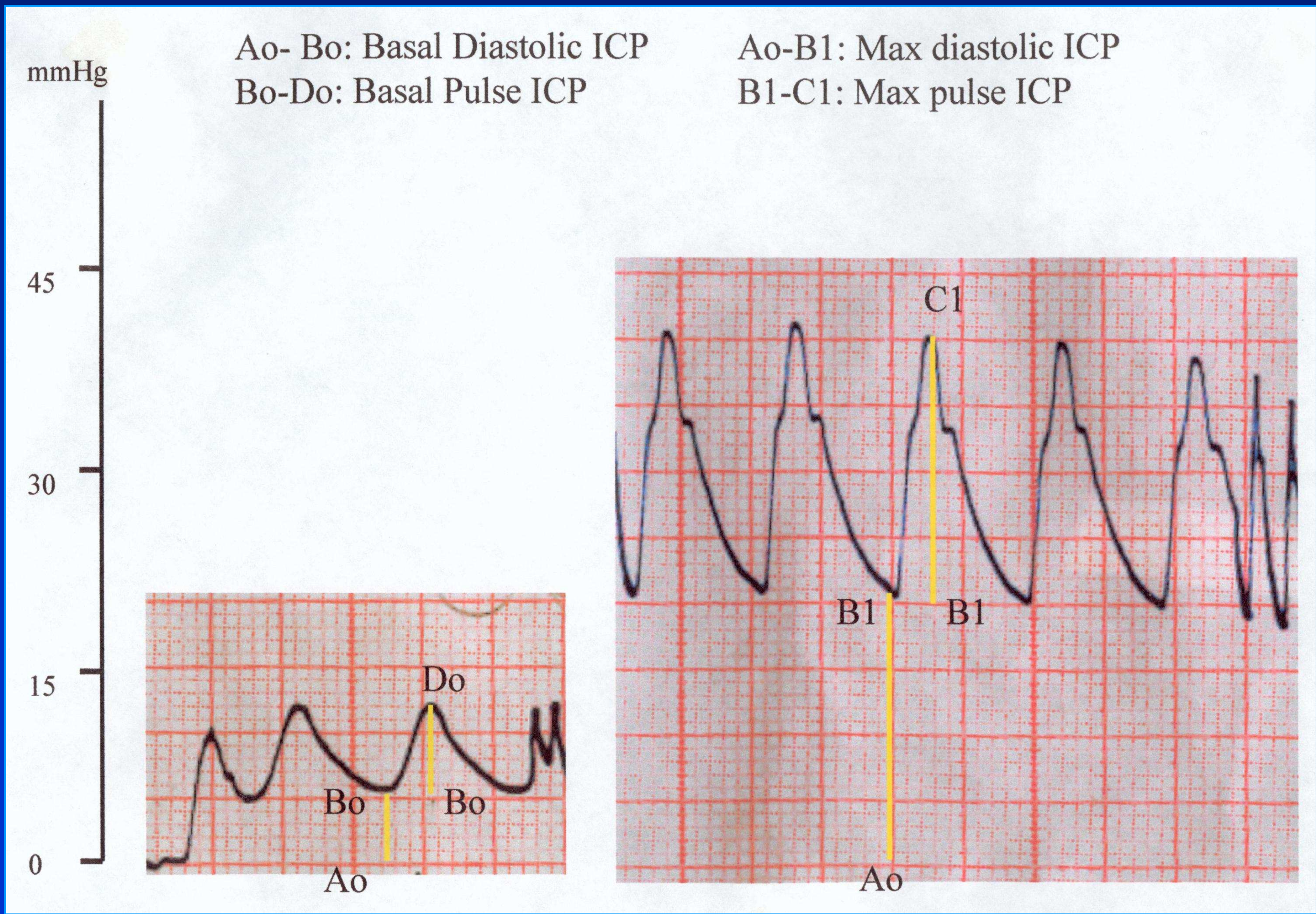
Infusion test

1st Series:

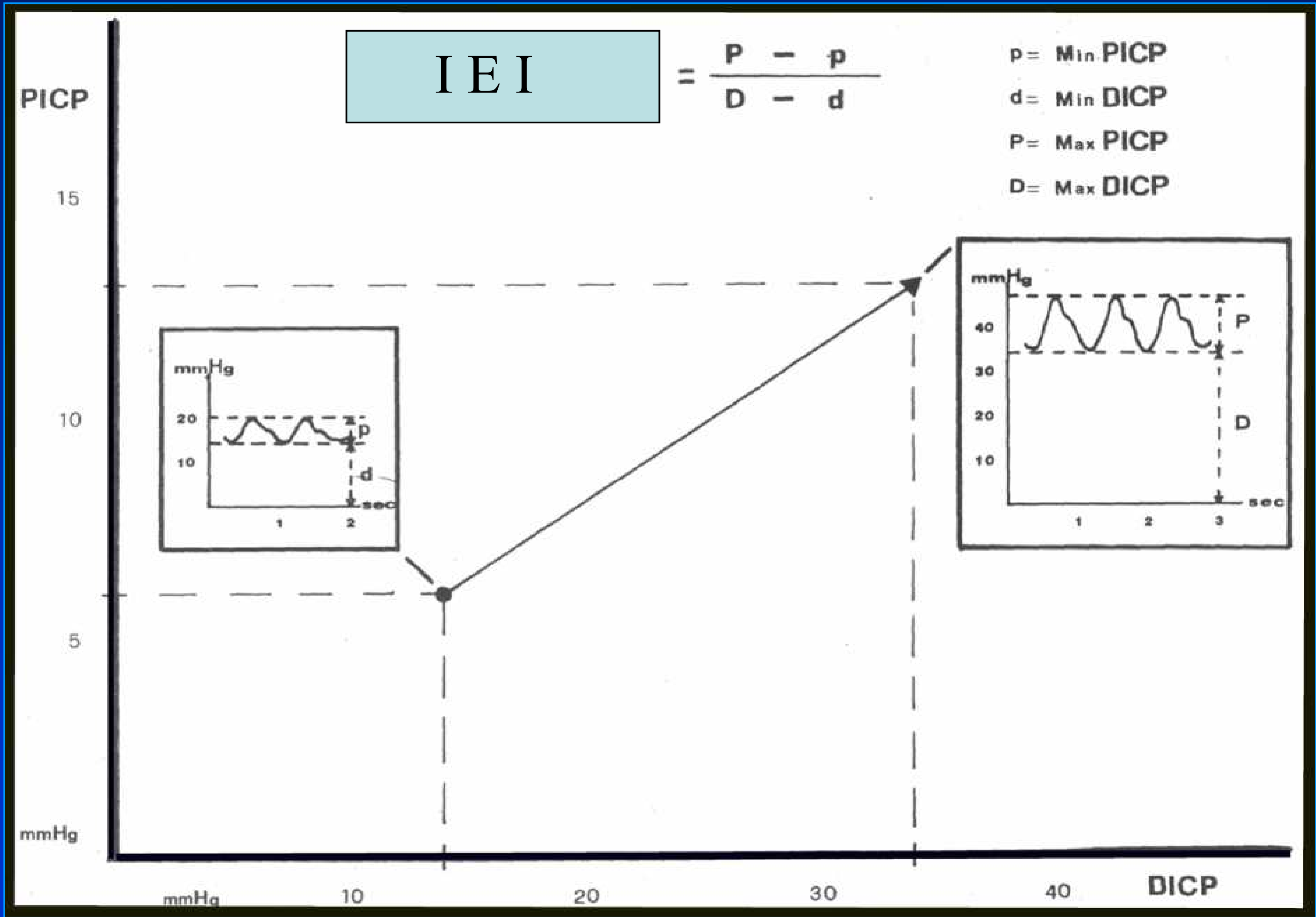
CSF Outflow Resistance



CSF pulse wave analysis



Intracranial elastance index

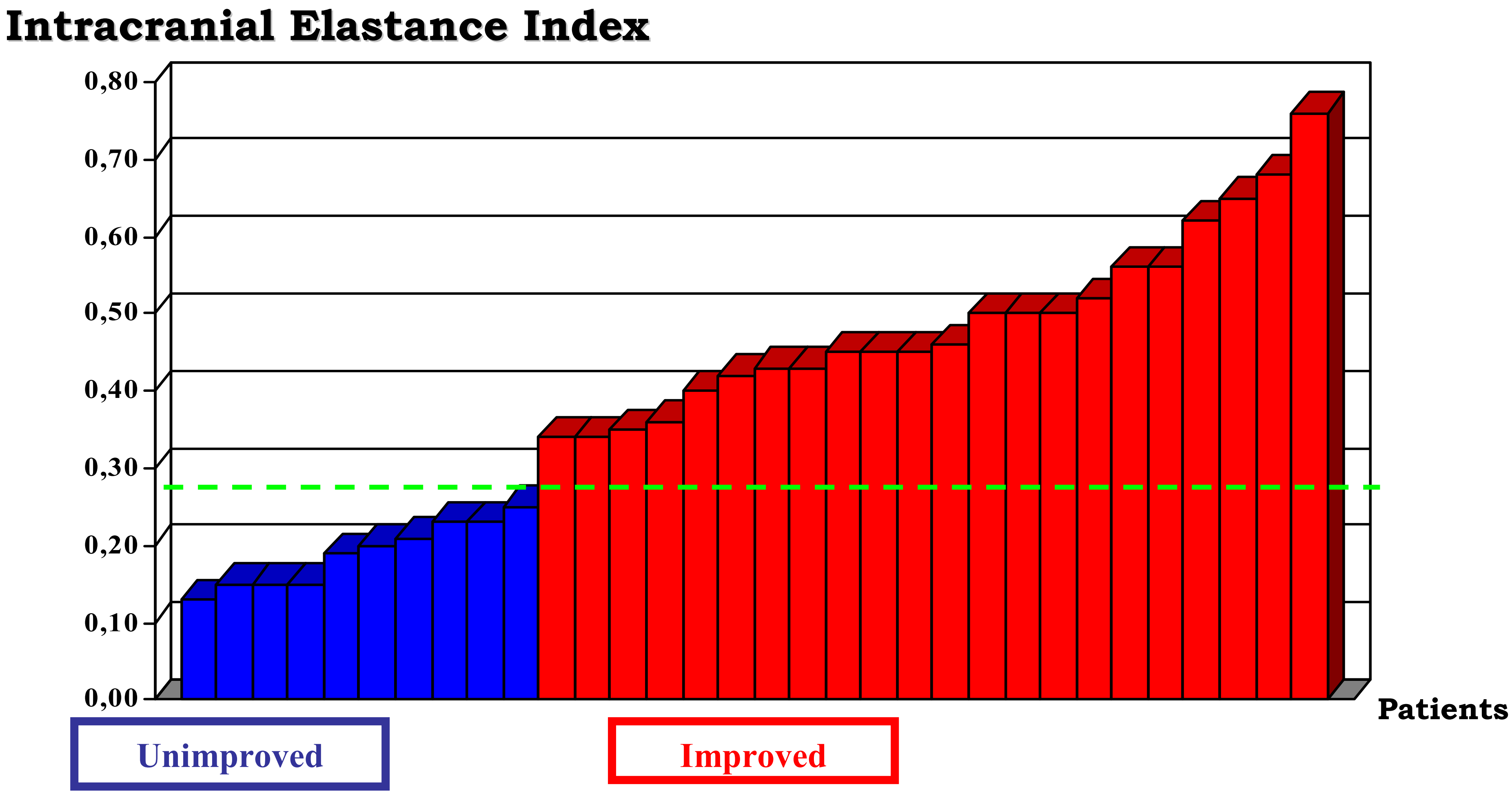


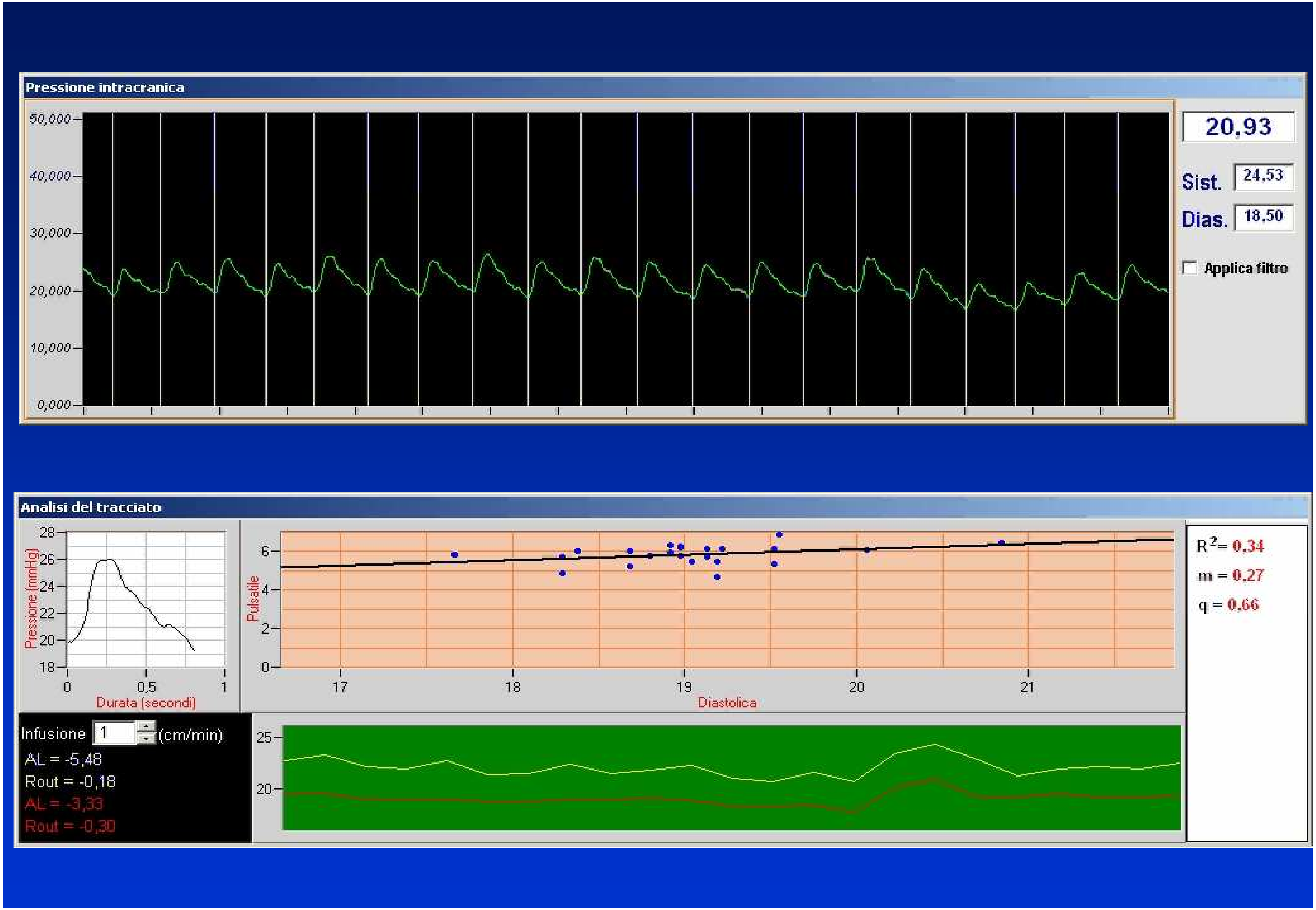
Intracranial Elastance Index calculation

$$\text{IEI:} \quad \frac{\text{Max Pulse ICP} - \text{Basal Pulse ICP}}{\text{Max Diastolic ICP} - \text{Basal Diastolic ICP}}$$

Infusion test

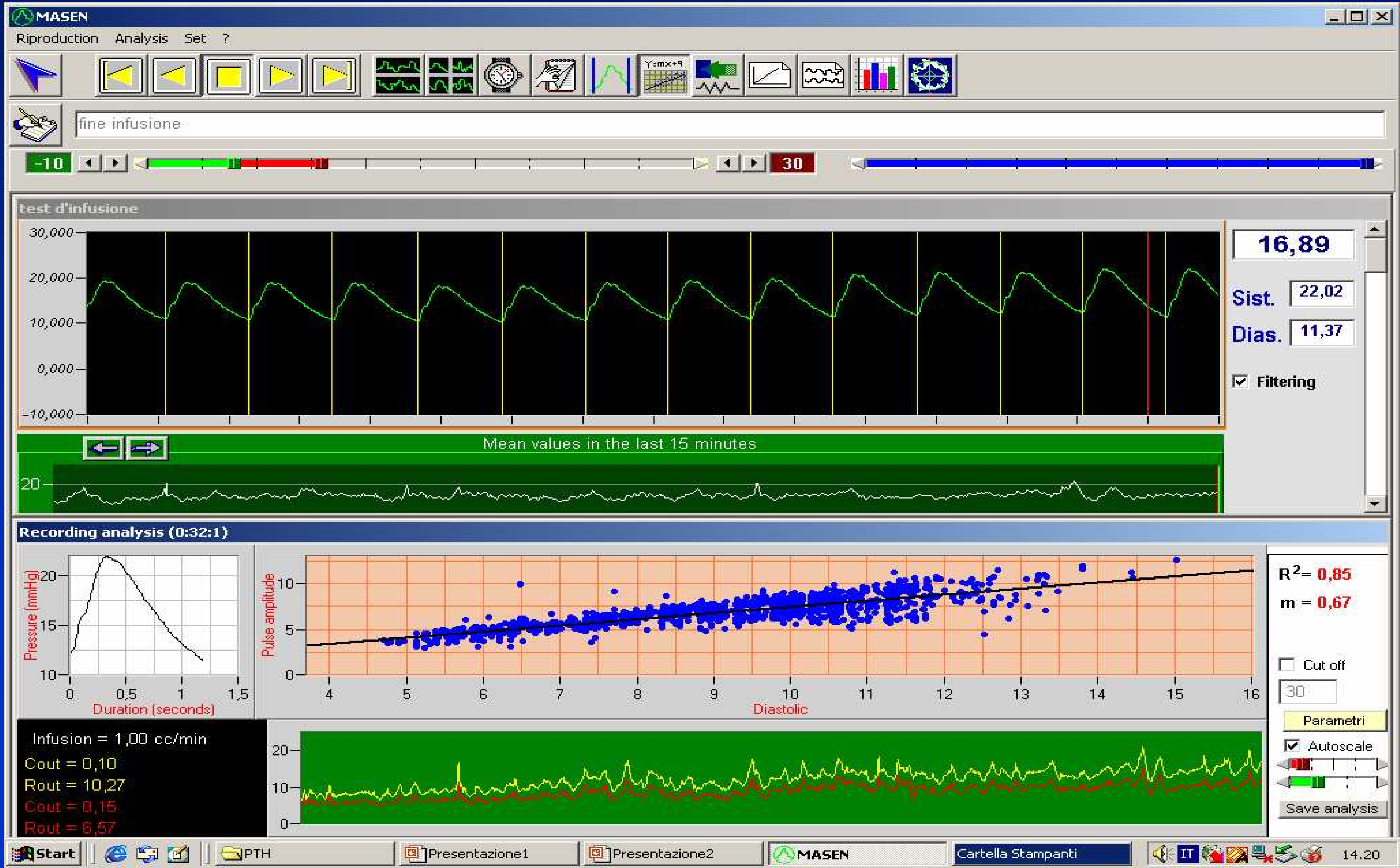
1st Series:



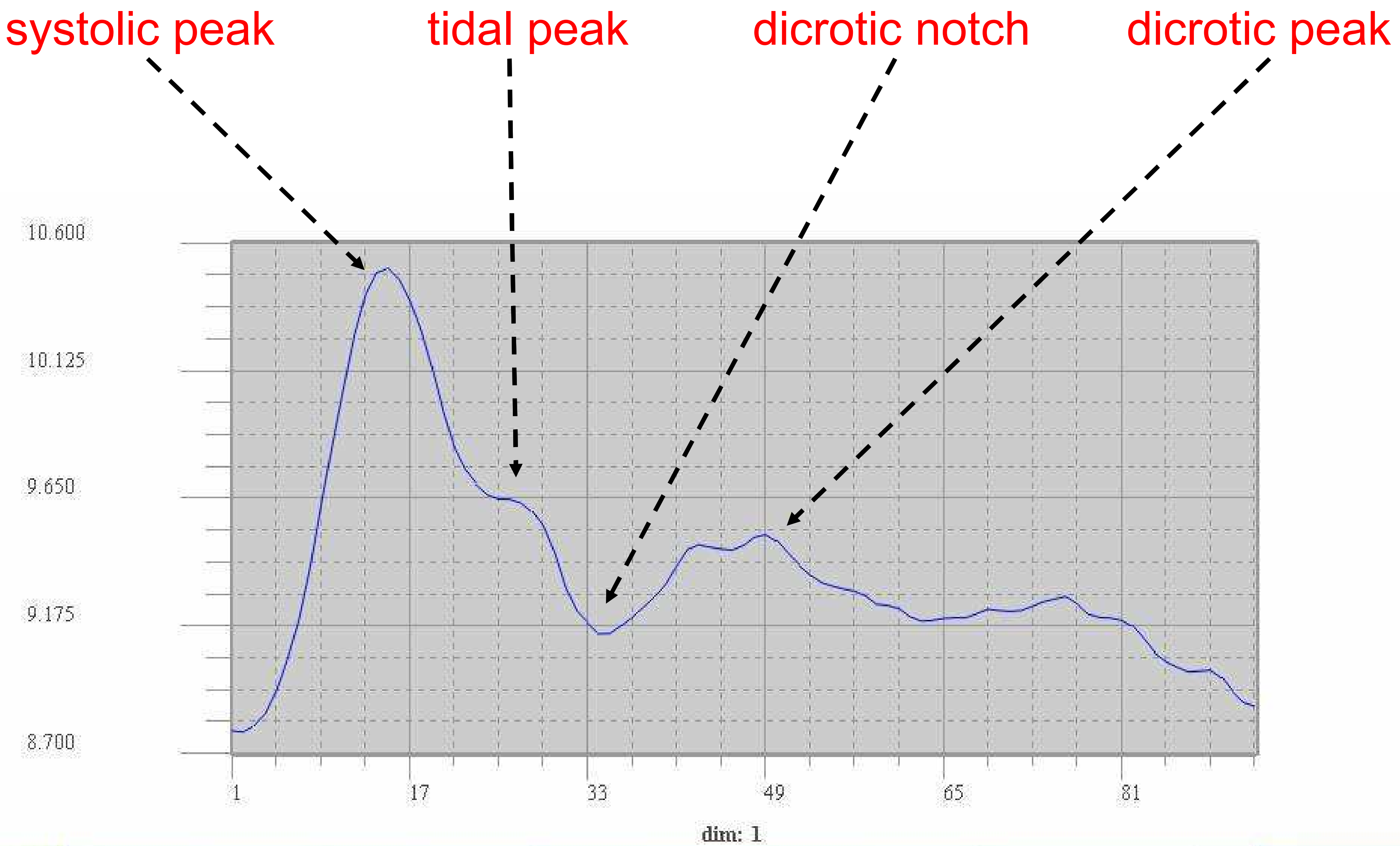


Pressione intracranica
50,000
40,000
30,000
20,000
10,000
0,000
20,93
Sist. 24,53
Dias. 18,50
Applica filtro
Analisi del tracciato
Pressione [mmHg]
Durata (secondi)
Pulsatile
Diastolica
R2= 0,34
m = 0,27
q = 0,66
Infusione 1 (cm/min)
AL = -5,48
Rout = -0,18
AL = -3,33
Rout = -0,30

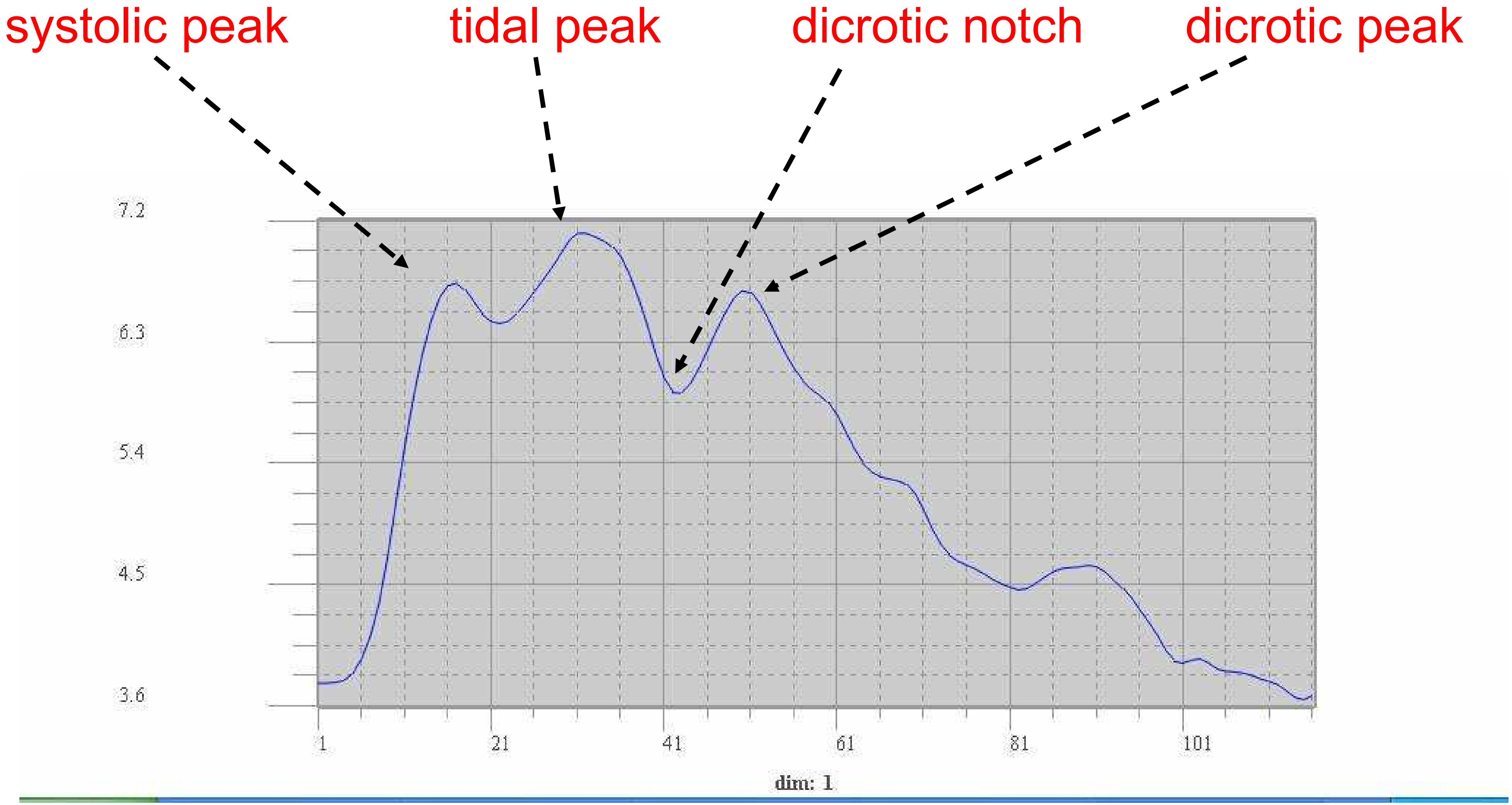
Selection of Patients: our approach



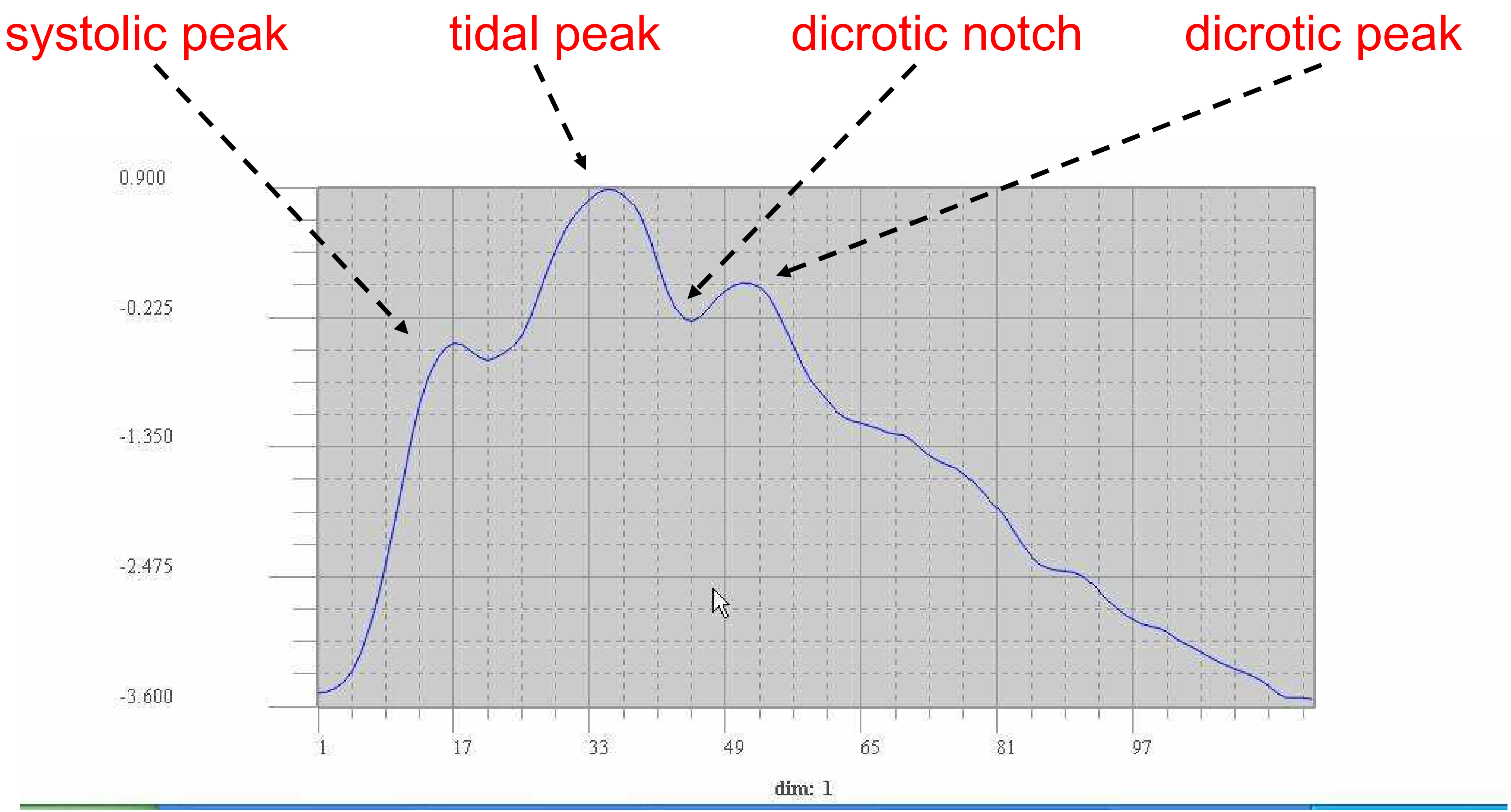
Class 1 - *Normal*



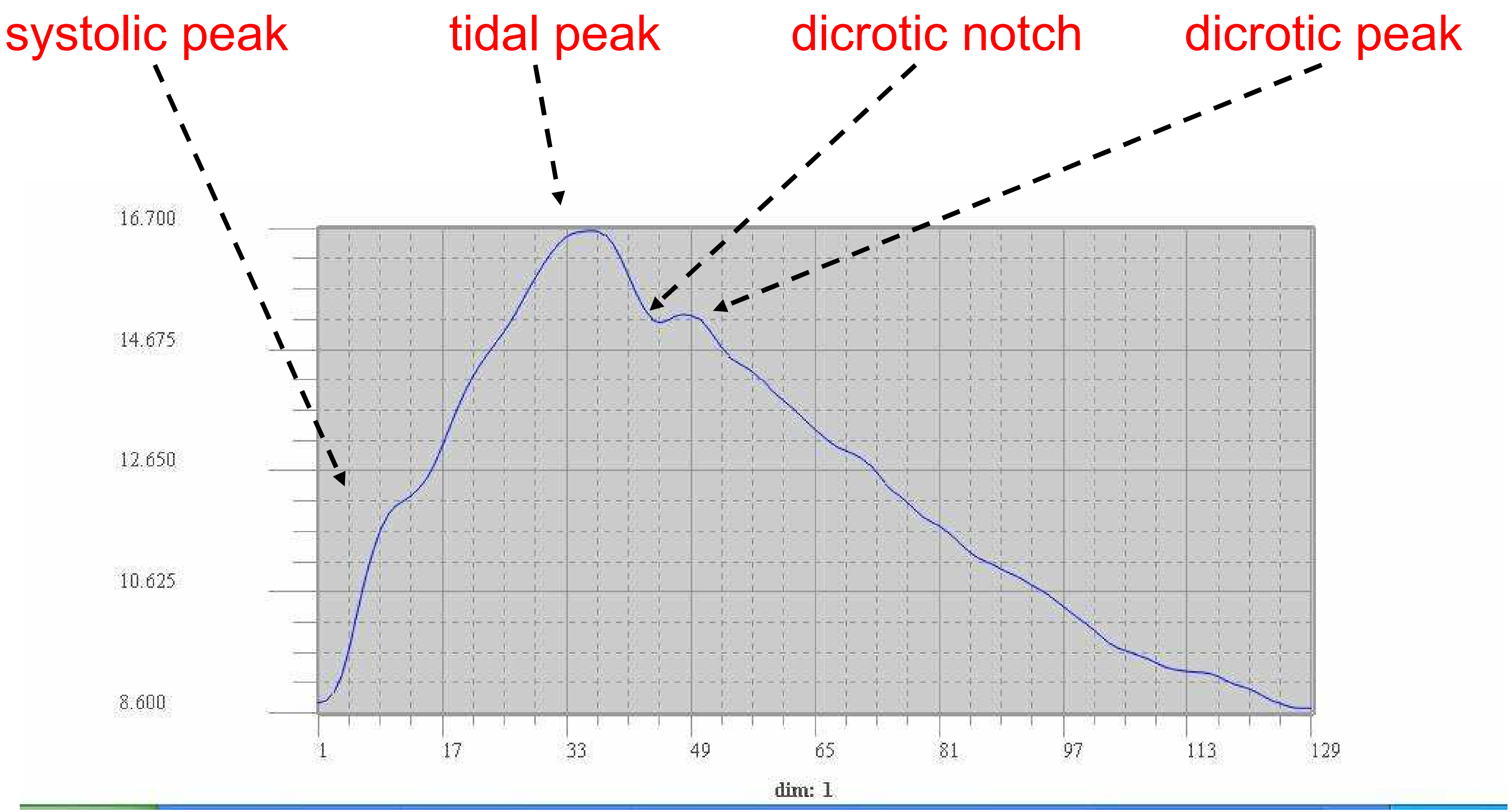
Class 2 – *Possible pathological*

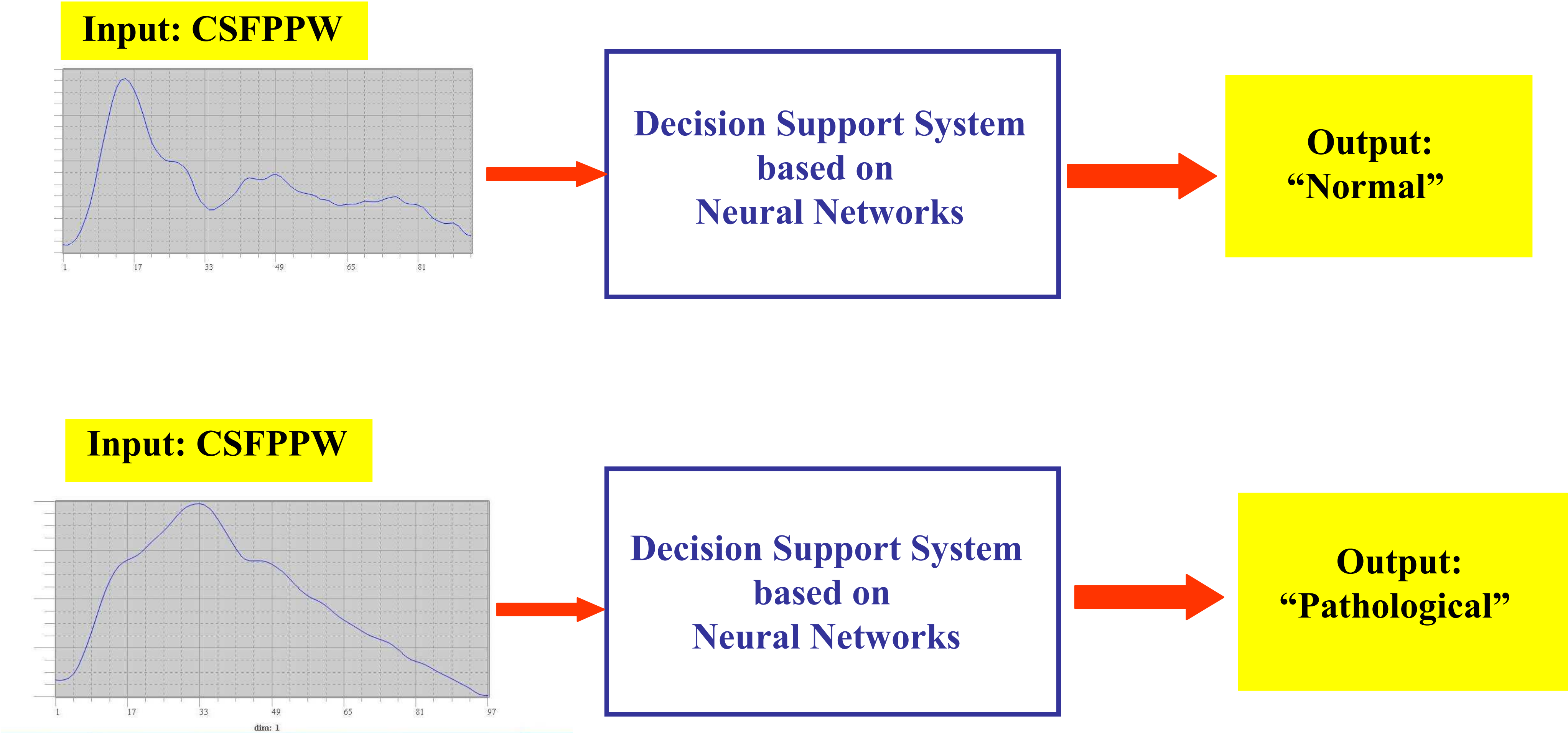


Class 3 – *Probable pathological*



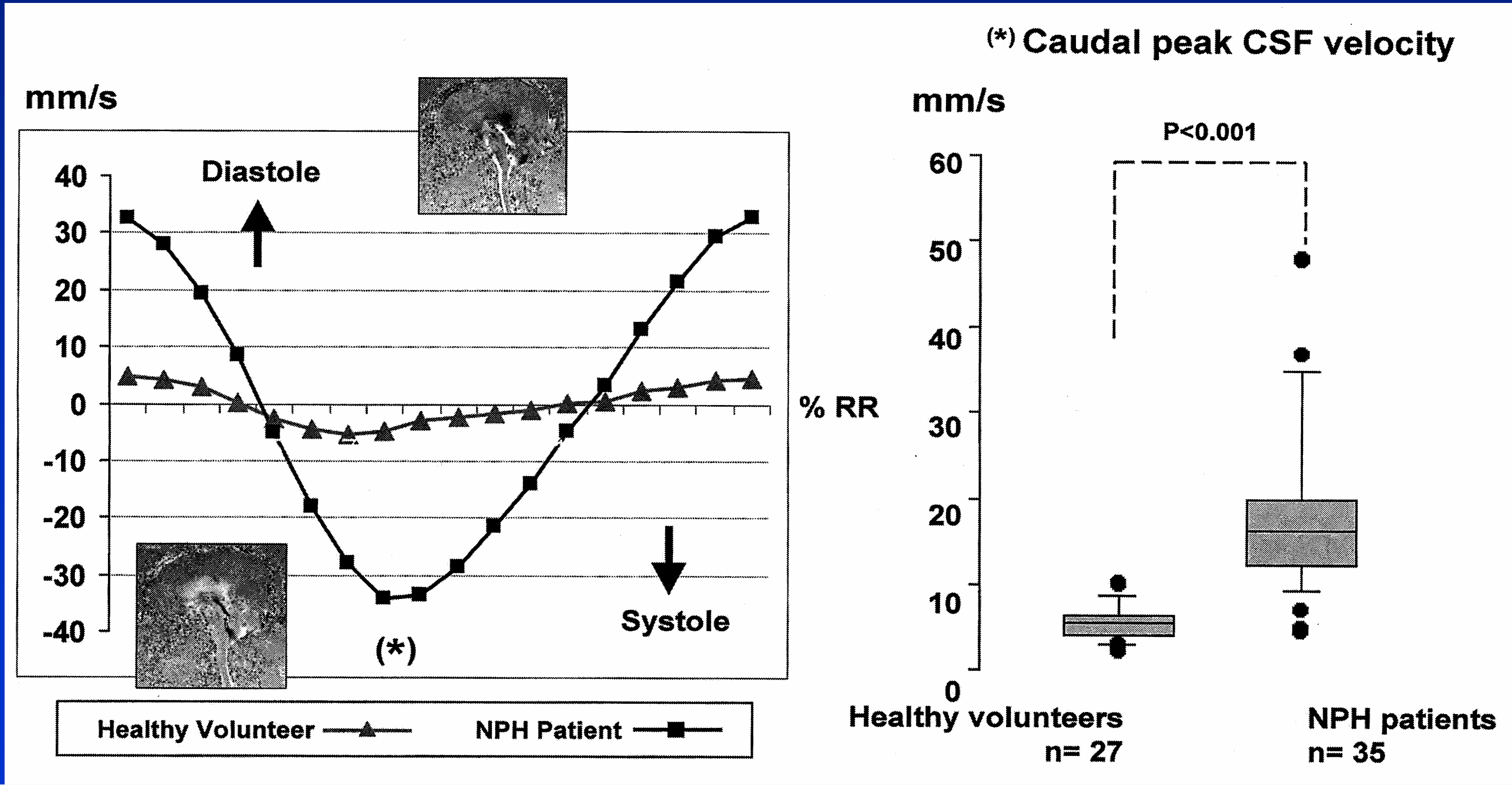
Class 4 – *Pathological*

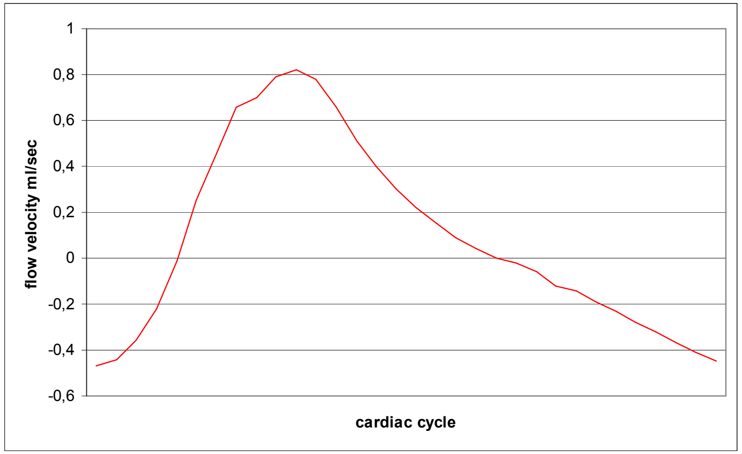



Input: CSFPPW
1
17
33
49
65
81
Decision Support System
based on
Neural Networks
Output:
“Normal”
Input: CSFPPW
1
17
33
49
65
81
97
dim: 1
Decision Support System
based on
Neural Networks
Output:
“Pathological”

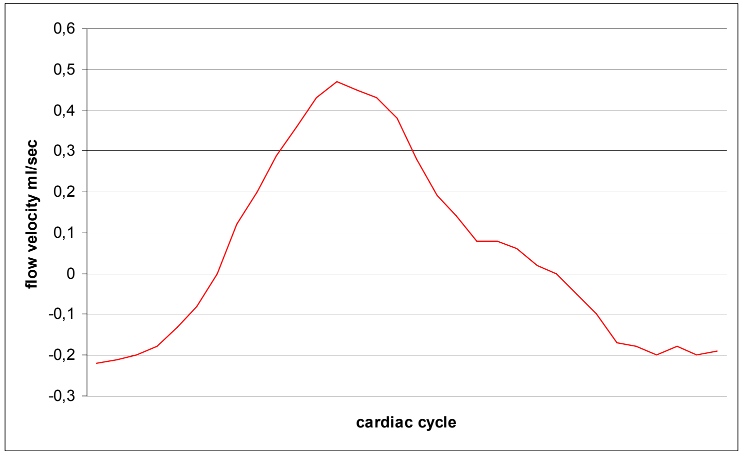
Correlation between waveform morphology and Intracranial Elastance

Agreement between CSF flow dynamics in MRI and ICP monitoring in the diagnosis of normal pressure hydrocephalus. Sensitivity and specificity of CSF dynamics to predict outcome. Poca MA et al., *Acta Neurochir [Suppl]* **81**:7-10, 2002.

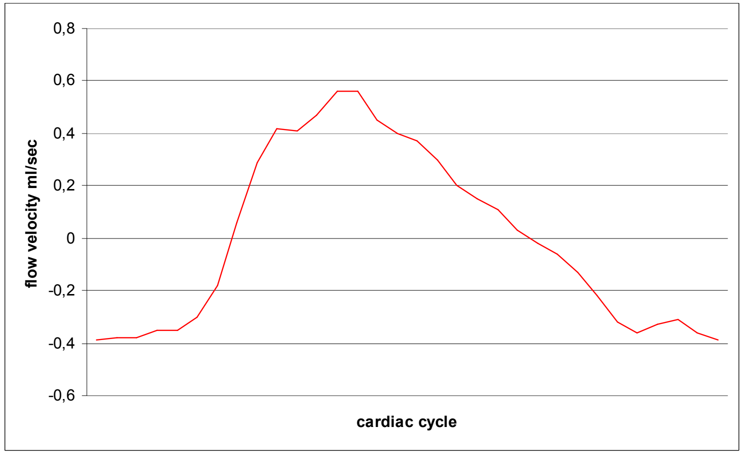




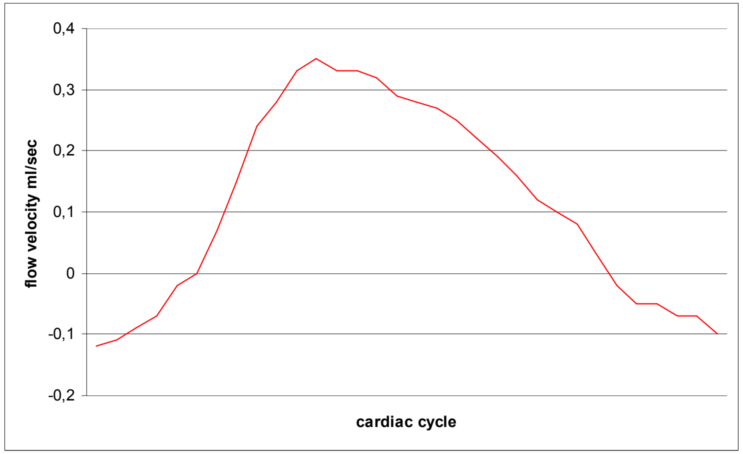
1
0,8
0,6
0,4
0,2
0
-0,2
-0,4
-0,6
flow velocity ml/sec
cardiac cycle



0,6
0,5
0,4
0,3
0,2
0,1
0
-0,1
-0,2
-0,3
flow velocity ml/sec
cardiac cycle



0,8
0,6
0,4
0,2
0
-0,2
-0,4
-0,6
flow velocity ml/sec
cardiac cycle

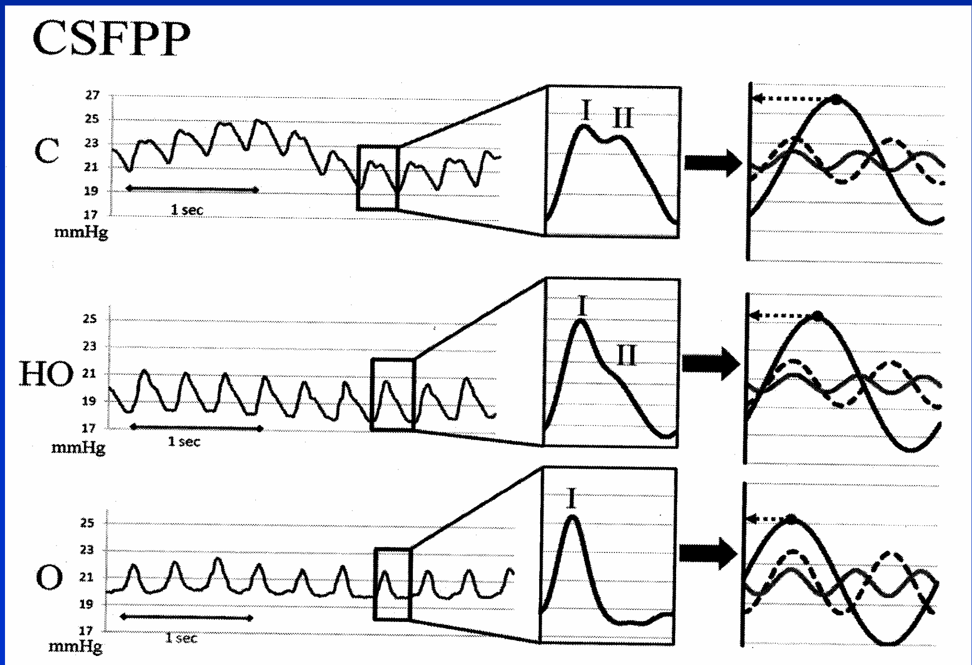


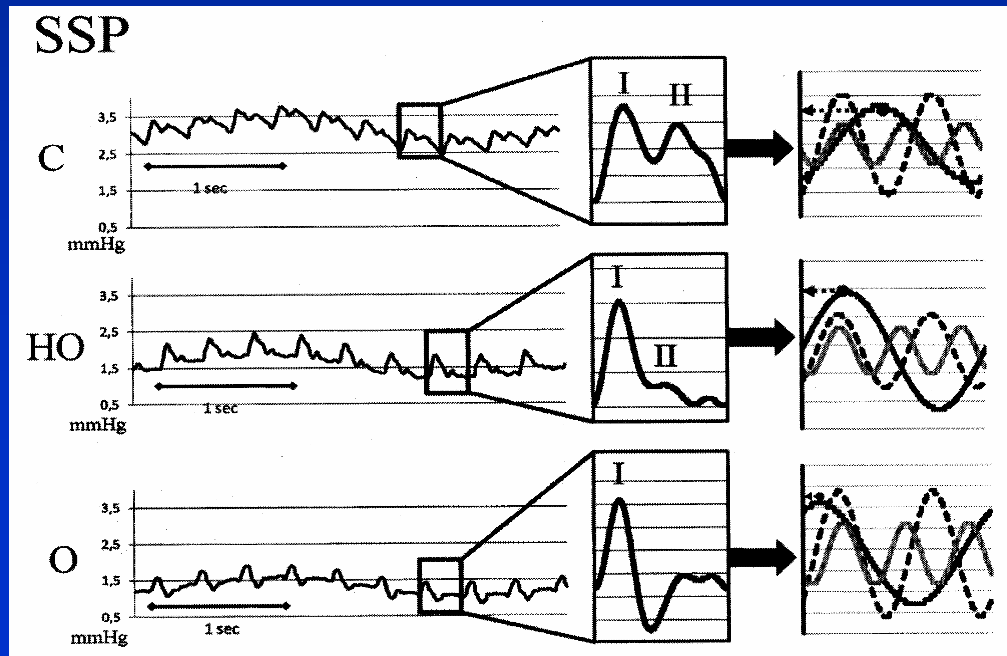
0,4
0,3
0,2
0,1
0
-0,1
-0,2
flow velocity ml/sec
cardiac cycle

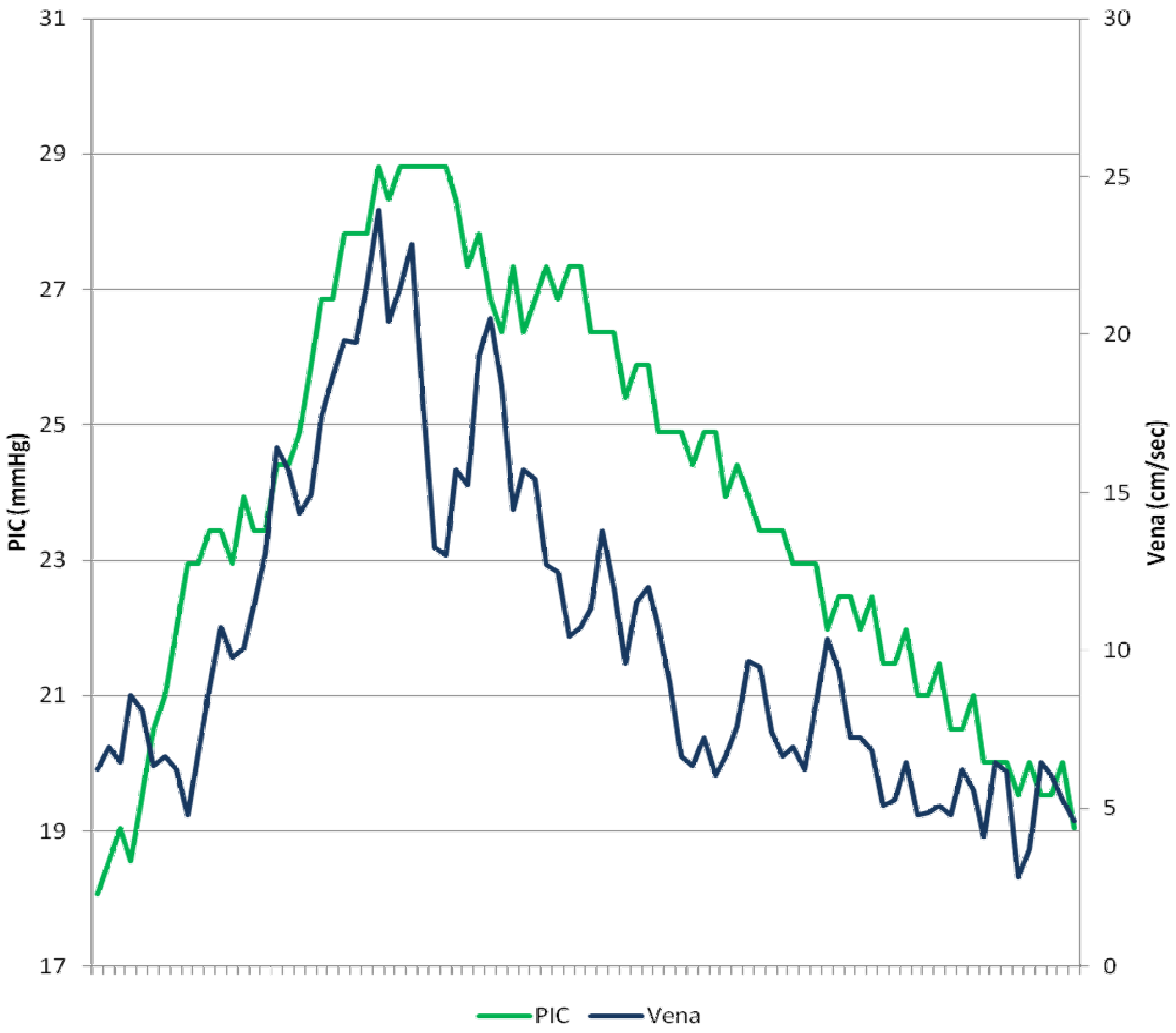
An experimental study on artificially induced CSF pulse waveform morphological modifications

Carmelo Anile[1], Pasquale De Bonis[1], Antonio Ficola[2], Pietro Santini[1], Annunziato Mangiola[1]

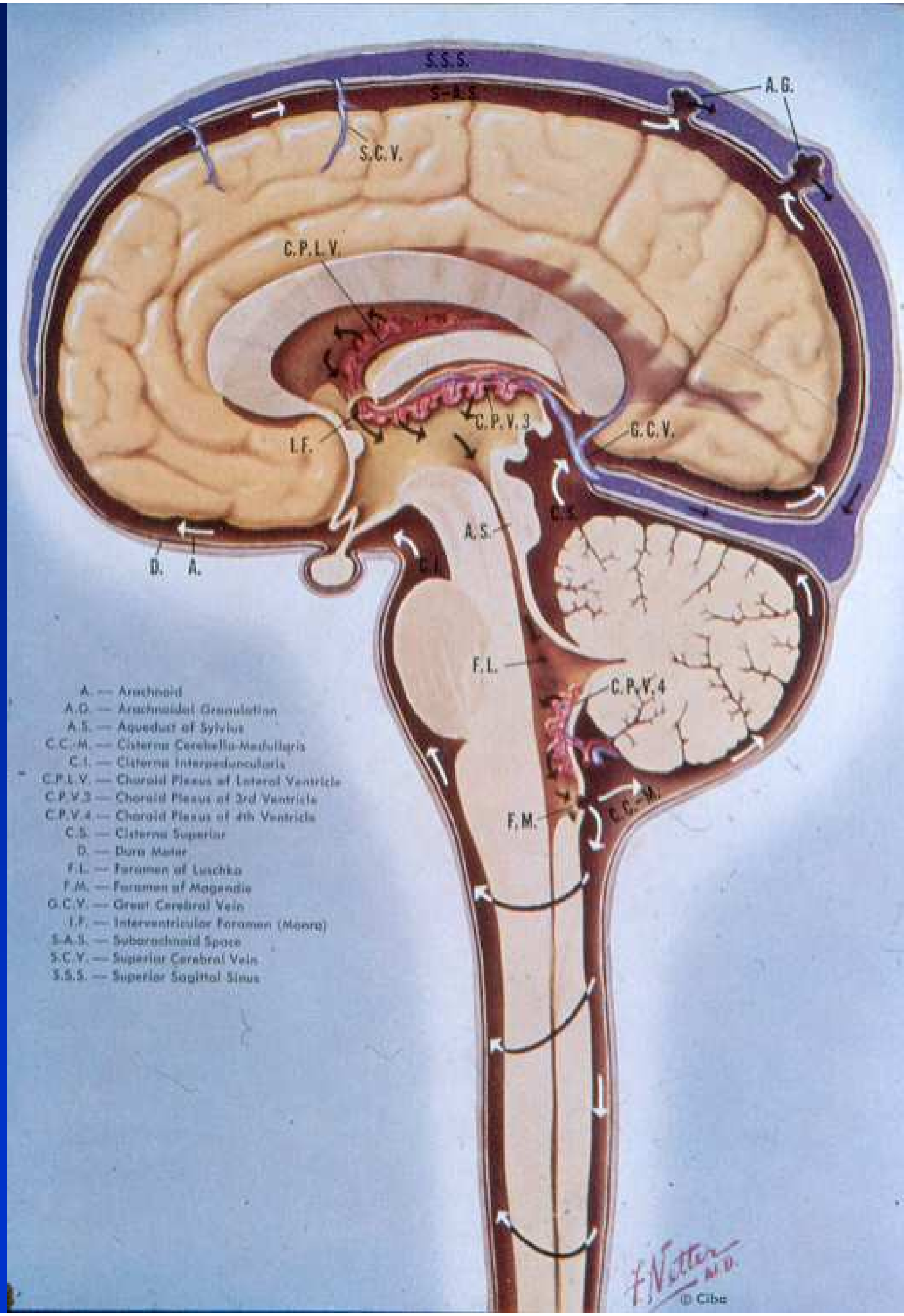
[1]Institute of Neurosurgery, Catholic University School of Medicine, Rome, Italy, [2]Department of Electronic and Information Engineering, University of Perugia, Perugia, Italy







31
29
27
25
23
21
19
17
PIC (mmHg)
30
25
20
15
10
5
0
Vena (cm/sec)
PIC
Vena


S.S.S.
S-A.S.
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C.P.V.3
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F. Netter M.D.
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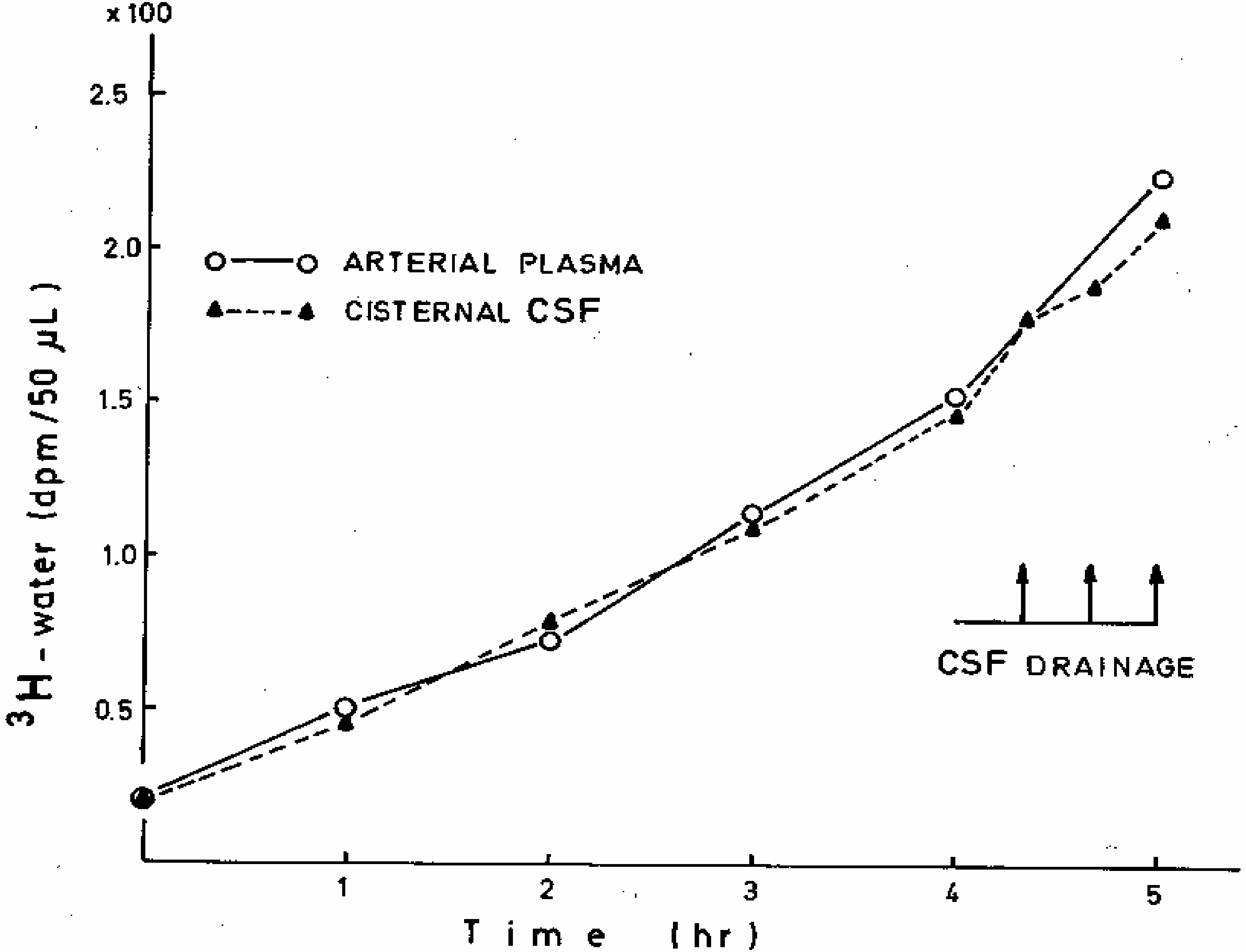
Three decades of normal pressure hydrocephalus: are we wiser now? Vanneste JAL. *J Neurol Neurosurg Psychiatry* **57**:1022-1024, 1994.

- *...defective CSF absorption through the arach-noid villi would not lead to ventricular enlarge-ment because it would not cause a pressure gra-dient between the ventricles and the subarachnoid space...there are neither physiological or patho-logical arguments to maintain the myth that ma-labsorption of CSF causes ventricular dilation.*

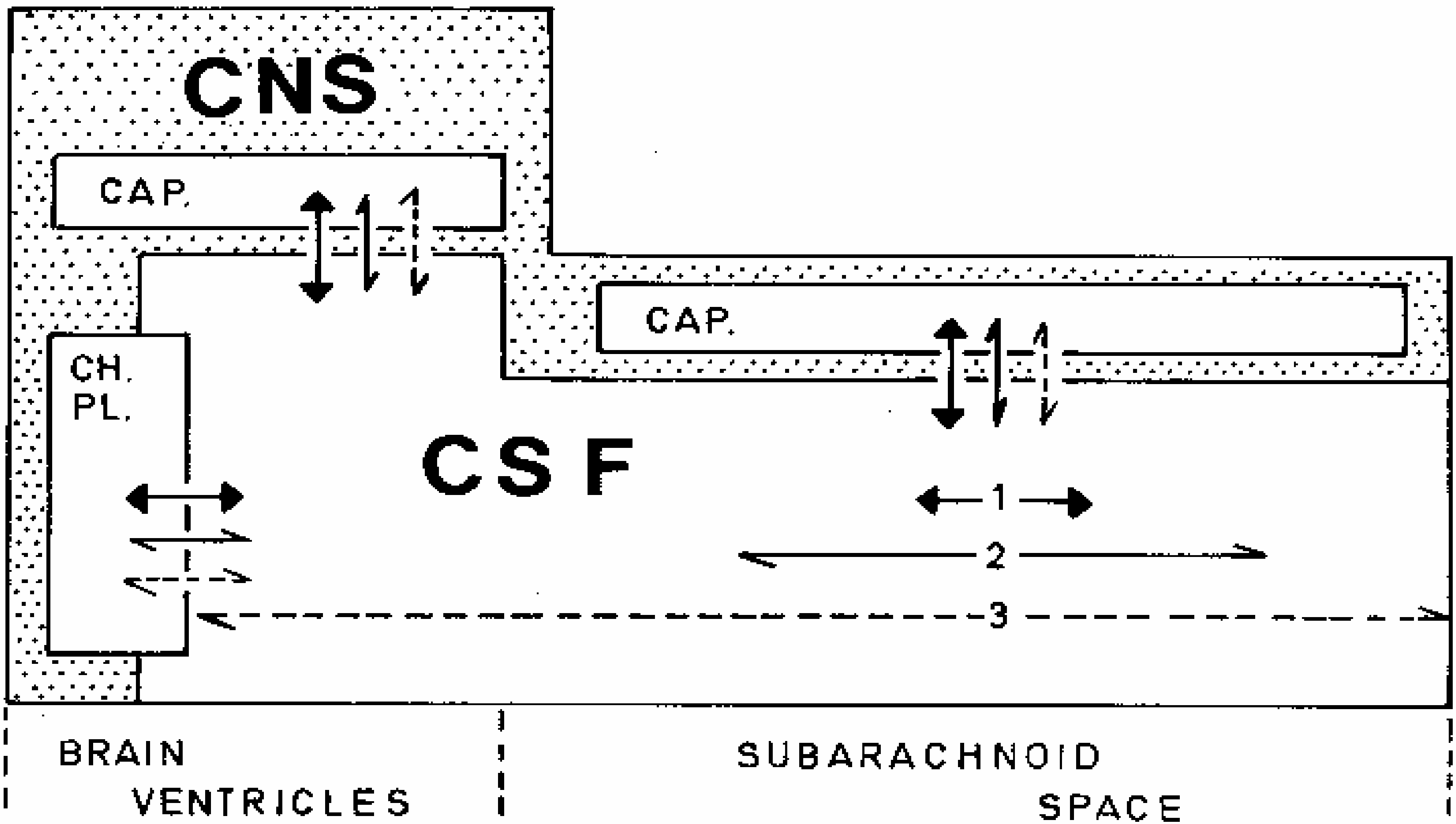
- *...malabsorption of CSF is associated* [non sem-pre] *with communicating hydrocephalus, but does not cause it.*

Dynamics and statics of the cerebrospinal fluid: the classical and a new hypothesis. Bulat M. *ICP VIII*, pp. 726-730, 1993.

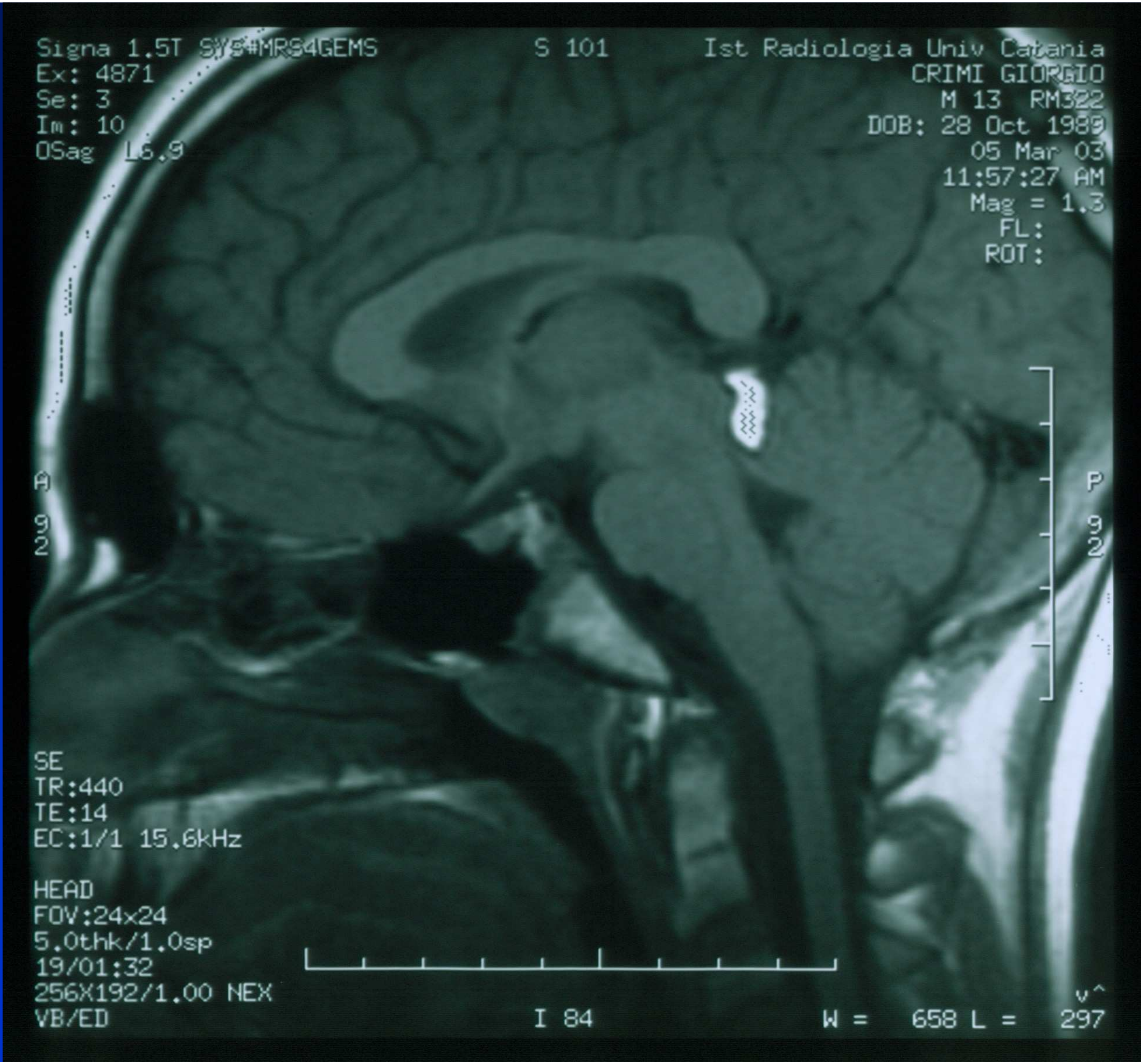
- *All data mentioned indicate that there is flow or circulation of CSF volume (water) between various CSF compartments but that a rapid exchange of water molecules occurs between these compartments and adjacent blood capillaries. Since water constitu-tes 99% of CSF volume it is obvious that the classi-cal circulation and absorption of CSF volume do not exist.*



x 100
2.5
2.0
1.5
1.0
0.5
^{3}H - water (dpm /50 μL)
ARTERIAL PLASMA
CISTERNAL CSF
CSF DRAINAGE
1
2
3
4
5
Time (hr)



CNS
CAP.
CAP.
CH.
PL.
CSF
1
2
3
BRAIN
VENTRICLES
SUBARACHNOID
SPACE


Signa 1.5T SYS#MRS4GEMS
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Se: 3
Im: 10
OSag L6.9
S 101
Ist Radiologia Univ Catania
CRIMI GIORGIO
M 13 RM322
DOB: 28 Oct 1989
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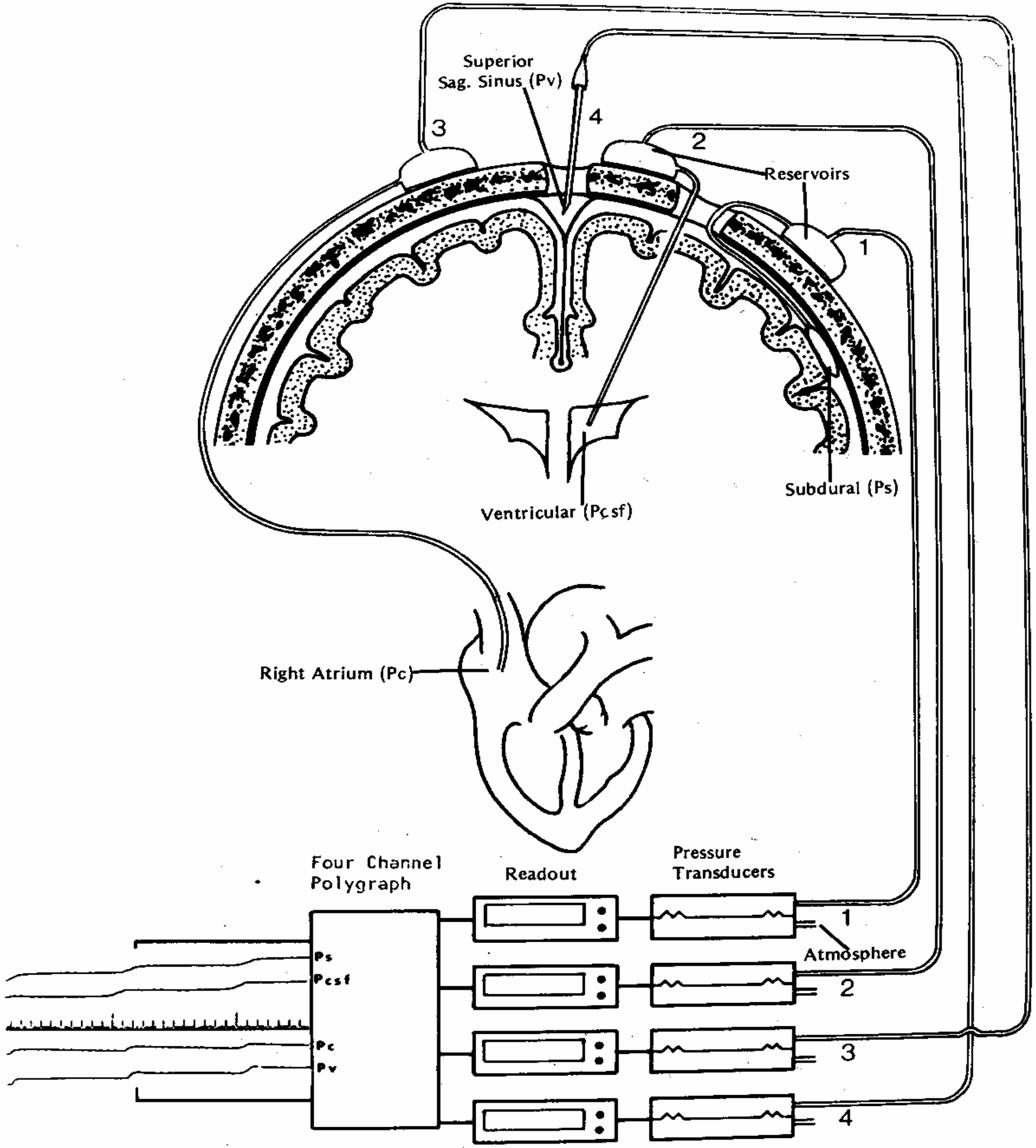
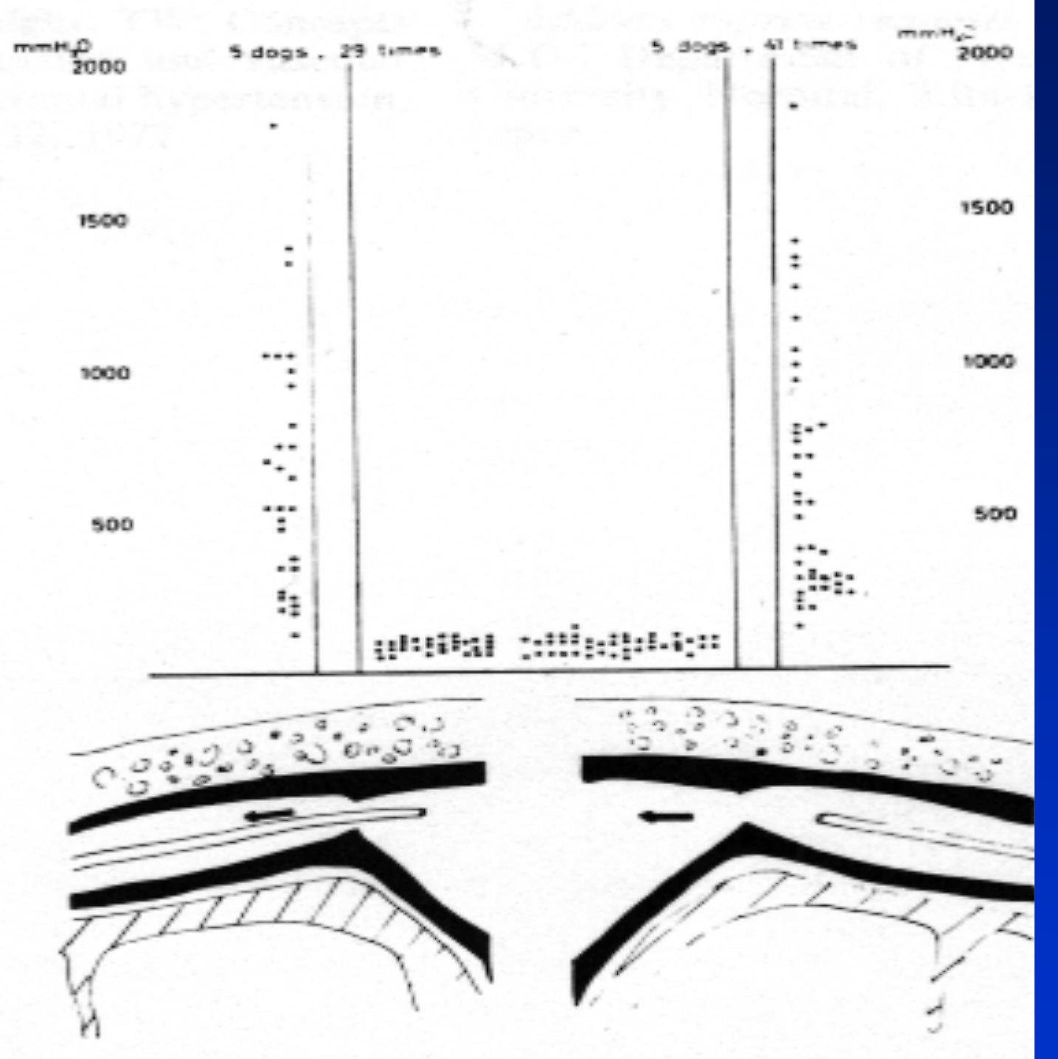
Mag = 1.3
FL:
ROT:
A
9
2
P
9
2
SE
TR:440
TE:14
EC:1/1 15.6kHz
HEAD
FOV:24x24
5.0thk/1.0sp
19/01:32
256X192/1.00 NEX
VB/ED
I 84
W = 658 L = 297

Effect of aqueductal blockage on cerebrospinal fluid formation in isolated brain ventricles. Klarica M et al. *3rd International Hydrocephalus Worshop* - Kos, 17-20 May 2001.

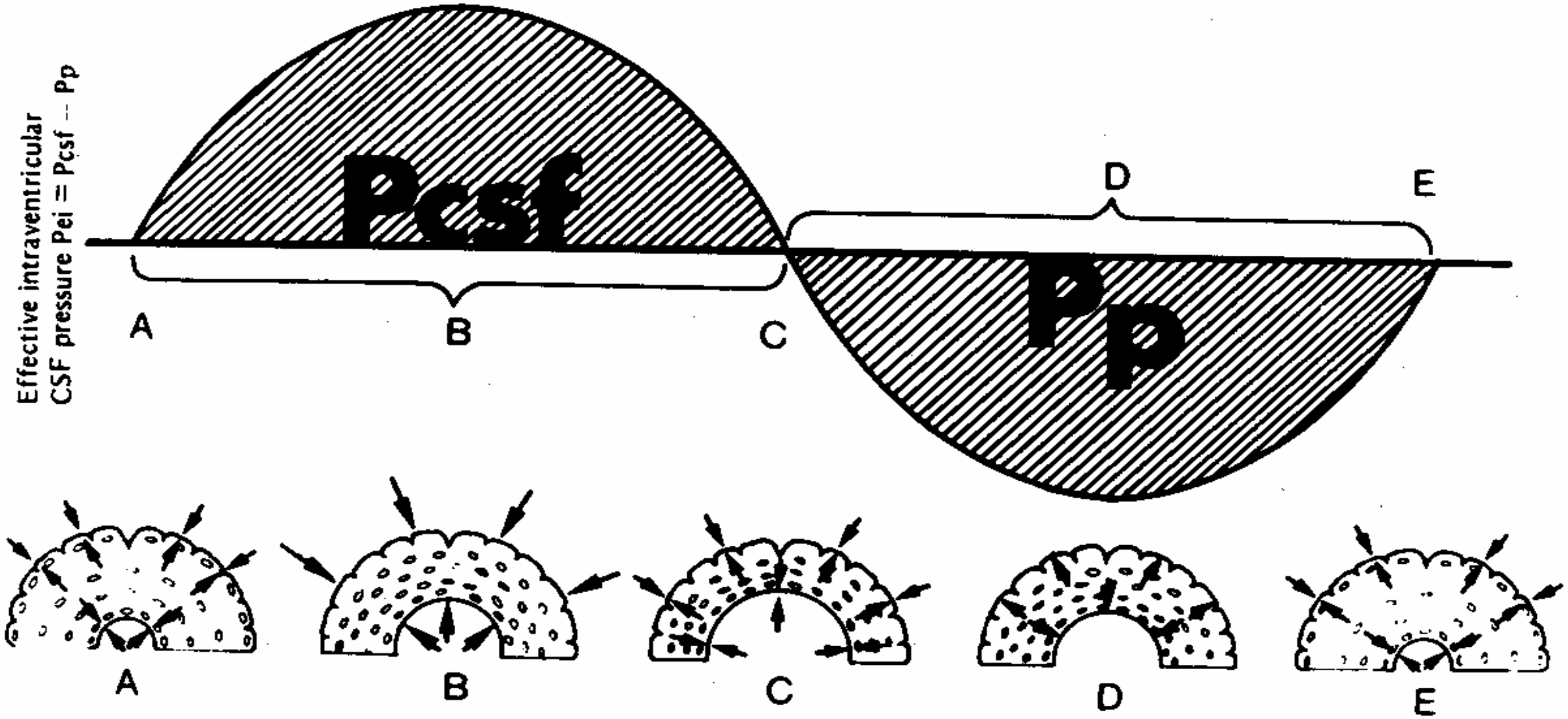
•*After blockage of aqueduct, the CSF pressure in iso-lated ventricles and cisterna magna were not diffe-rent from control value and cerebral transmantle pressure gradient did not develop over several hours.*

•*The results indicate that there is not net formation and accumulation of CSF in isolated ventricles and suggest that some other factor is responsible for development of hydrocephalus after blockage of aqueduct.*


Superior
Sag. Sinus (Pv)
3
4
2
Reservoirs
1
Subdural (Ps)
Ventricular (Pcsf)
Right Atrium (Pc)
Four Channel
Polygraph
Readout
Pressure
Transducers
Ps
Pcsf
Pc
Pv
1
Atmosphere
2
3
4



mmH2O
5 dogs , 29 times
5 dogs , 41 times
mmH2O
2000
1500
1000
500



A	B	?	C	D	E
$P_{csf} = P_p$	$P_{csf} > P_p$		$P_{csf} = P_p$	$P_{csf} < P_p$	$P_{csf} = P_p$
$P_{ei} = 0$	$P_{ei} > 0$		$P_{ei} = 0$	$P_{ei} < 0$	$P_{ei} = 0$

Fig. 29. The development, maintenance and reversal of hydrocephalus. Analysis of the pressure changes, fluid movement, and stress distribution within the brain parenchyma.

A: Normal ventricle, steady state, no deformation.

B: Ventricular dilatation in progress, positive gradient, distortion of parenchyma.

C: Enlarged ventricles, steady state, plastic deformation.

D: Hydrocephalus under shunt treatment, reversed gradient, expansion of parenchyma.

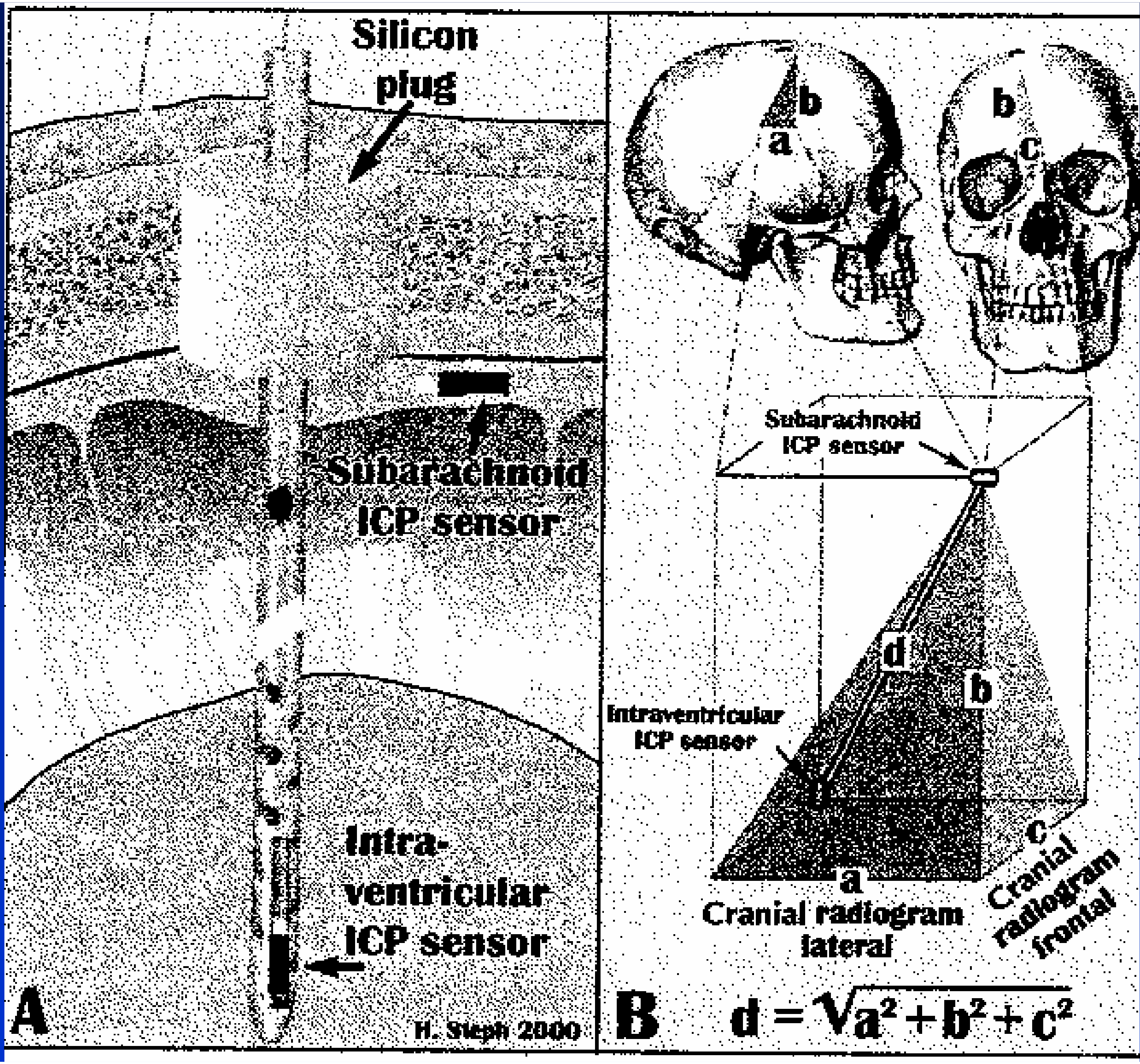
E: Normal ventricle, steady state, no deformation.

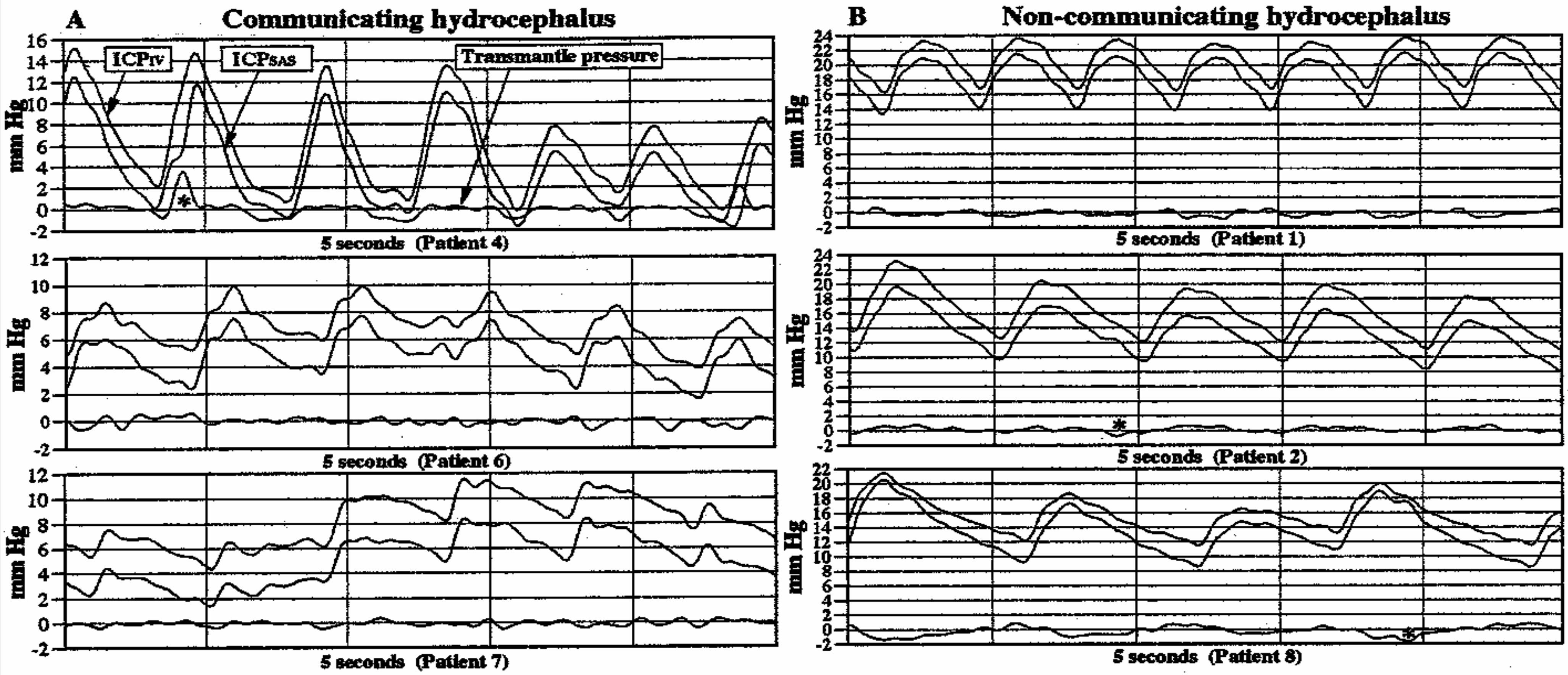
There is no transmantle pressure gradient in communicating or noncommunicating hydrocephalus.
Stephensen H et al. *Neurosurgery* **50**:763-773, 2002.

- *There is no transmantle pressure gradient in patients with communicating and noncommunica-ting hydrocephalus, and ICP in these patients be-haves in accordance with the Pascal principle. The chief factor for this is the pulsation and mo-vements of the brain during the cardiac cycle, which equalizes all possible pressure differences between different parts of the CSF system, even when there is no direct communication.*

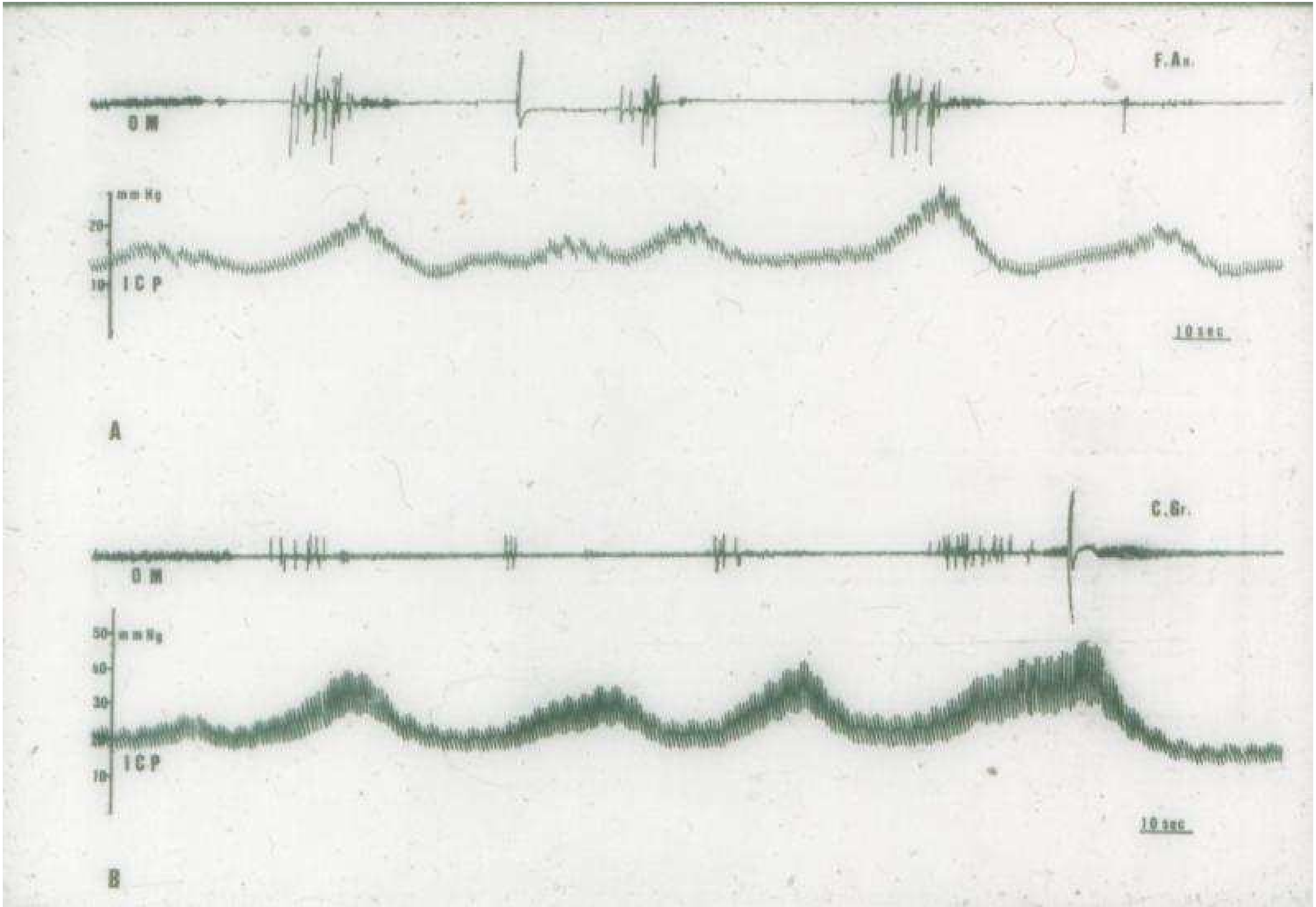
There is no transmantle pressure gradient in communicating or noncommunicating hydrocephalus. Stephensen H et al. *Neurosurgery* **50**:763-773, 2002.

- *Our results lead us to propose that brain pulsa-tion simultaneously exerts the same force on the subarachnoid space and the ventricles during the entire cardiac cycle, as is reflected by the identi-cal pulse pressure wave forms in both spaces.*


Silicon plug
Subarachnoid ICP sensor
Intra-ventricular ICP sensor
A
H. Steph 2000
b
a
b
c
Subarachnoid ICP sensor
d
b
Intraventricular ICP sensor
a
c
Cranial radiogram lateral
Cranial radiogram frontal
B
$d = \sqrt{a^2 + b^2 + c^2}$



A
Communicating hydrocephalus
ICPIV
ICPSAS
Transmantle pressure
mm Hg
5 seconds (Patient 4)
5 seconds (Patient 6)
5 seconds (Patient 7)
B
Non-communicating hydrocephalus
5 seconds (Patient 1)
5 seconds (Patient 2)
5 seconds (Patient 8)

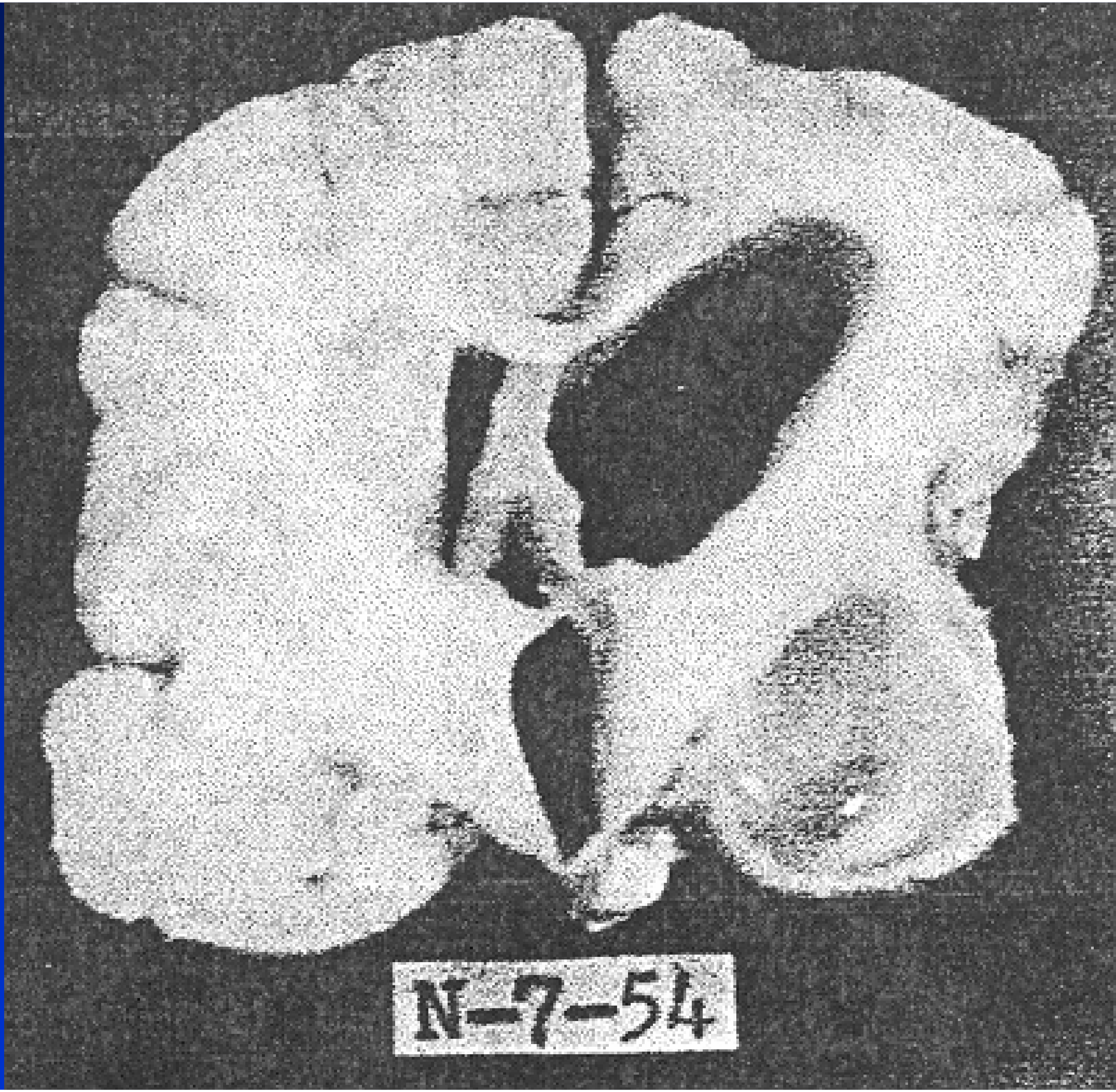

F.An.
OM
mm Hg
20
10
ICP
10 sec
A
C.Gr.
OM
50
mm Hg
40
30
10
ICP
10 sec
B

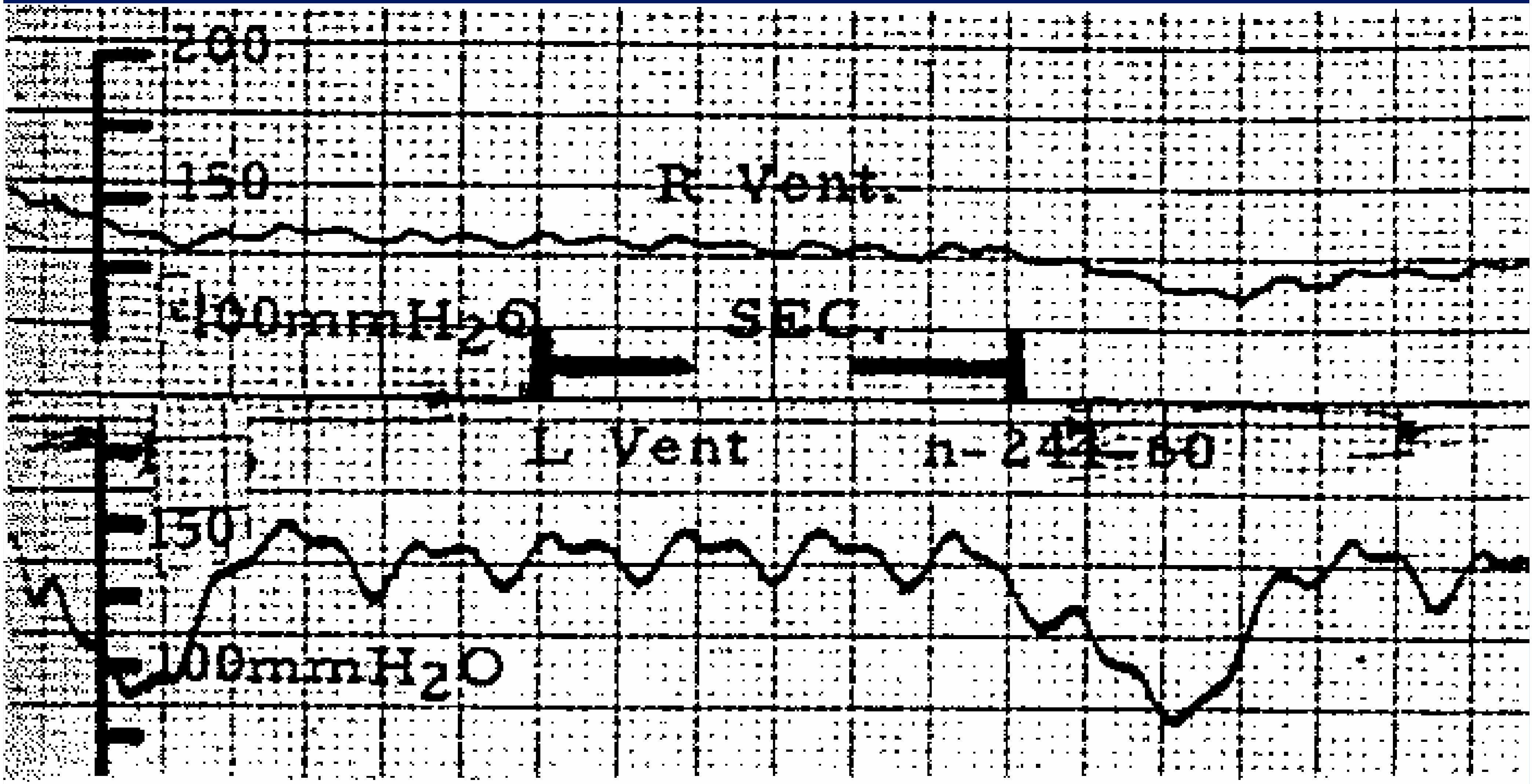
Experimental hydrocephalus. Dandy WE. *Ann Surg* **70**:129-142, 1919.

•*In 1919, in a study of experimental hydroepha-lus, Dandy occluded the foramen of Monro on one side in normal dogs,* and the ispilateral ven-tricle enlarged. *Then, he occluded the foramen of Monro after choroid plexectomy,* and the ventri-cle did not enlarge. *He concluded that the cho-roid plexus was the source of CSF, and that en-largement of the ventricle was due to the back pressure of the accumulated CSF in the ventricle.*

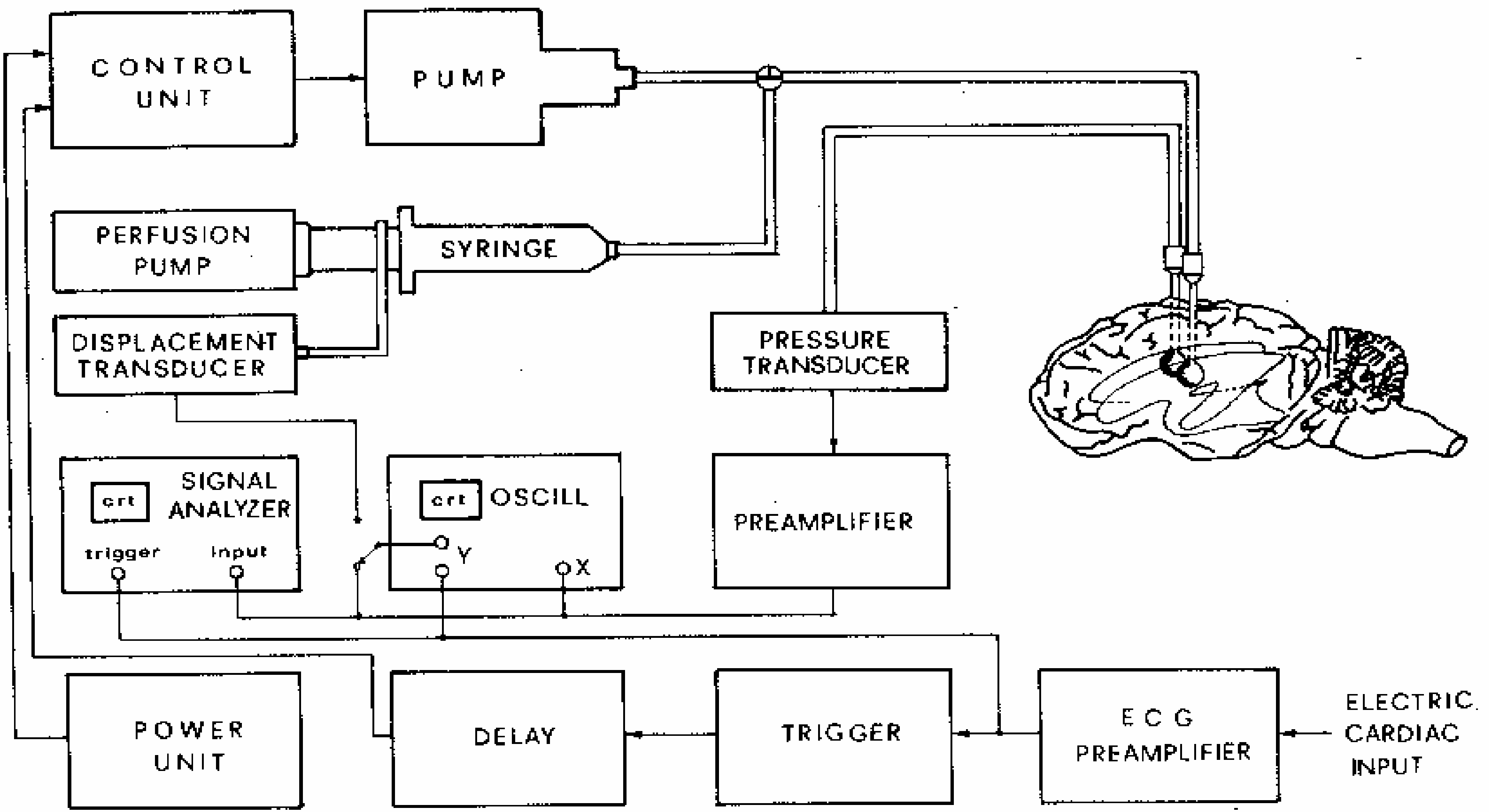
Circulation of the cerebrospinal fluid: demonstra-tion of the choroid plexus as the generator of the force for flow of fluid and ventricular enlarge-ment. Bering EA. *J Neurosurg* **19**:405-413, 1962.

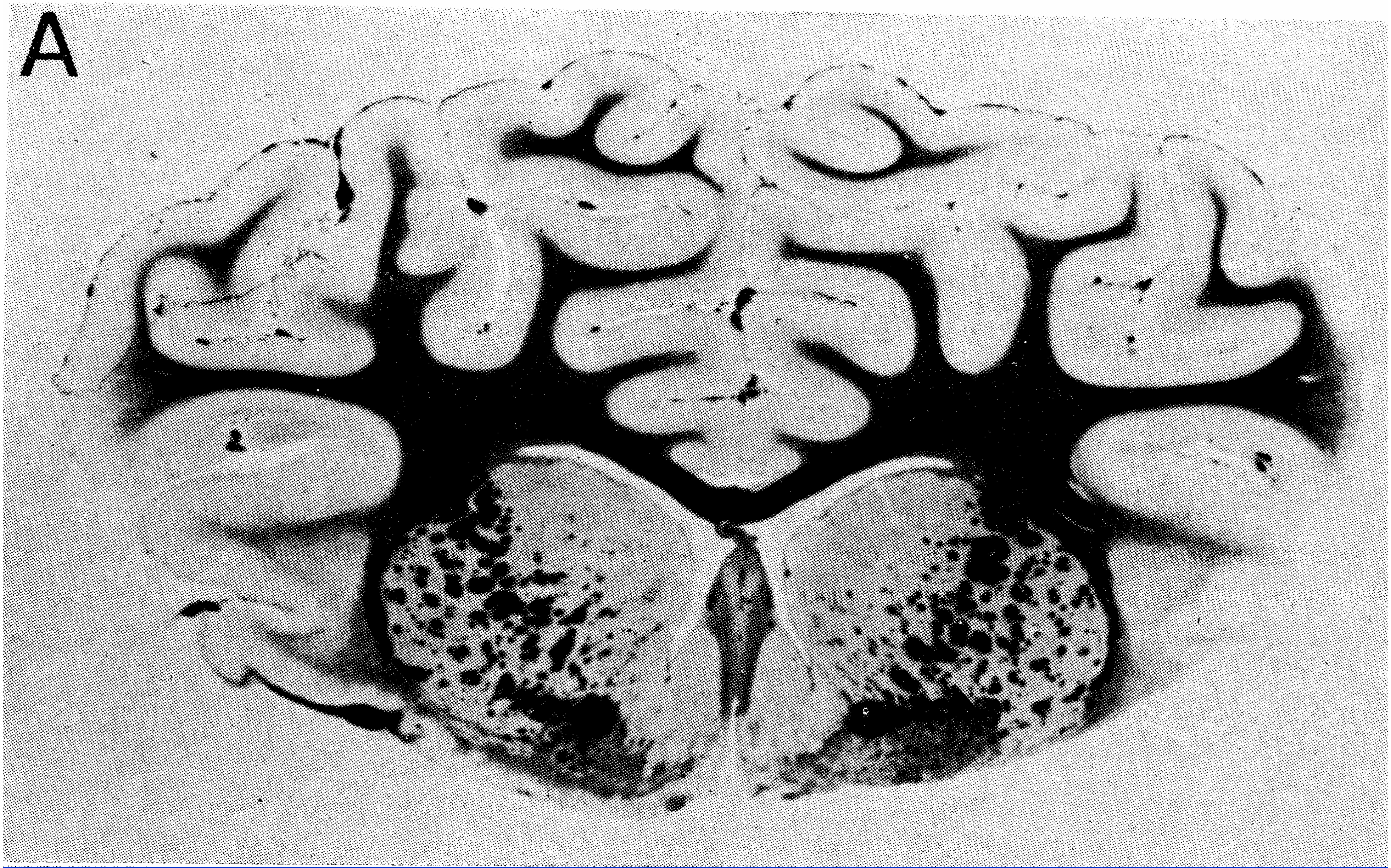
•*He produced hydrocephalus in dogs by cisternal kaolin injection and removed the choroid plexus from one lateral ventricle. ... The ventricle with-out the choroid plexus remained small; only the ventricle with the choroid plexus enlarged. Bering concluded that ventricular enlargement was not the result of increased intraventricular pressure from accumulated CSF; ...both the ventricle(s)... were subject to the same static fluid pressures.*

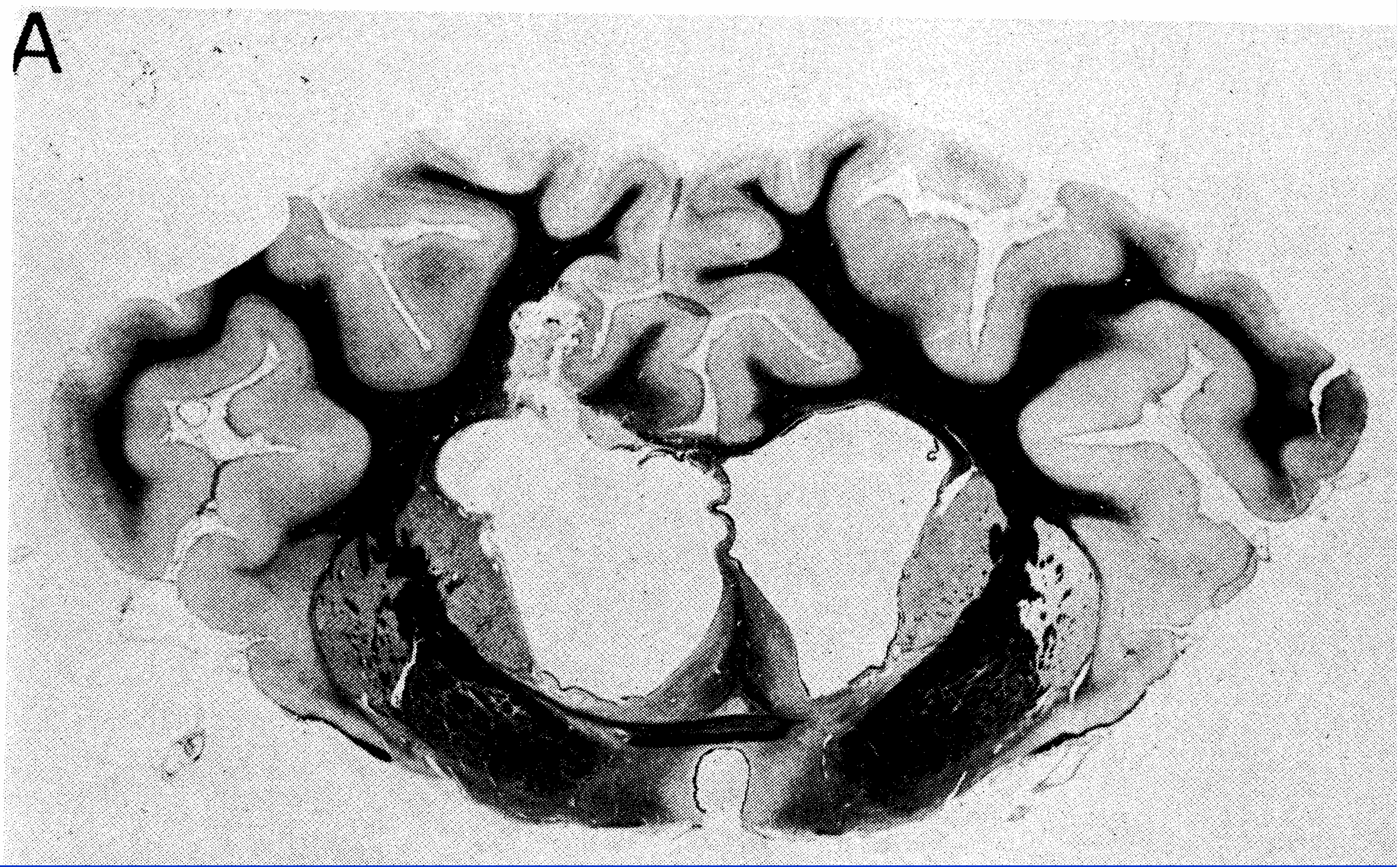

N-7-54


200
150
R Vent.
100mmH2O
SEC.
L Vent
100mmH2O

HYDROCEPHALUS MODEL




A

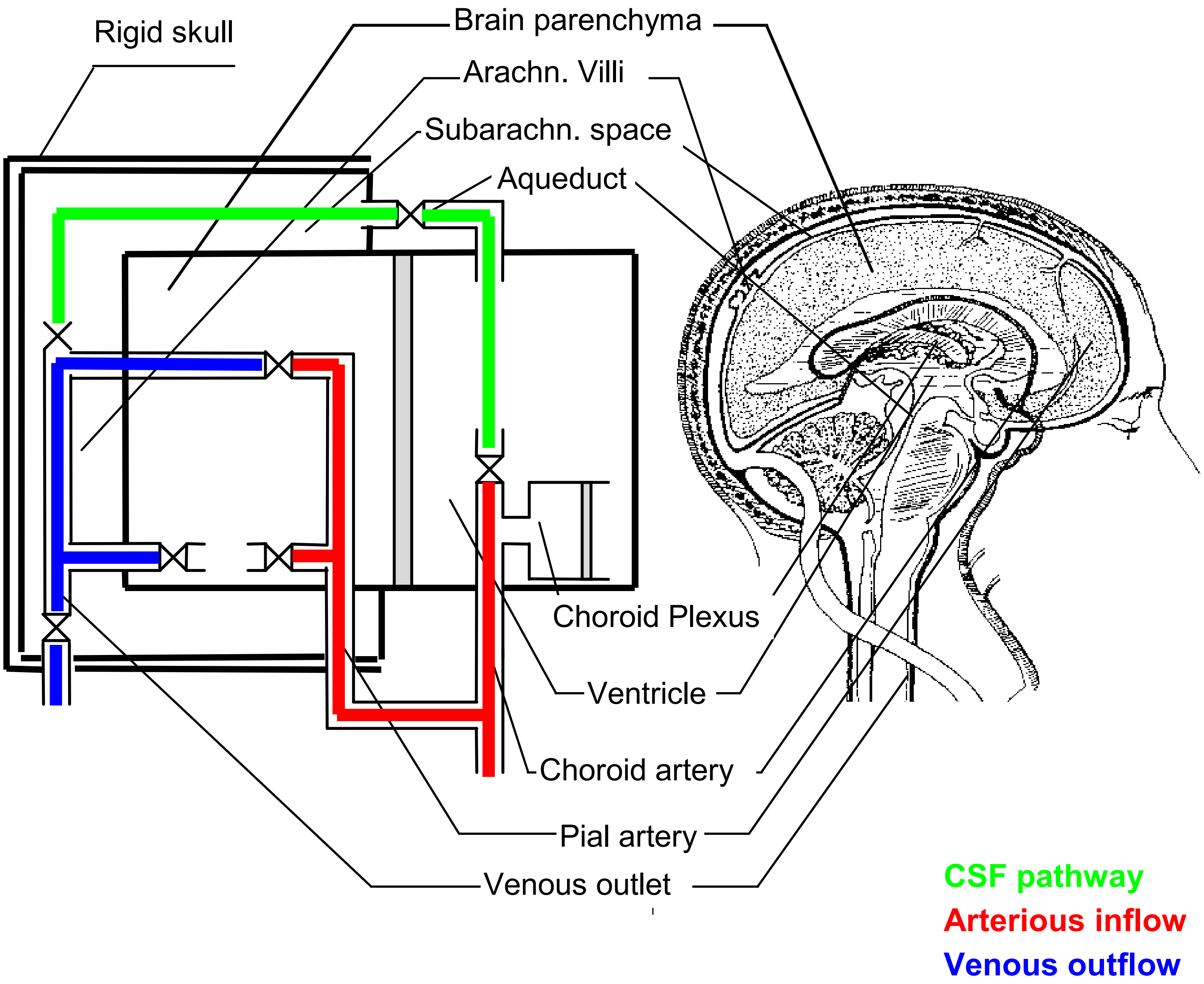

A

A mathematical model to explain ventricular enlargement in NPH

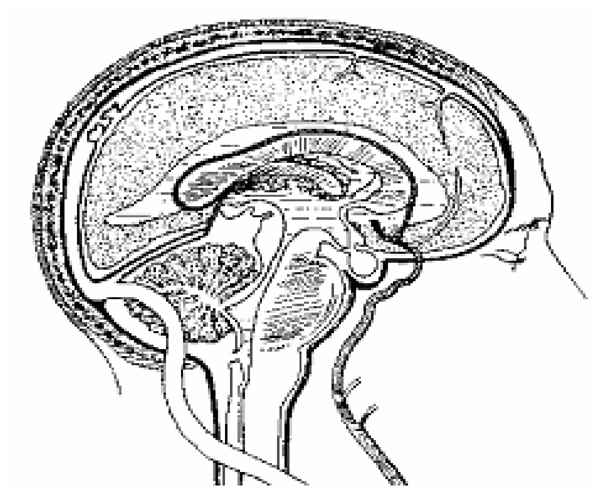
Antonio FICOLA[1] and Carmelo ANILE[2]

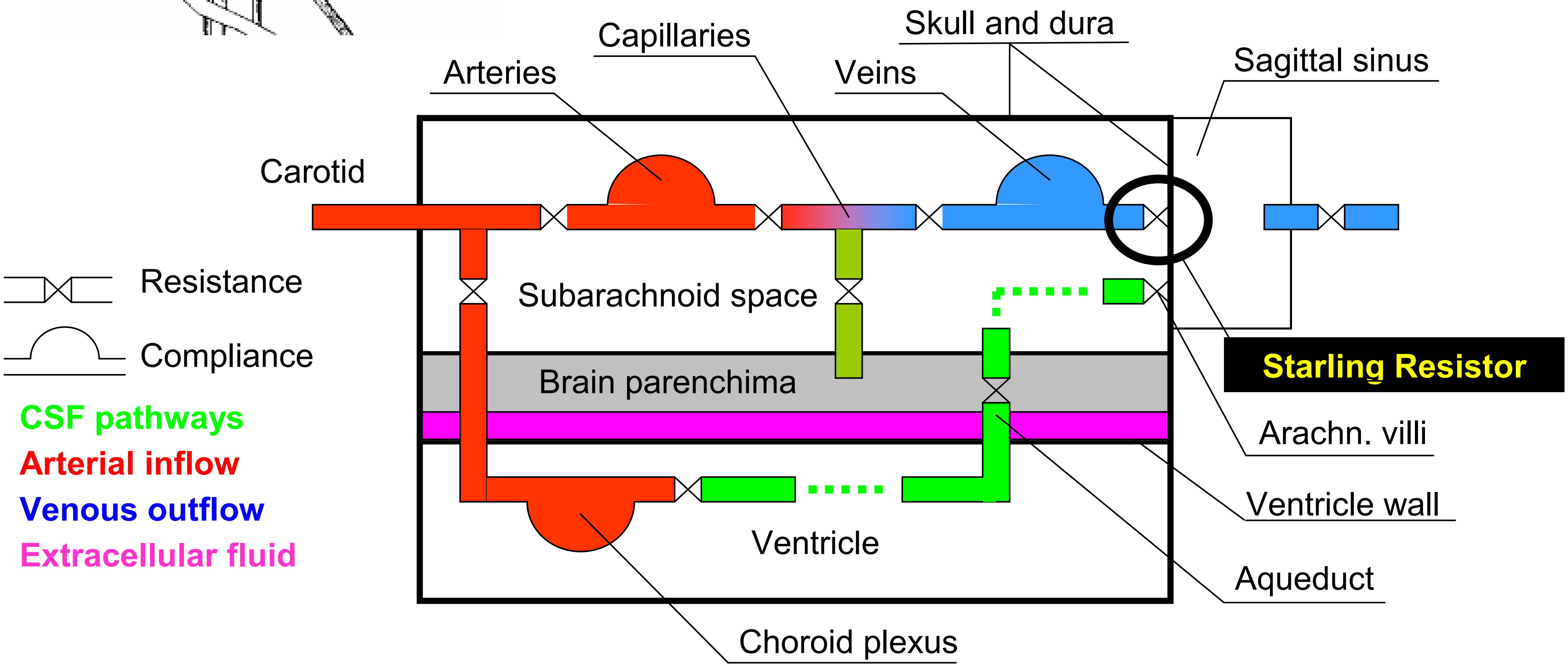
[1]University of Perugia, Dept. of Electronic and Information Engineering, Perugia, Italy

[2]Catholic University of Rome, Institute of Neurosurgery, Rome, Italy


Rigid skull
Brain parenchyma
Arachn. Villi
Subarachn. space
Aqueduct
Choroid Plexus
Ventricle
Choroid artery
Pial artery
Venous outlet
CSF pathway
Arterious inflow
Venous outflow

THE INTRACRANIAL SYSTEM MODEL





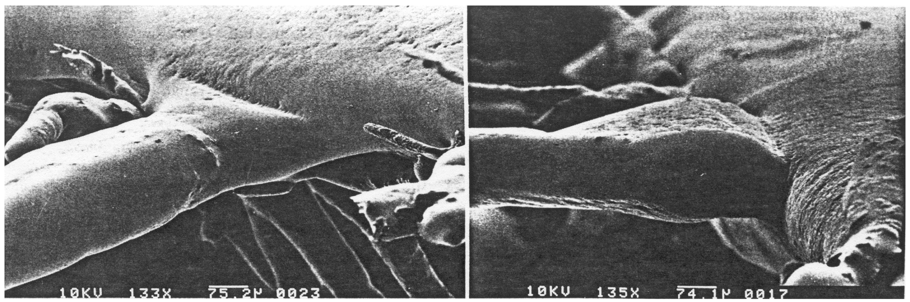
MODEL ASSUMPTIONS

- The model implements the Monro-Kellie doctrine:

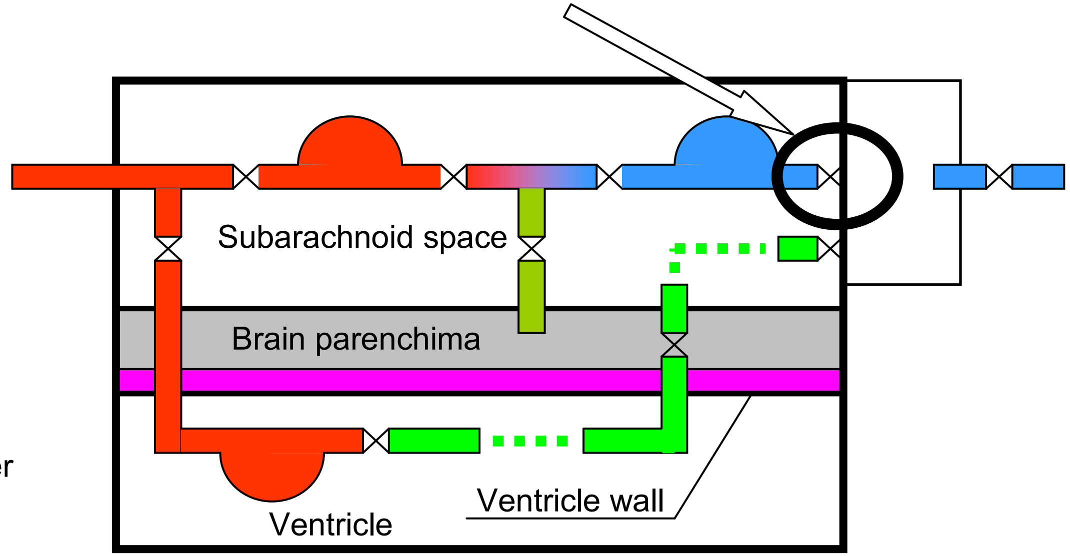
Blood + CSF + Brain parenchima = Const.

Brain parenchima = Cell volume + ExtraCellular Fluid (ECF)

- The venous outflow is regulated by a Starling Resistor.



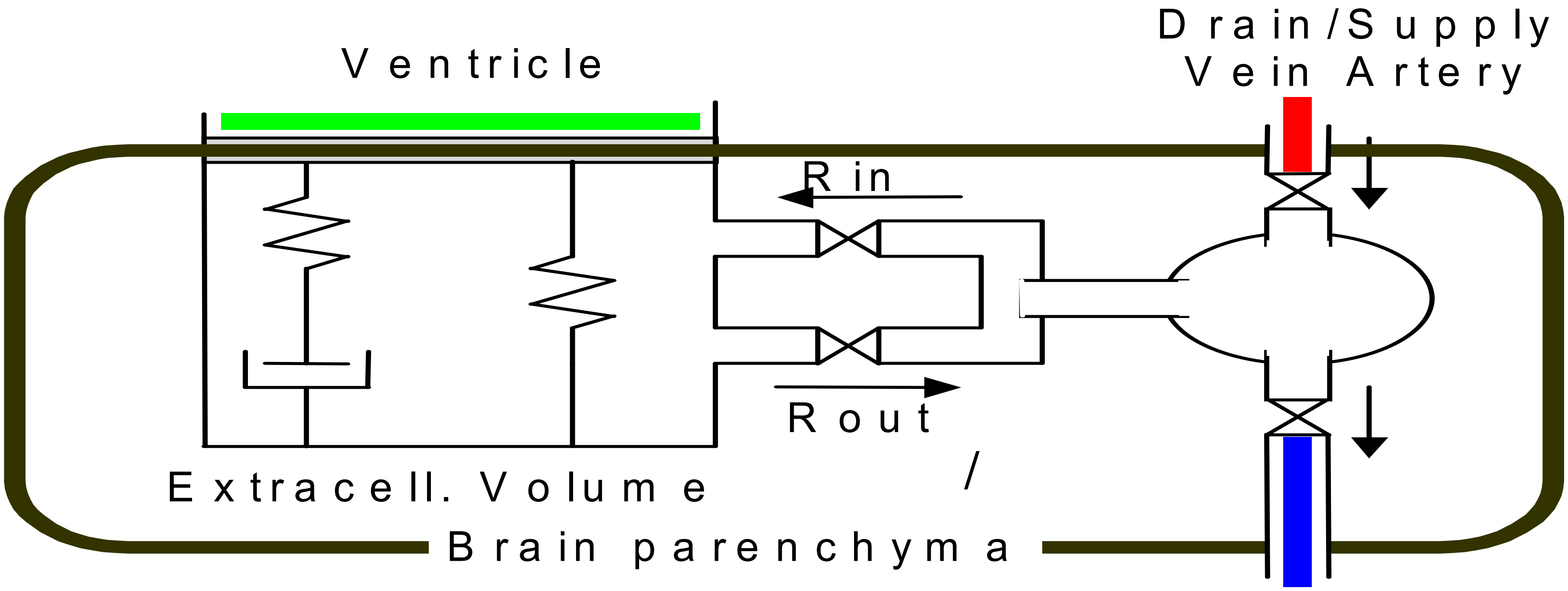
From: L.M. Auer, N. Ishiyama, K.C. Hodde, R. Kleinert, R. Pucher
Effect of intracranial pressure on bridging veins in rats.



Brain parenchyma under variable loads:

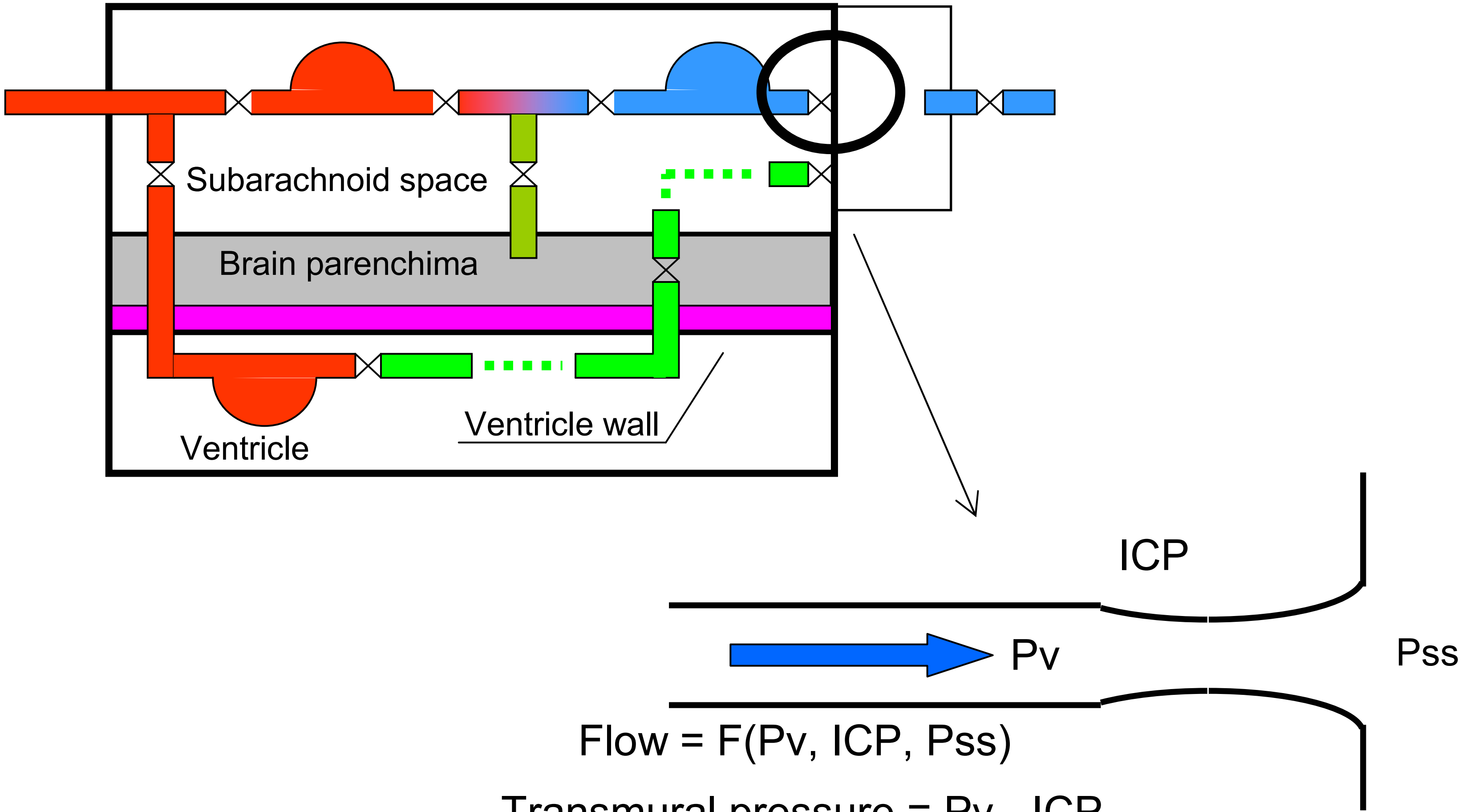
- the parenchyma is modeled like a sponge;
- it is assumed that *it is easier to squeeze it than to make it suck in.*

VISCOELASTIC MODEL OF THE BRAIN TISSUE



Rin>Rout

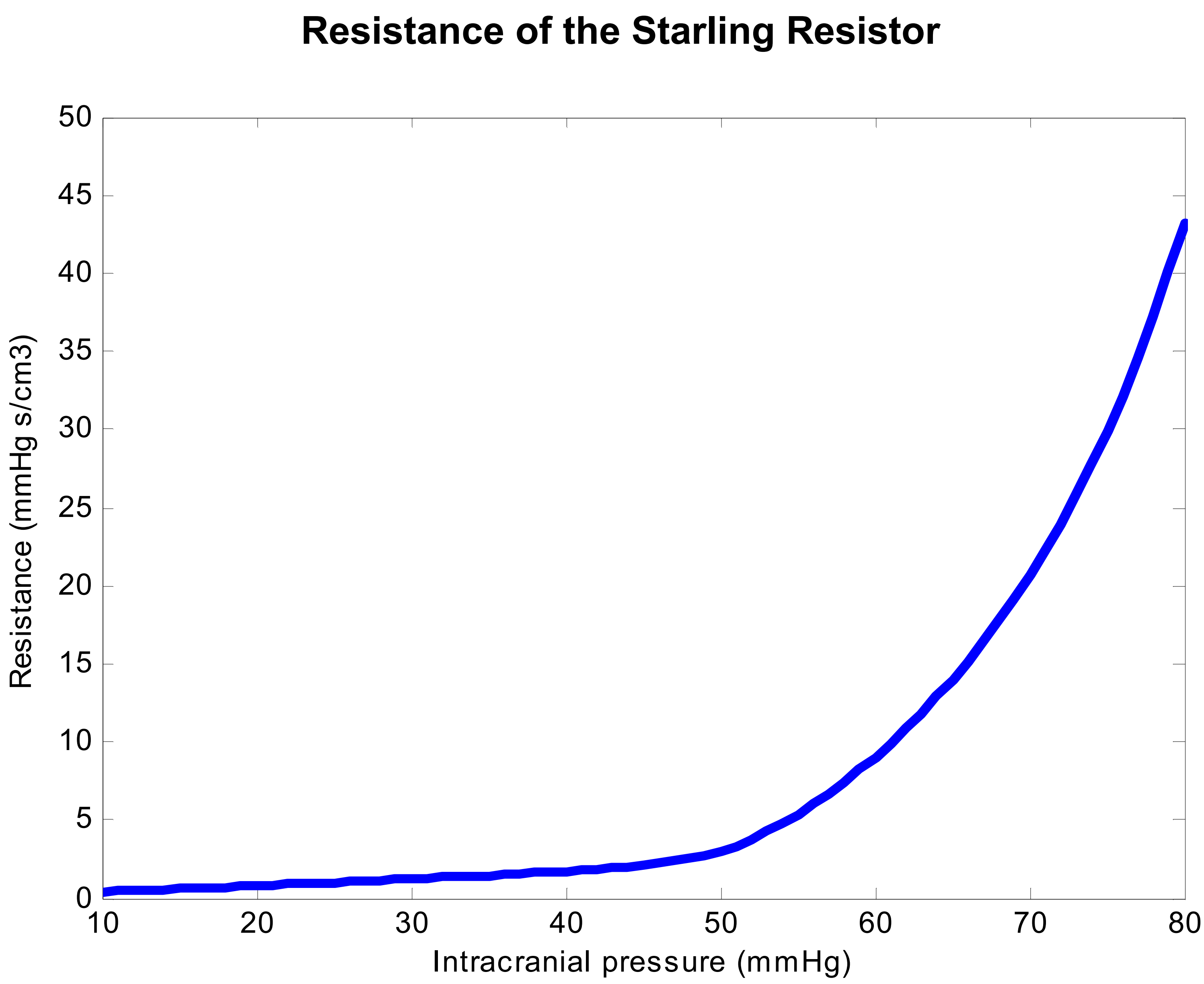
The Starling Resistor



Flow = F(Pv, ICP, Pss)

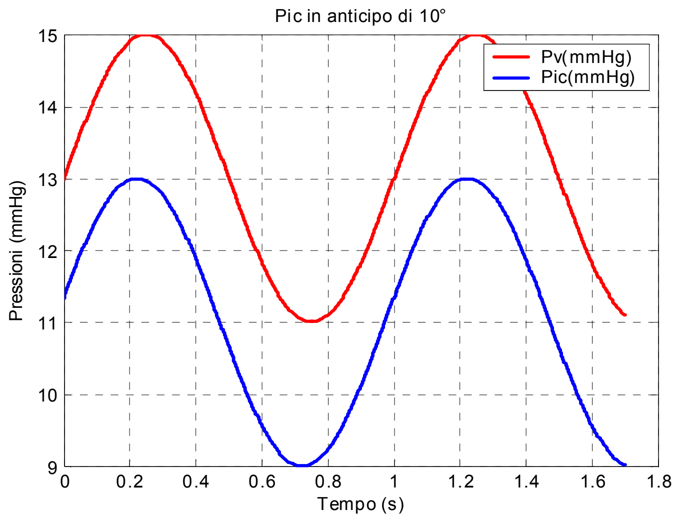
Transmural pressure = Pv - ICP

A.H. Shapiro, “Steady flow in collapsible tubes” J. Biomech. Eng.,1977



Resistance of the Starling Resistor
Resistance (mmHg s/cm3)
Intracranial pressure (mmHg)
0
5
10
15
20
25
30
35
40
45
50
10
20
30
40
50
60
70
80

Effetti del Resistore di Starling

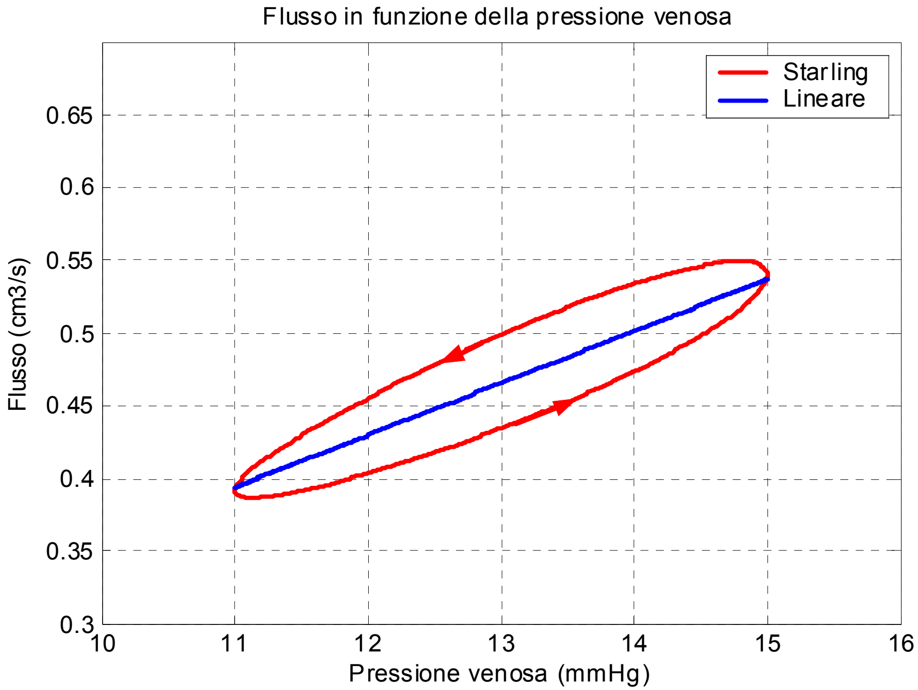


Pv e Pic sono sfasate di 10° (Pic in anticipo)

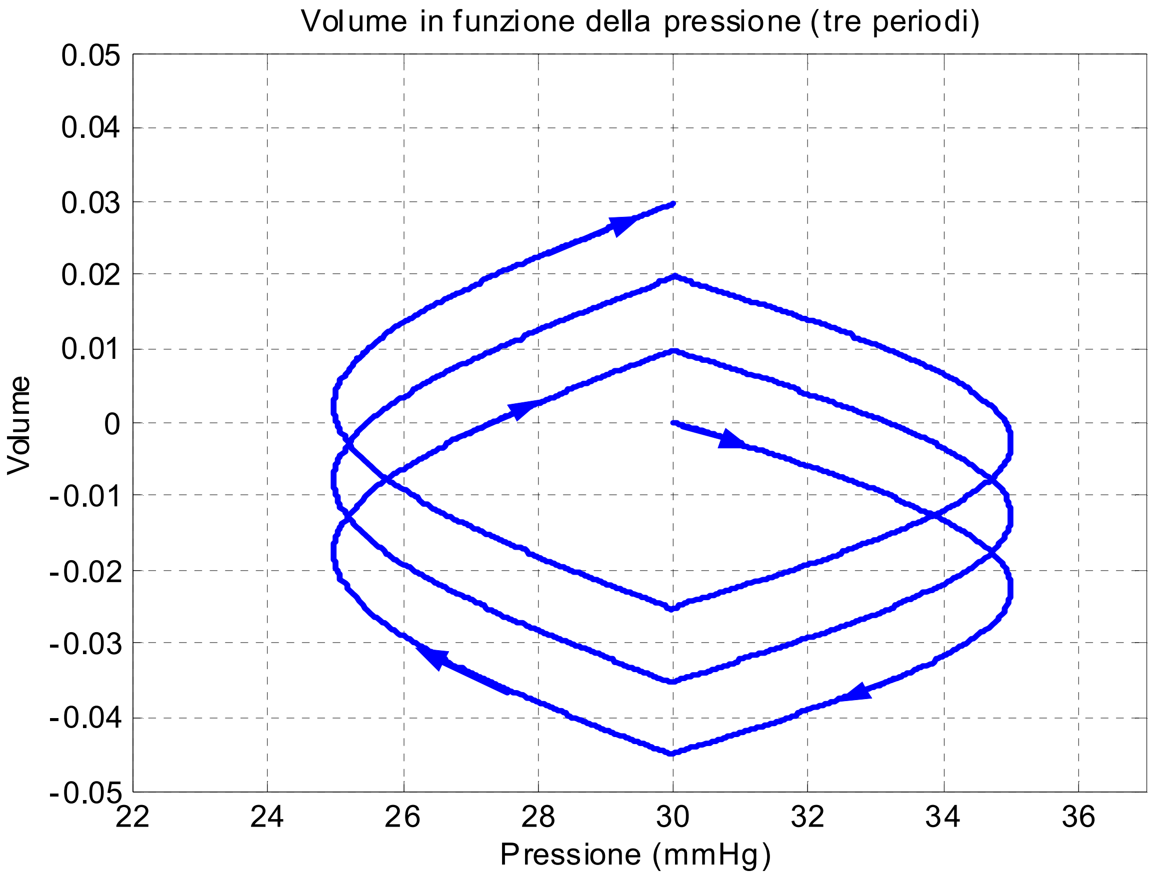
Durante l'aumento di Pv il flusso è minore di quello che si ha durante la diminuzione.
Es. quando Pv = 13 mmHg,
•se Pv aumenta il flusso è 0.42 cm3/s
•se Pv diminuisce il flusso è 0.50 cm3/s
La curva non è un'ellisse: la parte superiore è più distante della inferiore dalla linea media.

Resistore di Starling
Flusso in sistole: 0.2094 cm3
Flusso in diastole: 0.2573 cm3
Differenza: **0.0479 cm3**

Resistore lineare
Flusso in sistole: 0.2560 cm3
Flusso in diastole: 0.2560 cm3
Differenza: **0.0 cm3**



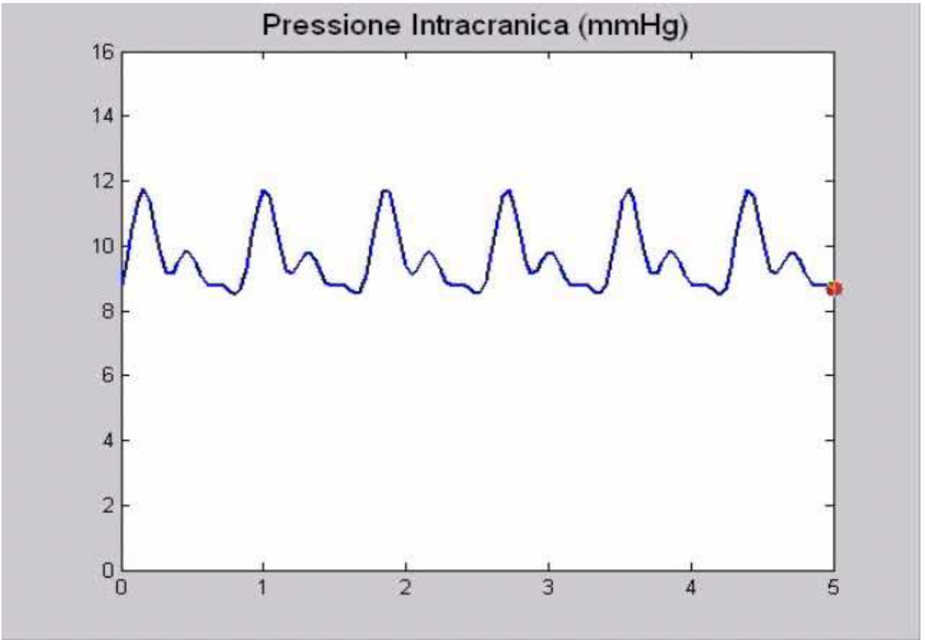
Asimmetria del parenchima cerebrale

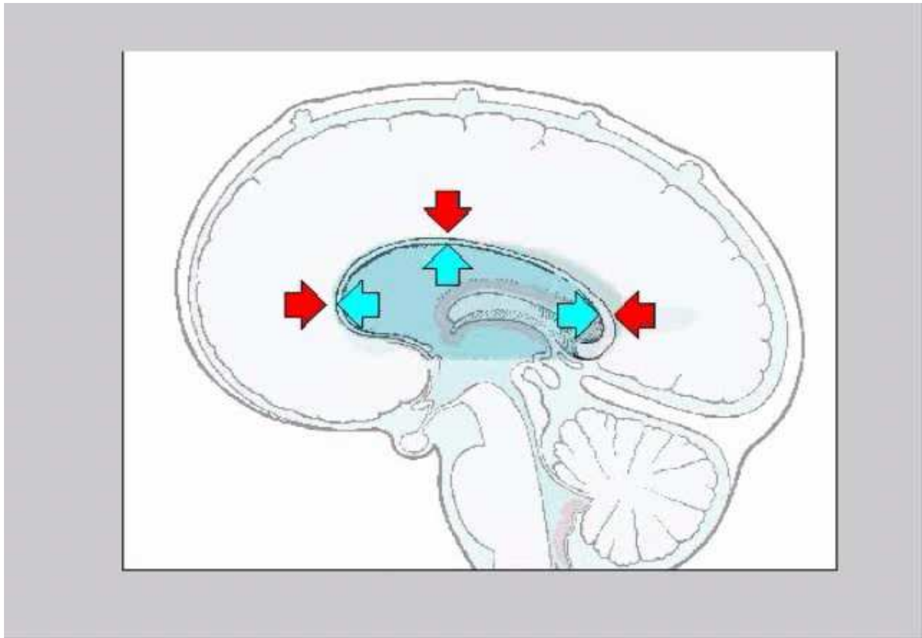


Alla fine di ogni ciclo il volume ventricolare aumenta

Si raggiunge un equilibrio in funzione delle pressioni medie e dell'ampiezza delle pulsazioni.

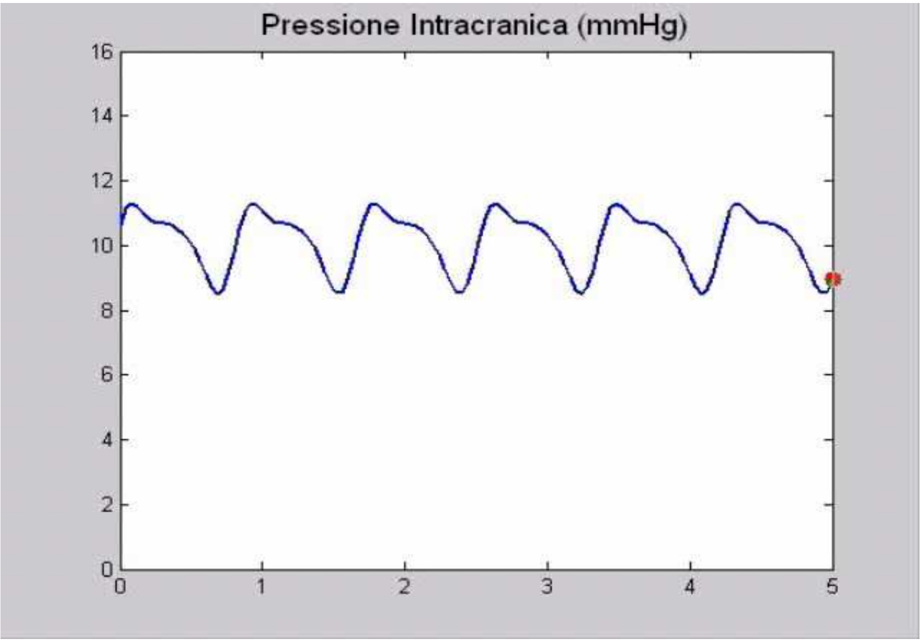
Condizione normale

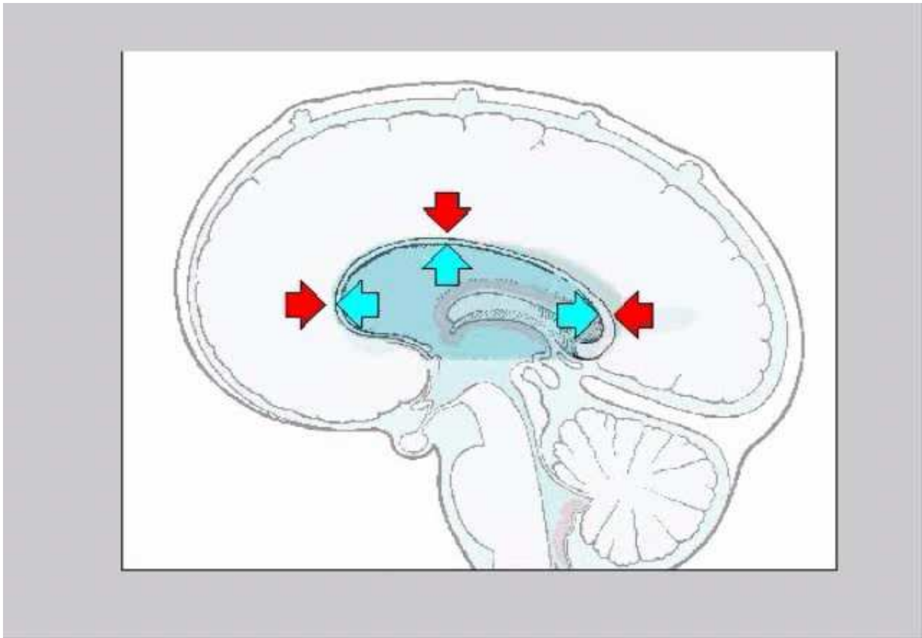




La pressione intracranica è bilanciata dalla pressione intraparenchimale.

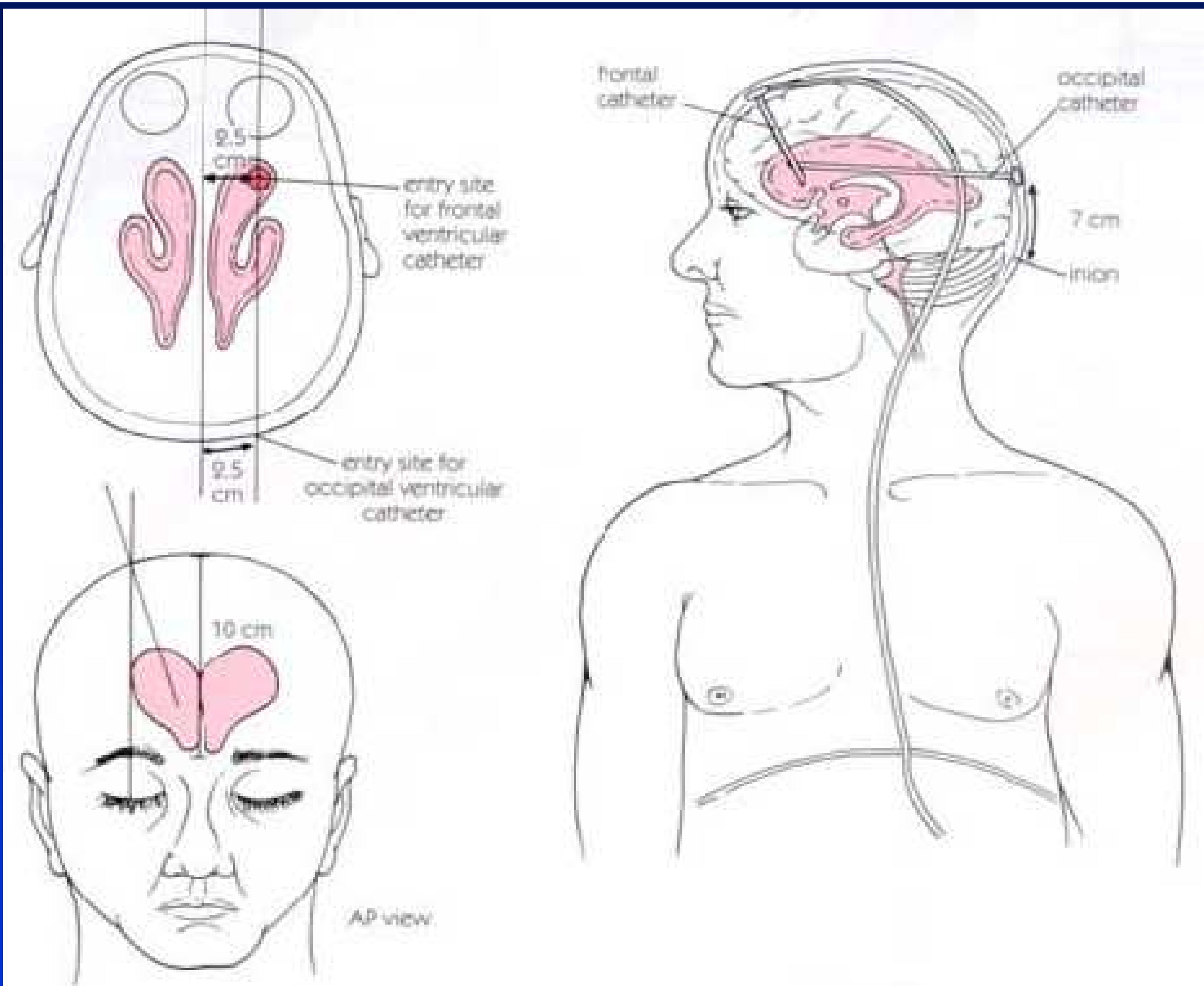
Condizione patologica





L'alterazione delle strutture venose di scarico (resistore di Starling) modifica la forma dell'onda della pressione intracranica.

Lo sbilanciamento con la pressione intraparenchimale produce la dilatazione ventricolare.



2.5 cm
entry site for frontal ventricular catheter
2.5 cm
entry site for occipital ventricular catheter
10 cm
AP view
frontal catheter
occipital catheter
7 cm
inion

Idiopathic normal pressure hydrocephalus: a systematic review of diagnosis and outcome. Hebb AO and Cusimano MD *Neurosurgery* **49**:1166-1186, 2001.

•*Overall, 59% (…24-100%) of patients improved after shunt placement, and 29% (…10-100%) of patients experienced prolonged or significant improvement.*

•*The …complication rate was 38% (…5-100%)…*

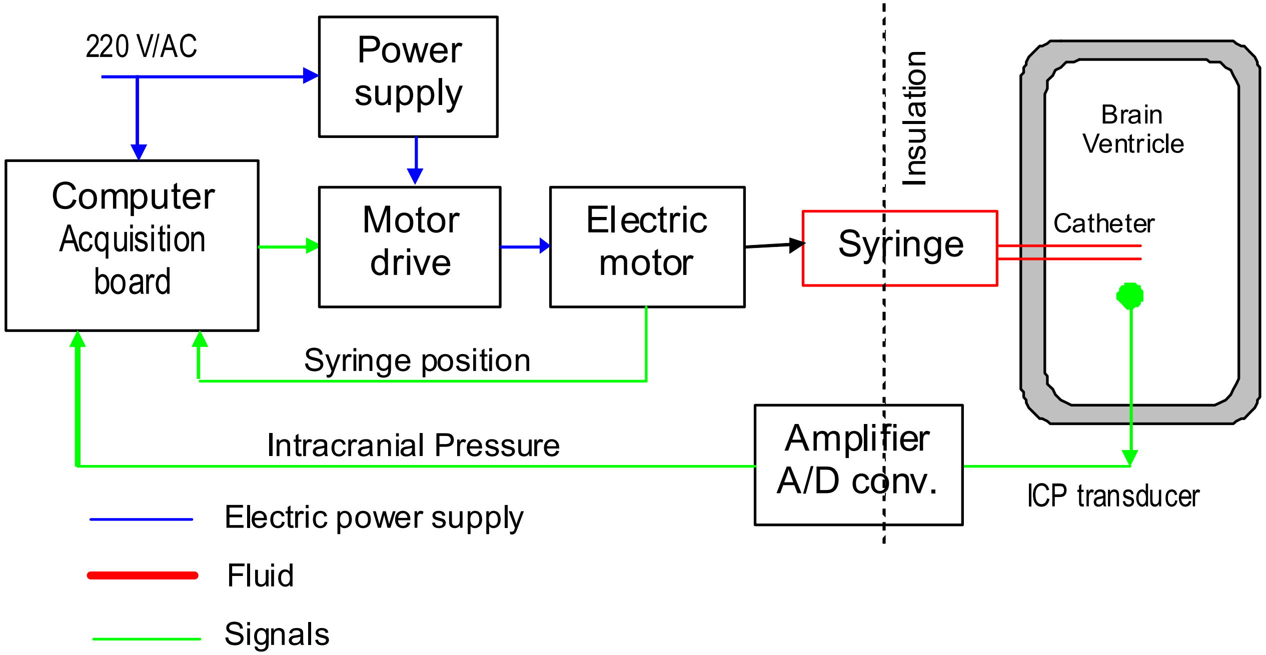
•*There was a 6% (…0-35%) combined rate of permanent neurological deficit and death.*

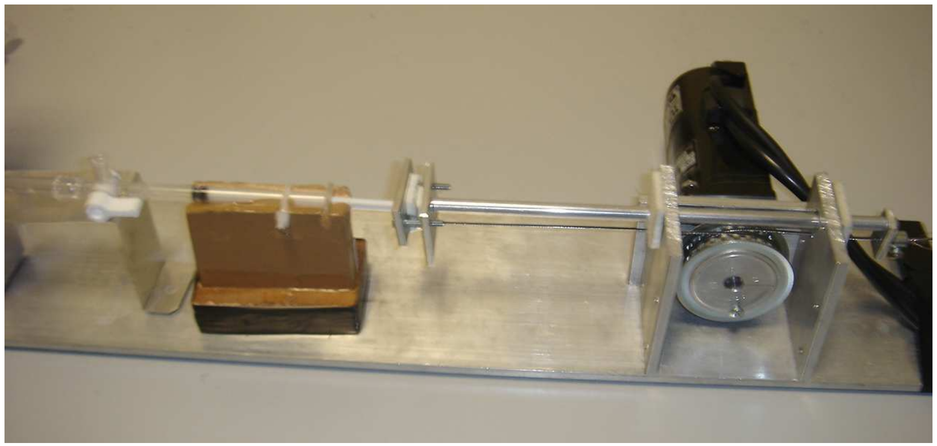
The future

- The future direction of the CSF shunting is aimed at reducing the morbidity of the overall management of shunt complications.

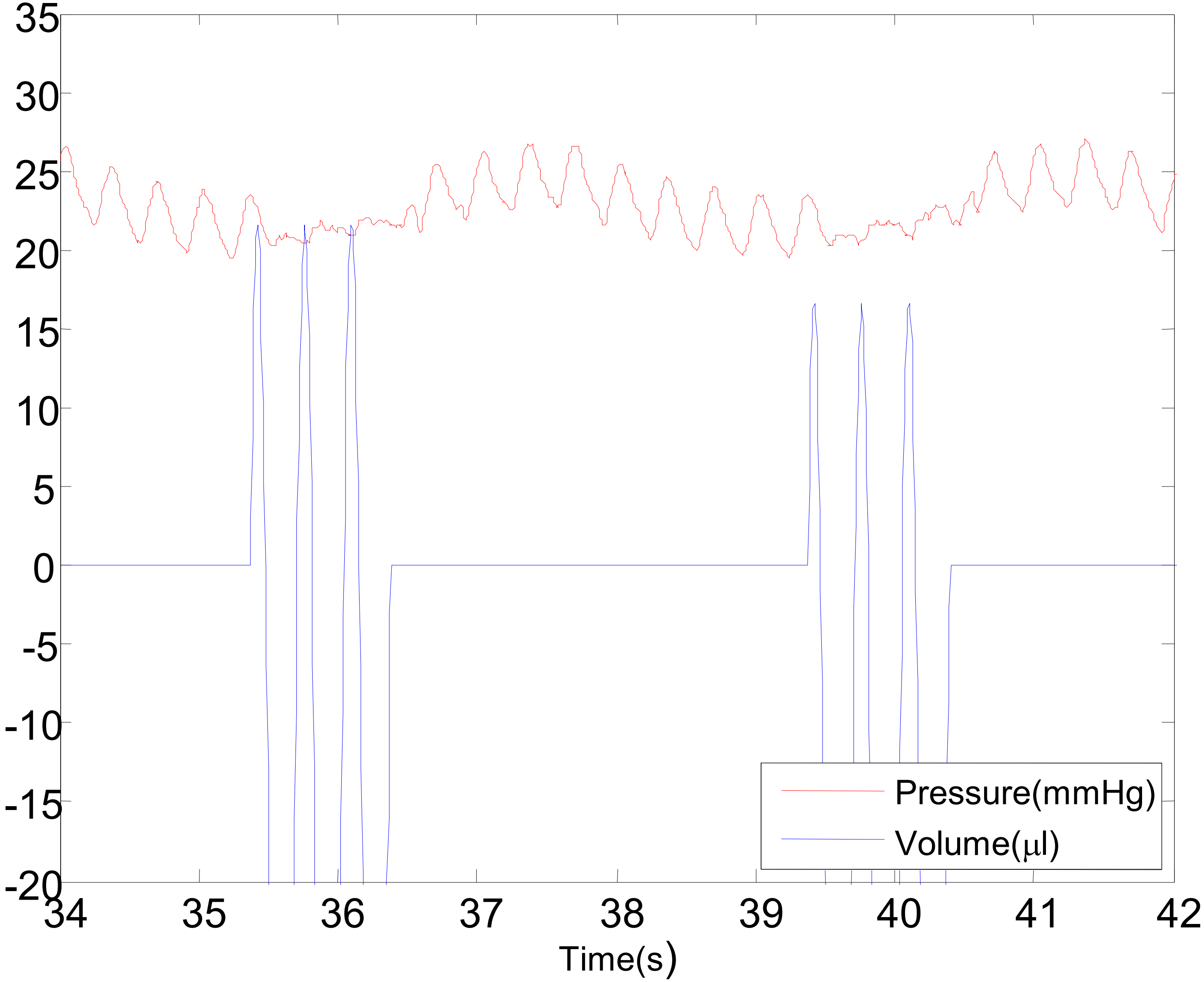
- The hope is a future in which a patient receives only one shunt in his lifetime that is sophisticated enough to control intracranial pressure within normal physiological limits, can be adjusted and monitored noninvasively, and is amenable to minimally noninvasive treatment for shunt obstruction.

The not-implantable system

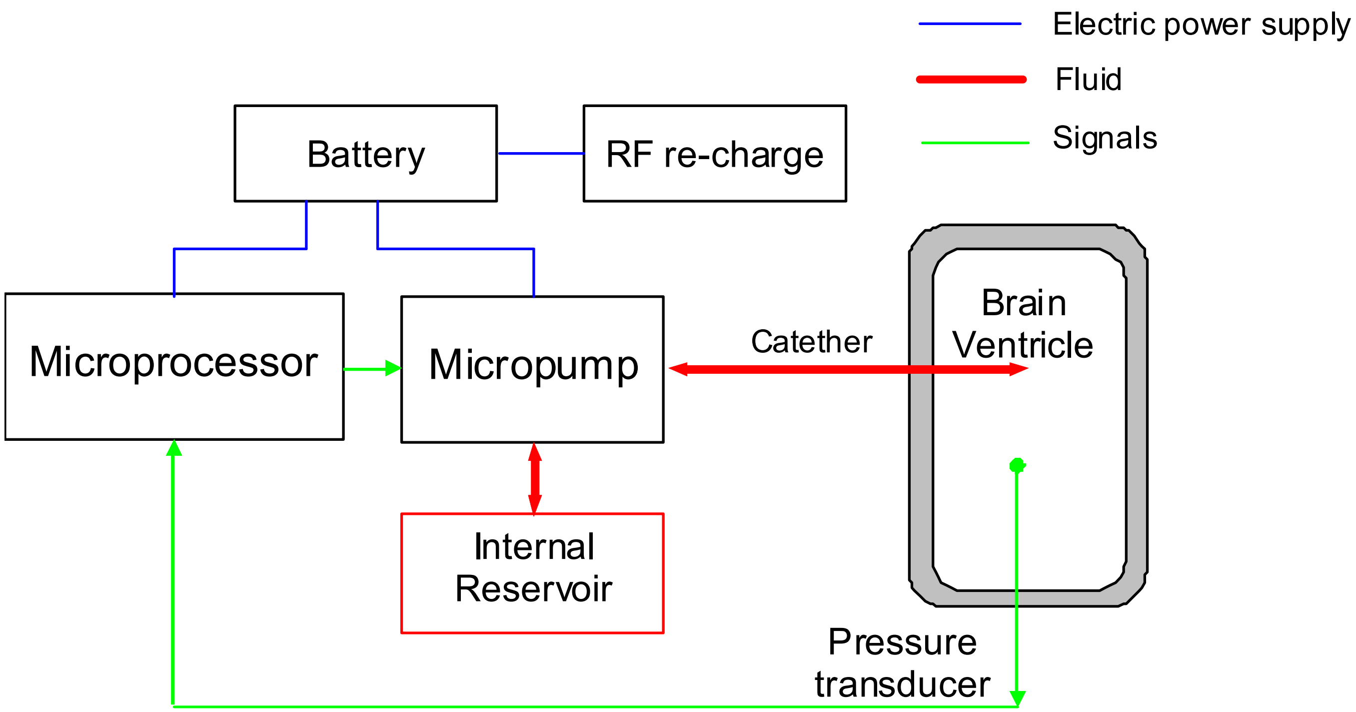




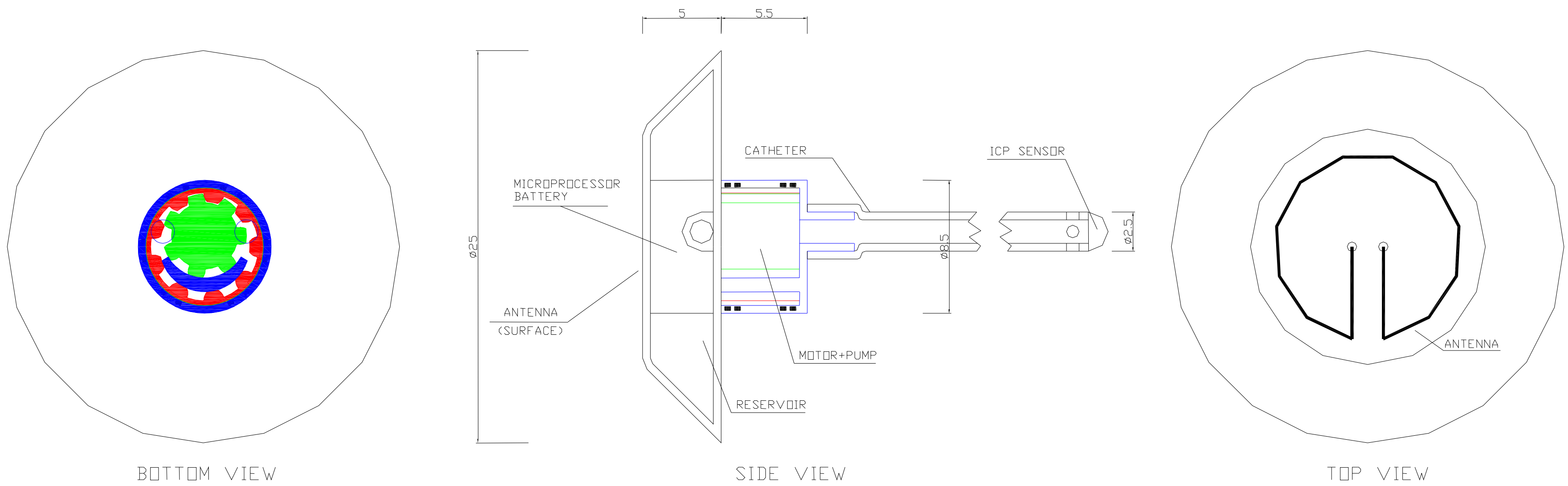
Experimental results (2)

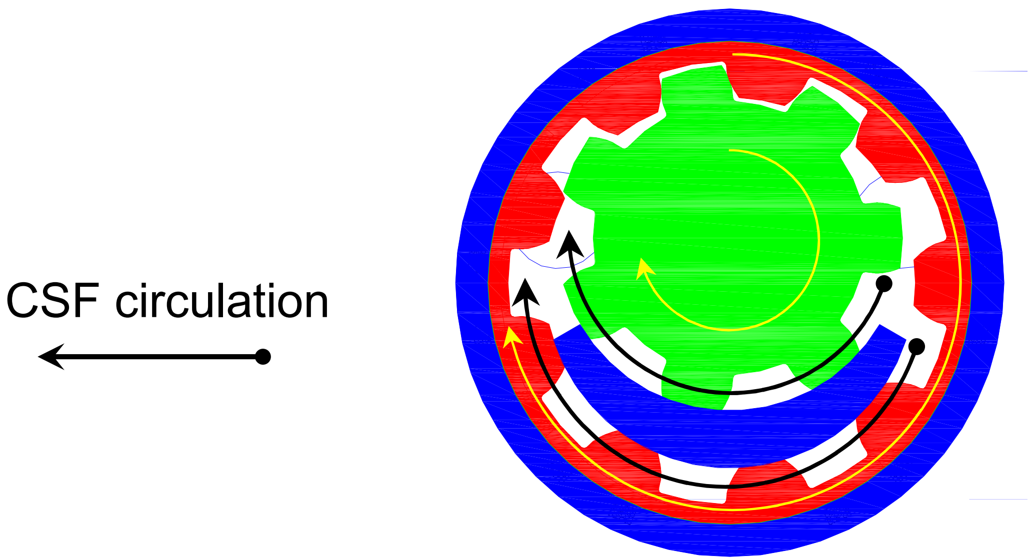


The implantable device



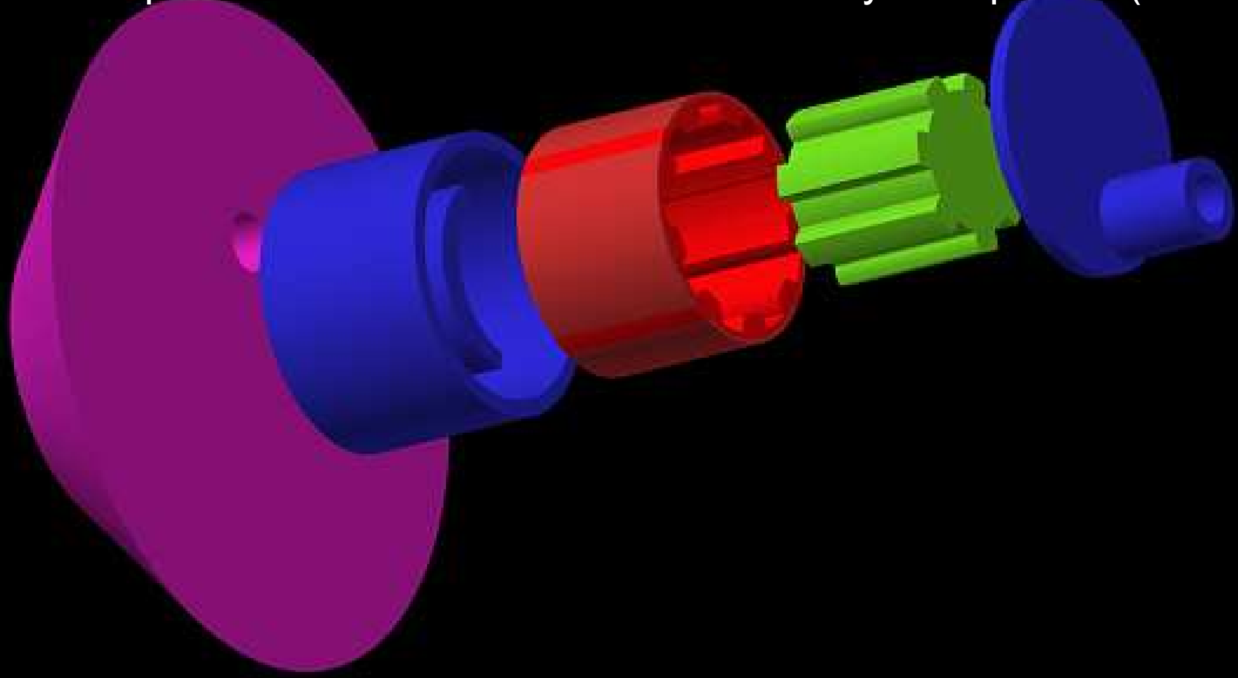
The implantable device

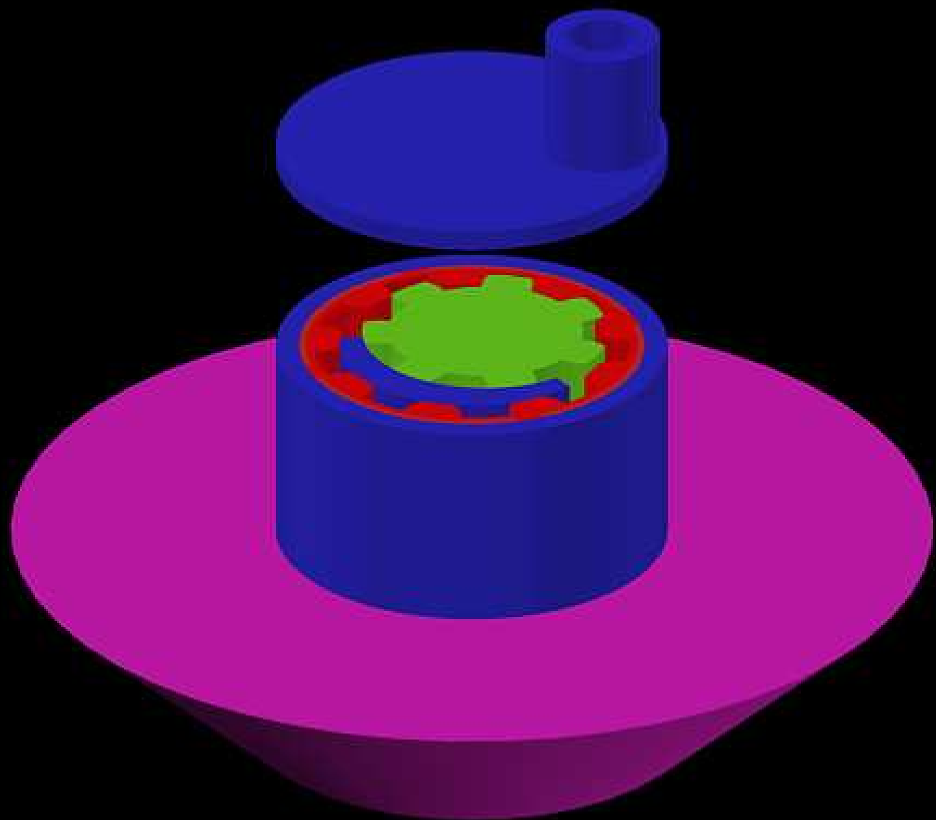


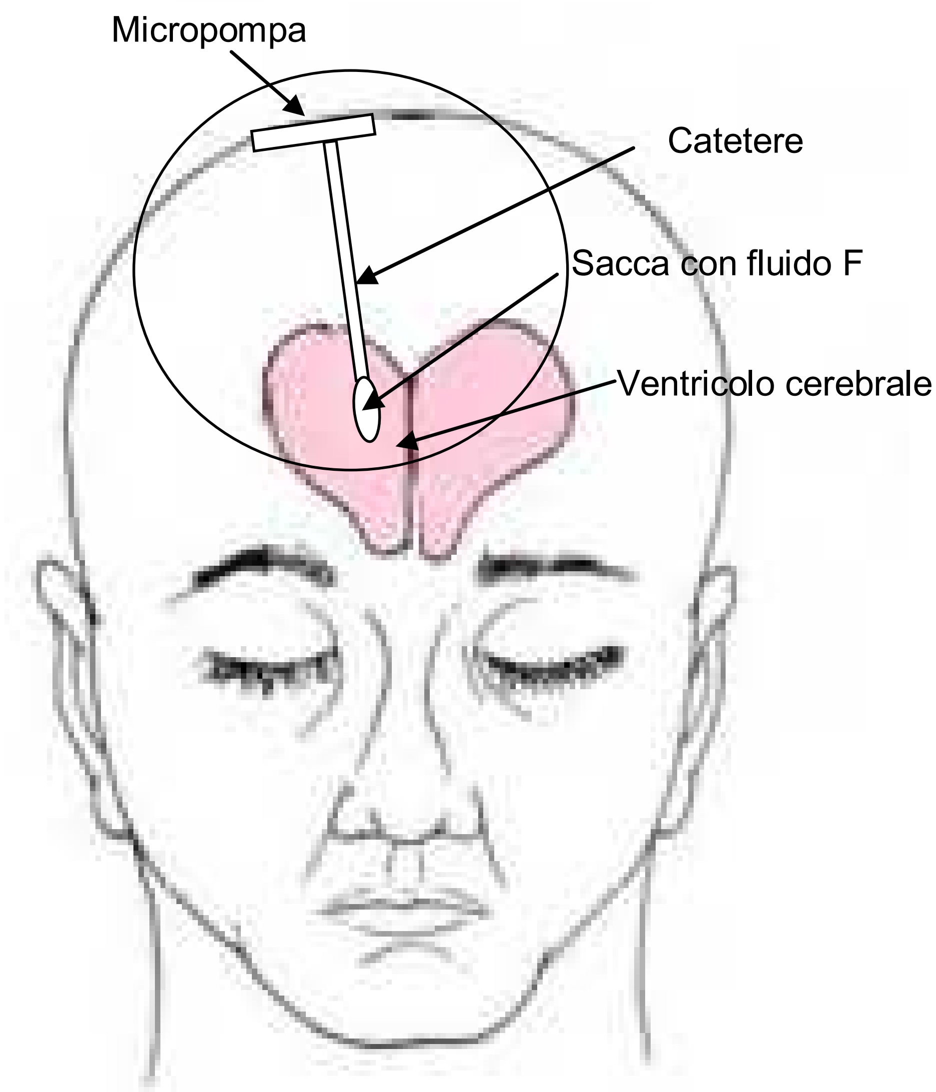


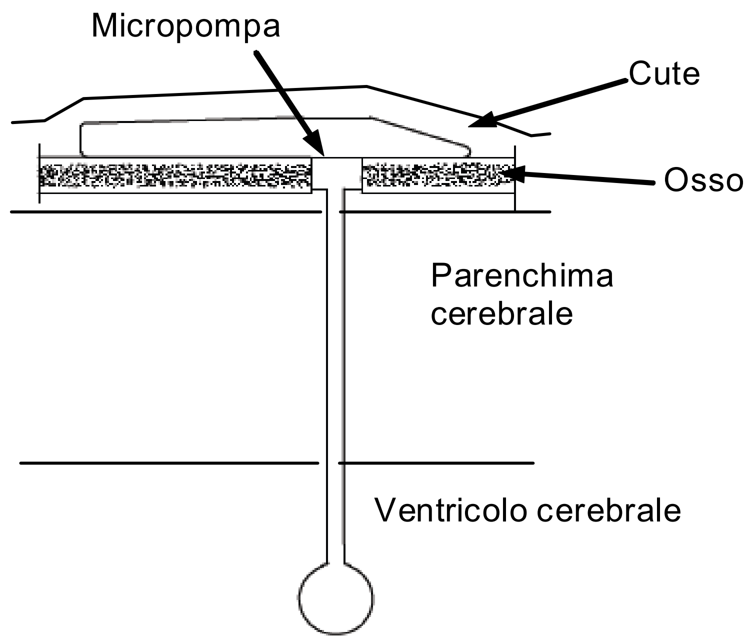
Implantable device for the treatment of hydrocephalus (Patent: IT2006RM00592 20061102)

Implantable device for the treatment of hydrocephalus (Patent: IT2006RM00592 20061102)






Micropompa
Catetere
Sacca con fluido F
Ventricolo cerebrale


Micropompa
Cute
Osso
Parenchima
cerebrale
Ventricolo cerebrale

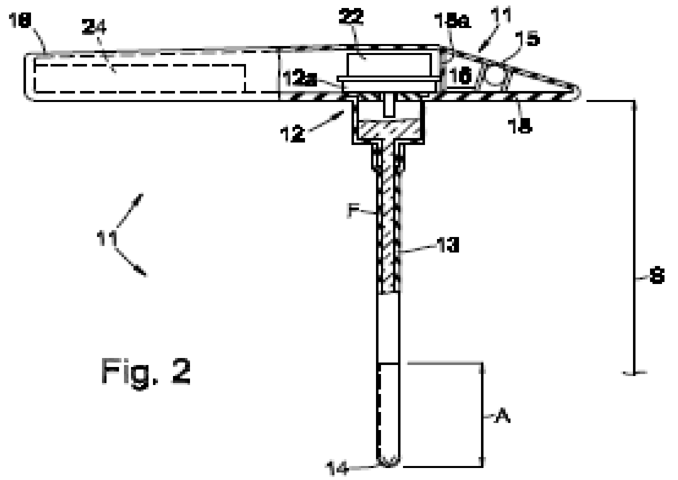


Fig. 2

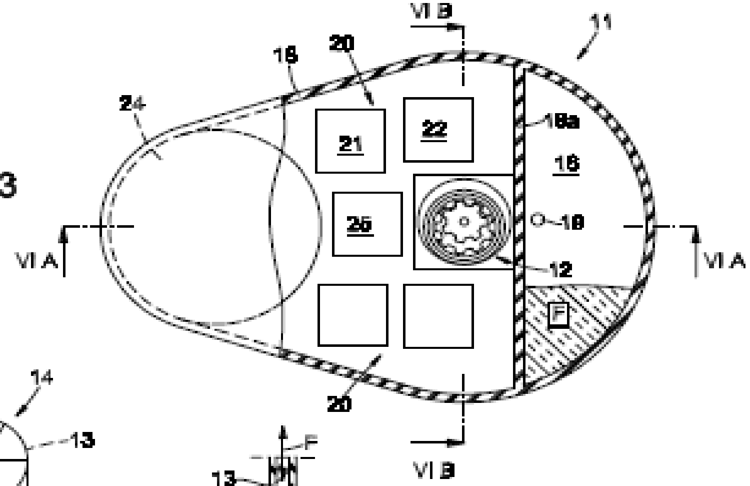


Fig. 3

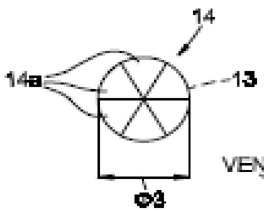


Fig. 4

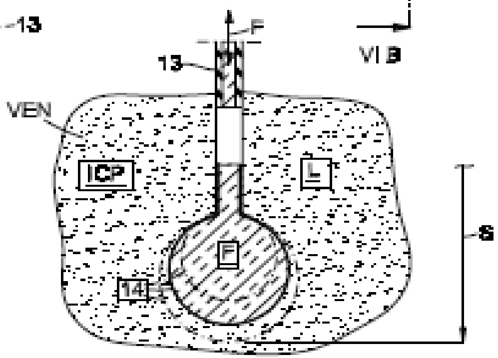


Fig. 5

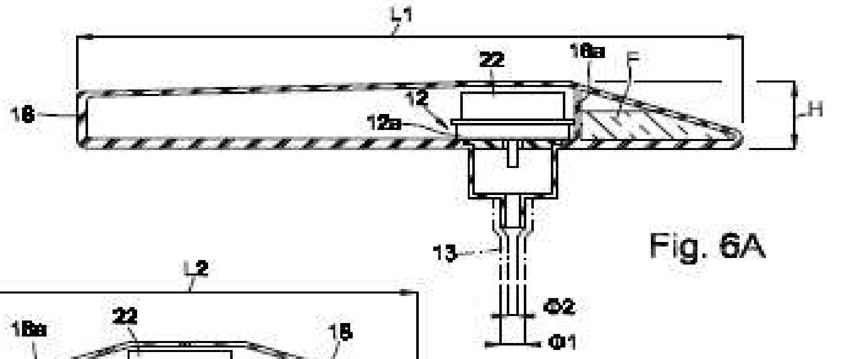


Fig. 6A

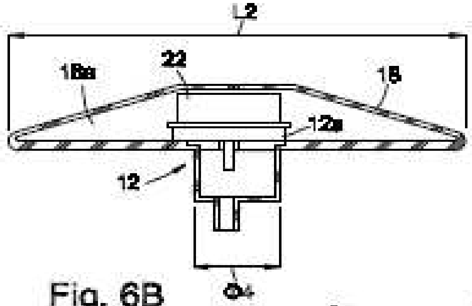


Fig. 6B

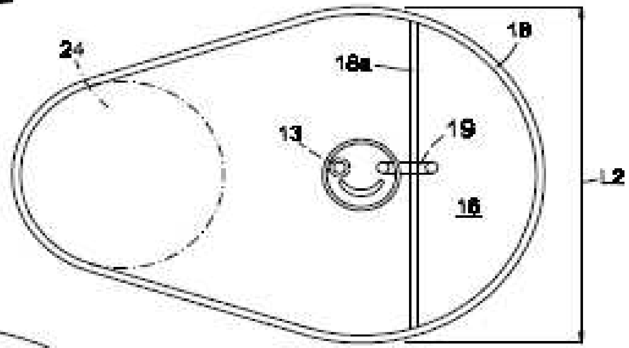


Fig. 6C

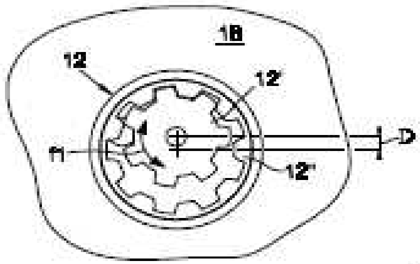


Fig. 7A

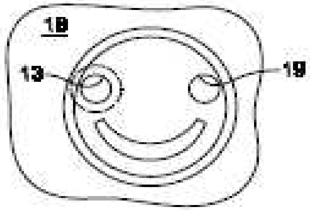
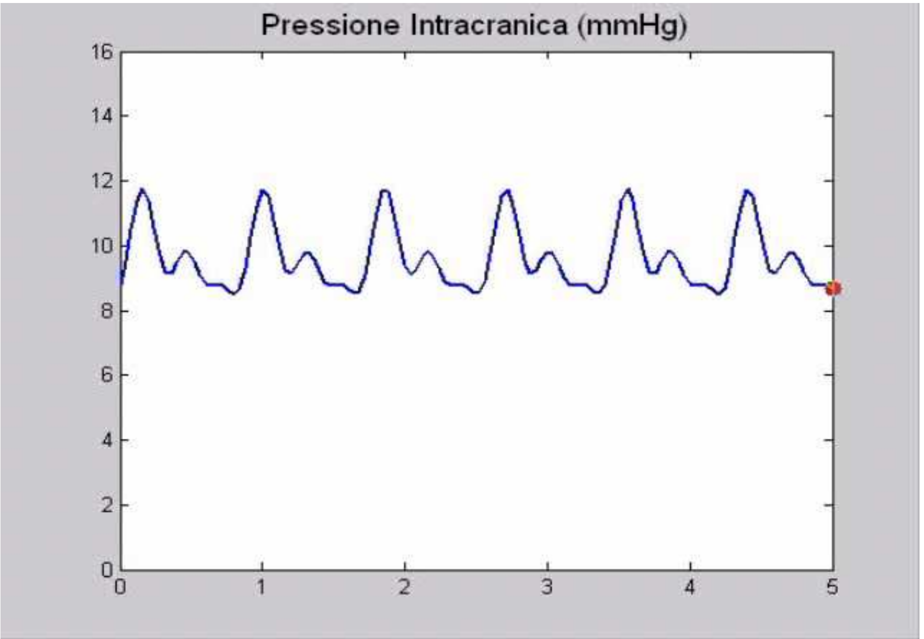


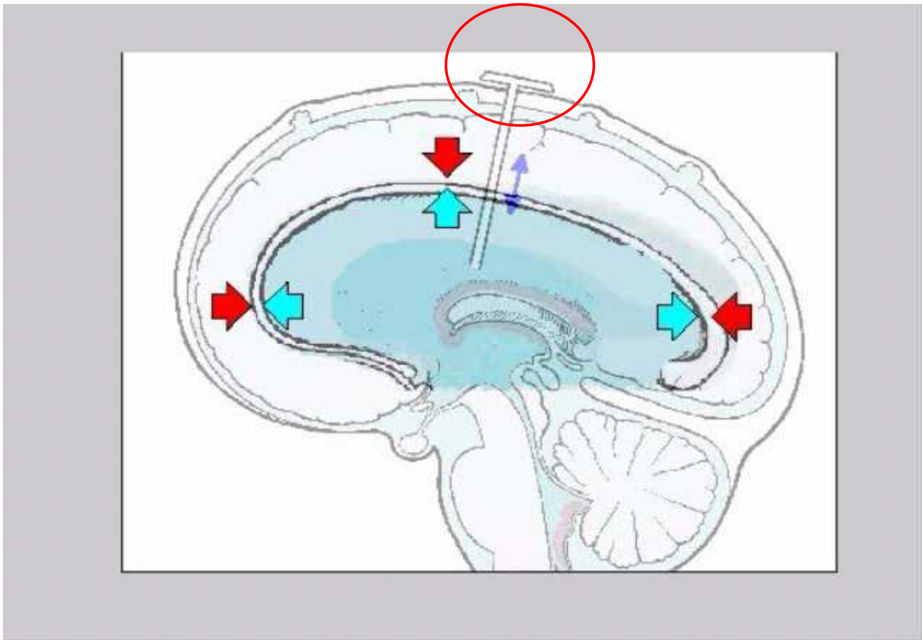
Fig. 7B

La terapia

Dispositivo impiantabile per il controllo della forma della componente pulsatile della pressione intracranica



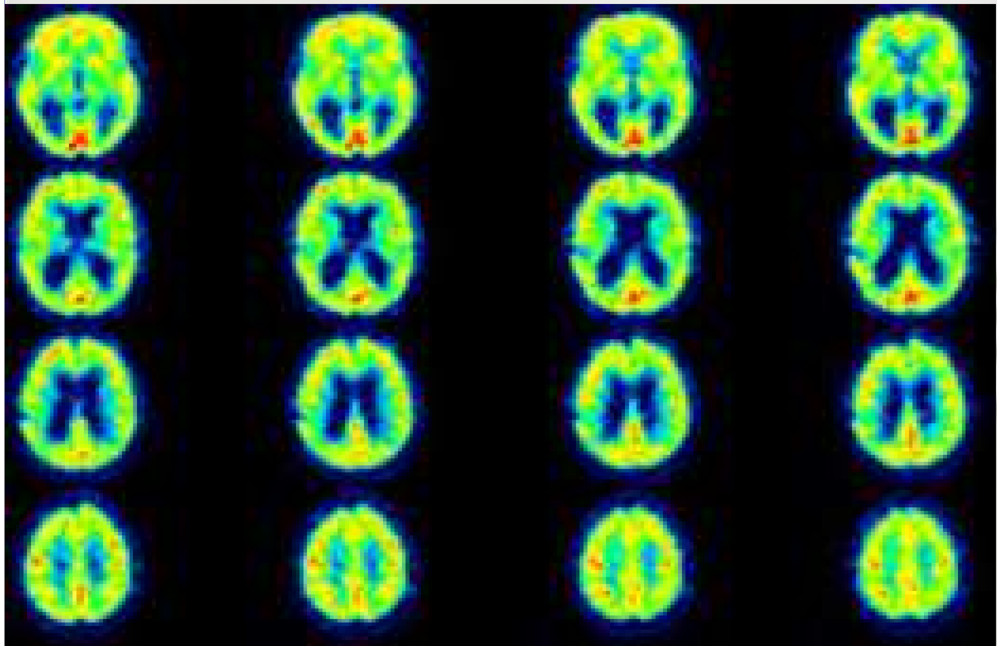
Dispositivo per il trattamento

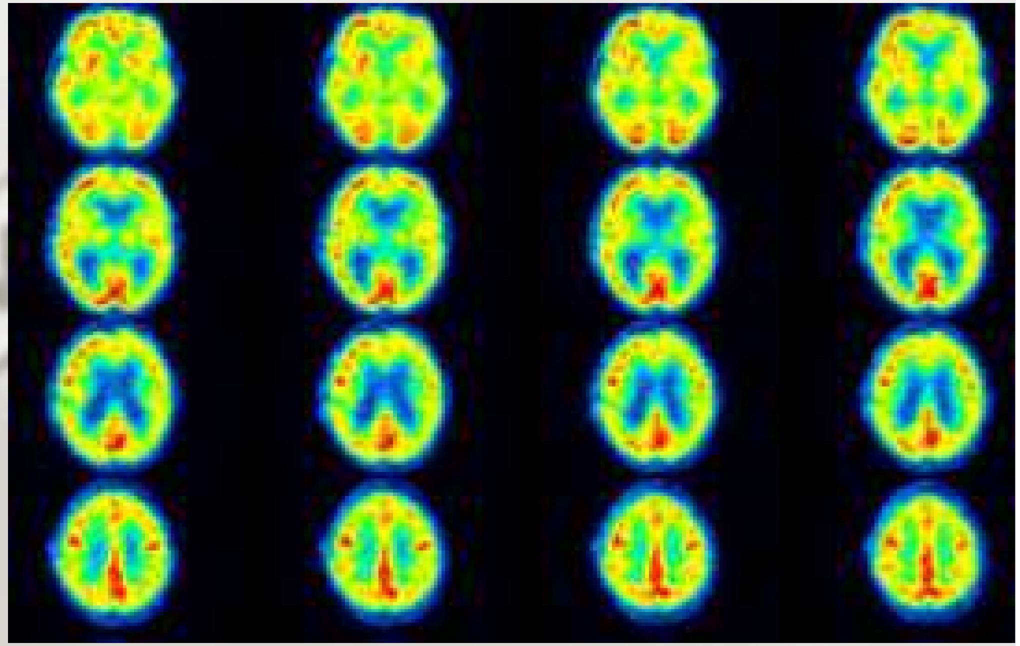


Ripristinando l'equilibrio tra pressione intracranica e pressione intraparenchimale, il ventricolo si riduce di volume.

Early evaluation of cerebral metabolic rate of glucose (CMRglu) with ^{18}F-FDG PET/CT and clinical assessment in idiopathic normal pressure hydrocephalus (INPH) patients before and after ventricular shunt placement: preliminary experience

Eur J Nucl Med Mol Imaging (2012) 39:236–241





Cerebral metabolic rate for glucose of NPH patients increases in shunt-reponders

J Neurol Neurosurg Psychiatry April 2012 Vol 83 No 4

Results: CMRglu