



**IL TRATTAMENTO CHIRURGICO DELL'EMORRAGIA  
INTRACEREBRALE : FINALITA' ED INDICAZIONI**

**DR . PIERPAOLO NINA**

**UOC DI NEUROCHIRURGIA OSPEDALE SAN GIOVANNI BOSCO NAPOLI**

# EMATOMI INTRACEREBRALI PRIMITIVI CLASSIFICAZIONE TOPOGRAFICA



Sovratentoriali



Infratentoriali

# SICH Cerebellari

*Vi e' un generale  
consenso sul ruolo  
positivo della chirurgia  
nonostante  
l'assenza di studi  
prospettici randomizzati!*  
**Intervento Chirurgico  
in Emergenza!**

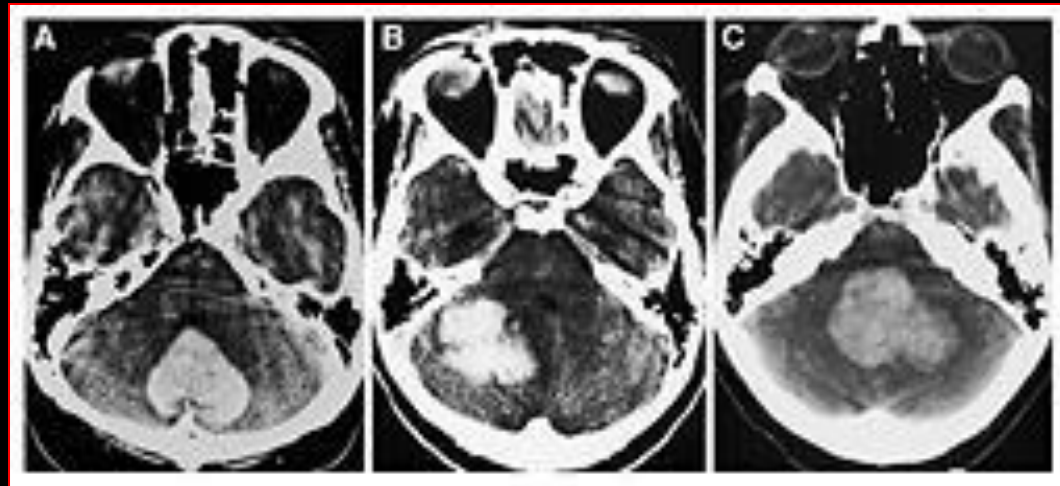




# SICH Cerebellari

## *Indicazioni Trattamento Chirurgico:*

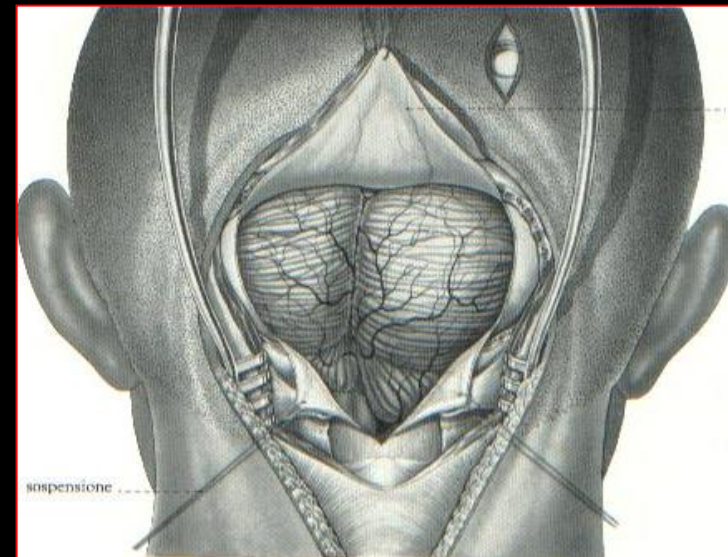
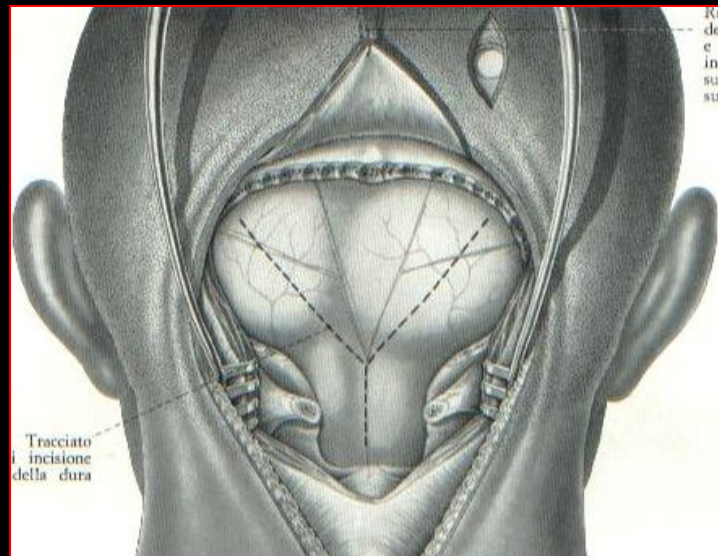
- Volume > 3 cm e/o
- GCS < 14 e/o
- Deterioramento clinico e/o
- Idrocefalo e/o
- Compressione del tronco encefalico



# SICH Cerebellari

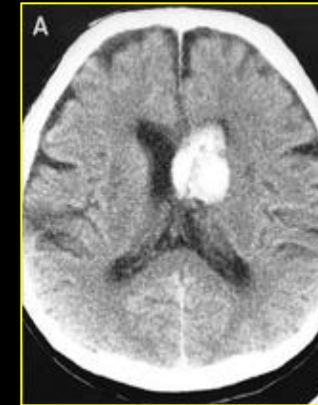
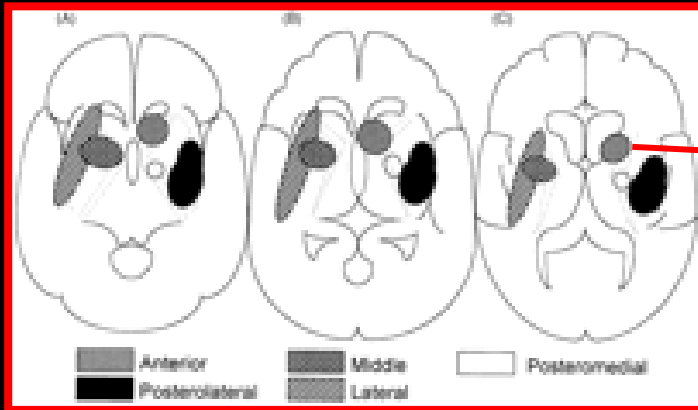
## *Tecnica Chirurgica:*

- ✓ Craniectomia standard
- ✓ Drenaggio ventricolare

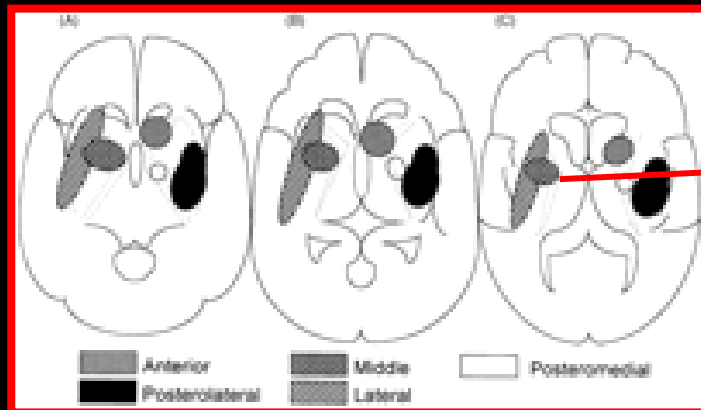


# Emorragie Cerebrali Primitive in Sede Tipica

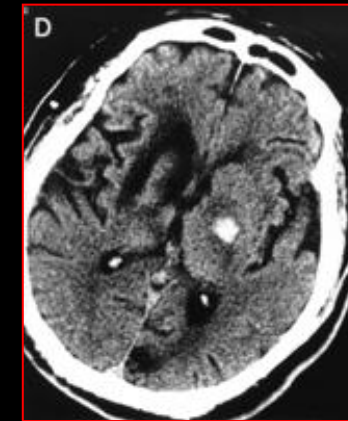
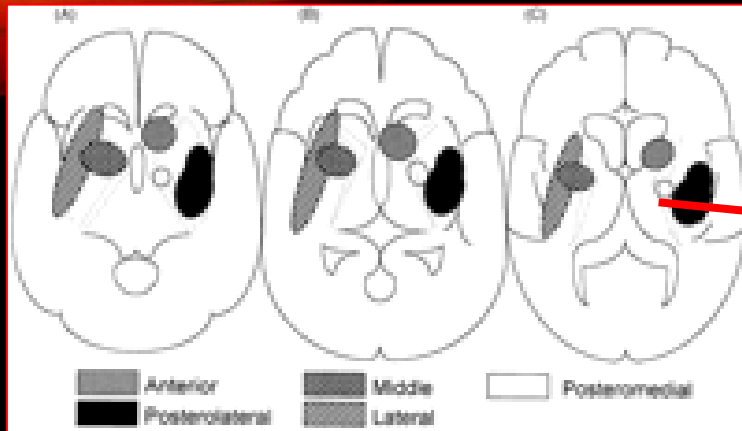
## 1. VARIANTE ANTERIORE



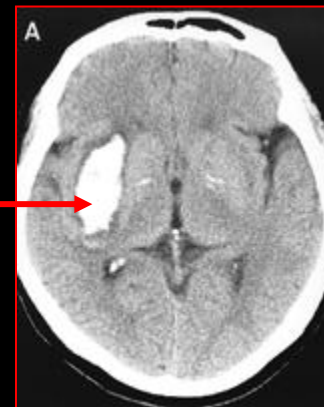
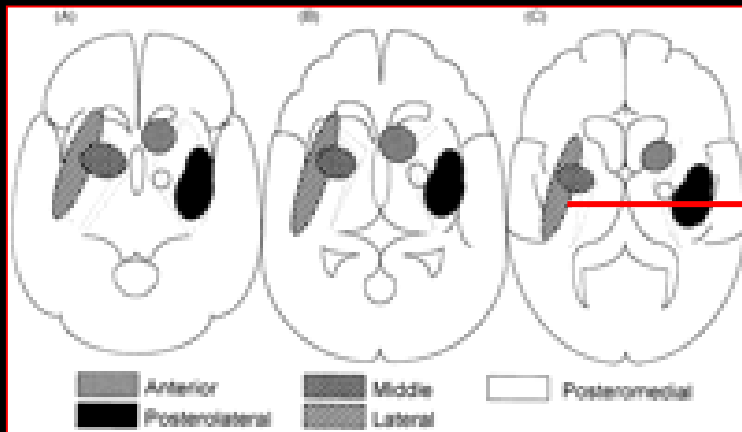
## 2. VARIANTE MEDIALE



### 3. VARIANTE POSTERO-MEDIALE

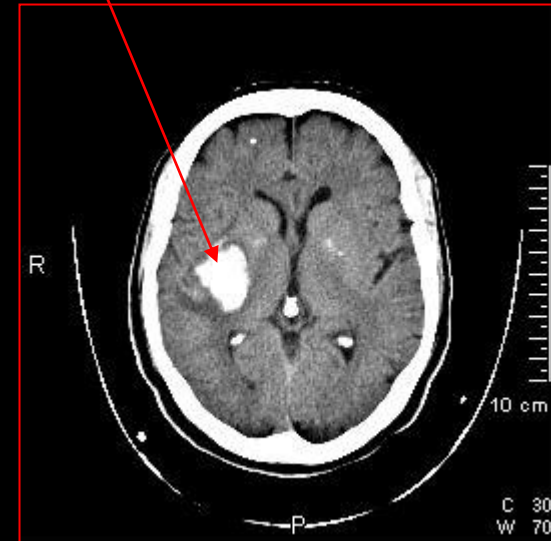
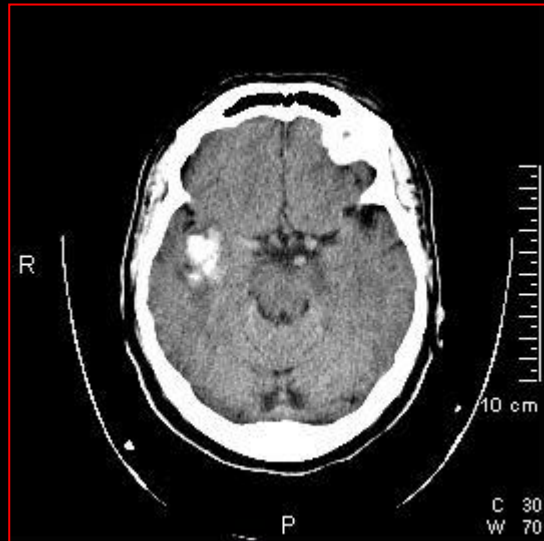
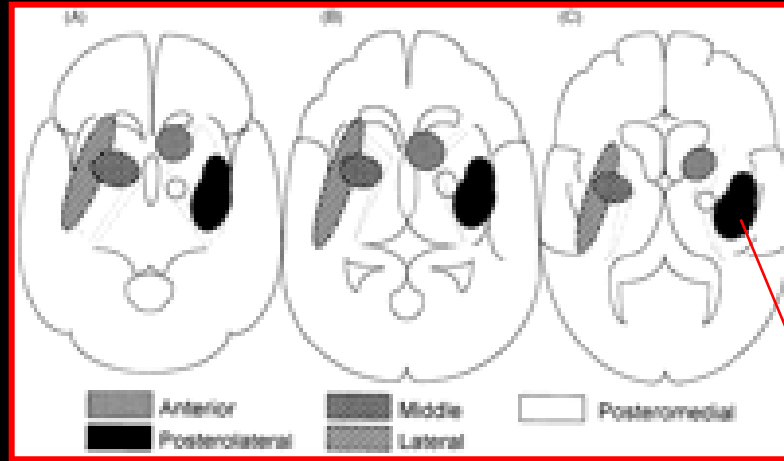


### 4. VARIANTE LATERALE



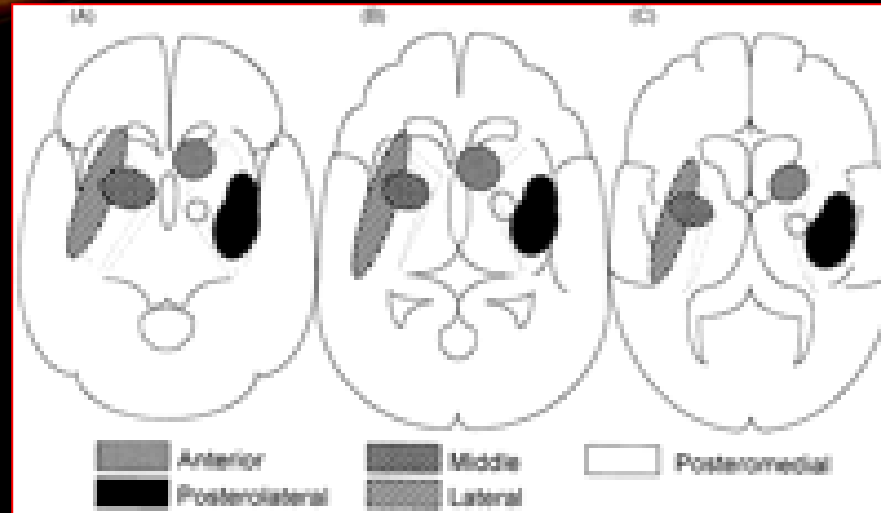


## 5. VARIANTE POSTERO-LATERALE





## 6. VARIANTE MASSIVA



A tutt'oggi  
l'emorragia cerebrale rappresenta,  
tra i diversi tipi di *Stroke*,  
quello che più di tutti ha disatteso i  
numerosi tentativi di individuare una  
terapia medica efficace



# Emorragie Cerebrali Primitive Sovratentoriali

*Tutt'oggi terapia medica inefficace!!!*

- ✓ *Mortalita' > 40 %*
- ✓ *Completa Autonomia Solo nel 20% dei Casi*

*Trattamento Chirurgico*



# Emorragie Cerebrali Primitive Sovratentoriali

## Trattamento Chirurgico: Basi Razionali Valide

- a) Ridurre l'effetto massa e quindi l'ICP;
- b) Prevenire l'espansione dell'ematoma;
- c) Diminuire l'edema e l'ischemia perilesionale;
- d) Ridurre gli effetti tossici dei metaboliti del sangue stravasato.



Studi Clinici *non* hanno dato Certezze sulla Efficacia del Trattamento Chirurgico!

# TRATTAMENTO CHIRURGICO VS TRATTAMENTO MEDICO

- 1.
- 2.
- 3.
- 4.
- 5.
- 6.
- 7.
- 8.
- 9.
- 10.



- 10 Trials clinici
- 1 Meta-analisi
- Numerosissimi lavori ( 1961-2005)



NESSUNA CONCLUSIONE PRECISA SUL REALE  
RUOLO DELLA TERAPIA CHIRURGICA

# Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral haematomas in the International Surgical Trial in Intracerebral Haemorrhage (STICH): a randomised trial

*A David Mendelow, Barbara A Gregson, Helen M Fernandes, Gordon D Murray, Graham M Teasdale, D Terence Hope, Abbas Karimi, M Donald M Shaw, and David H Barer for the STICH investigators\**

## Summary

**Background** Spontaneous supratentorial intracerebral haemorrhage accounts for 20% of all stroke-related sudden neurological deficits, has the highest morbidity and mortality of all stroke, and the role of surgery remains controversial. We undertook a prospective randomised trial to compare early surgery with initial conservative treatment for patients with intracerebral haemorrhage.

**Methods** A parallel-group trial design was used. Early surgery combined haematoma evacuation (within 24 h of randomisation) with medical treatment. Initial conservative treatment used medical treatment, although later evacuation was allowed if necessary. We used the eight-point Glasgow outcome scale obtained by postal questionnaires sent directly to patients at 6 months follow-up as the primary outcome measure. We divided the patients into good and poor prognosis groups on the basis of their clinical status at randomisation. For the good prognosis group, a favourable outcome was defined as good recovery or moderate disability on the Glasgow outcome scale. For the poor prognosis group, a favourable outcome also included the upper level of severe disability. Analysis was by intention to treat.

**Findings** 1033 patients from 83 centres in 27 countries were randomised to early surgery (503) or initial conservative treatment (530). At 6 months, 51 patients were lost to follow-up, and 17 were alive with unknown status. Of 468 patients randomised to early surgery, 122 (26%) had a favourable outcome compared with 118 (24%) of 496 randomised to initial conservative treatment (odds ratio 0.89 [95% CI 0.66–1.19],  $p=0.414$ ); absolute benefit 2.3% (–3.2 to 7.7), relative benefit 10% (–13 to 33).

**Interpretation** Patients with spontaneous supratentorial intracerebral haemorrhage in neurosurgical units show no overall benefit from early surgery when compared with initial conservative treatment.



# TRATTAMENTO CHIRURGICO: INDICAZIONI

- ✓ Enorme variabilità di trattamento a livello internazionale;
- ✓ Nello studio STICH :
  - in Ungheria: operati 2% degli ematomi
  - in Lituania : operati 90% degli ematomi

	Early surgery (n=503)	Initial conservative treatment (n=530)
Site of haematoma		
Lobar	196 (39%)	214 (40%)
Basal ganglia/thalamic	210 (42%)	224 (42%)
Both	94 (19%)	90 (17%)
Not assessable	3 (1%)	2
Haematoma volume (mL)*	40 (24-63)	37 (23 - 60)
Age (years)	62 (52-70)	62 (53-71)
Glasgow coma score		
5-8	99 (20%)	106 (20%)
9-12	199 (40%)	211 (40%)
13-15	205 (41%)	213 (40%)
Past medical history*		
Hypertension	341 (69%)	378 (72%)
On antihypertensives	225 (46%)	263 (50%)
Previous myocardial infarction	28 (6%)	44 (8%)
Previous stroke	30 (6%)	43 (8%)
Smoker	146 (30%)	134 (26%)
Other medical disorders	132 (27%)	143 (27%)

STICH:  
1033 PAZIENTI

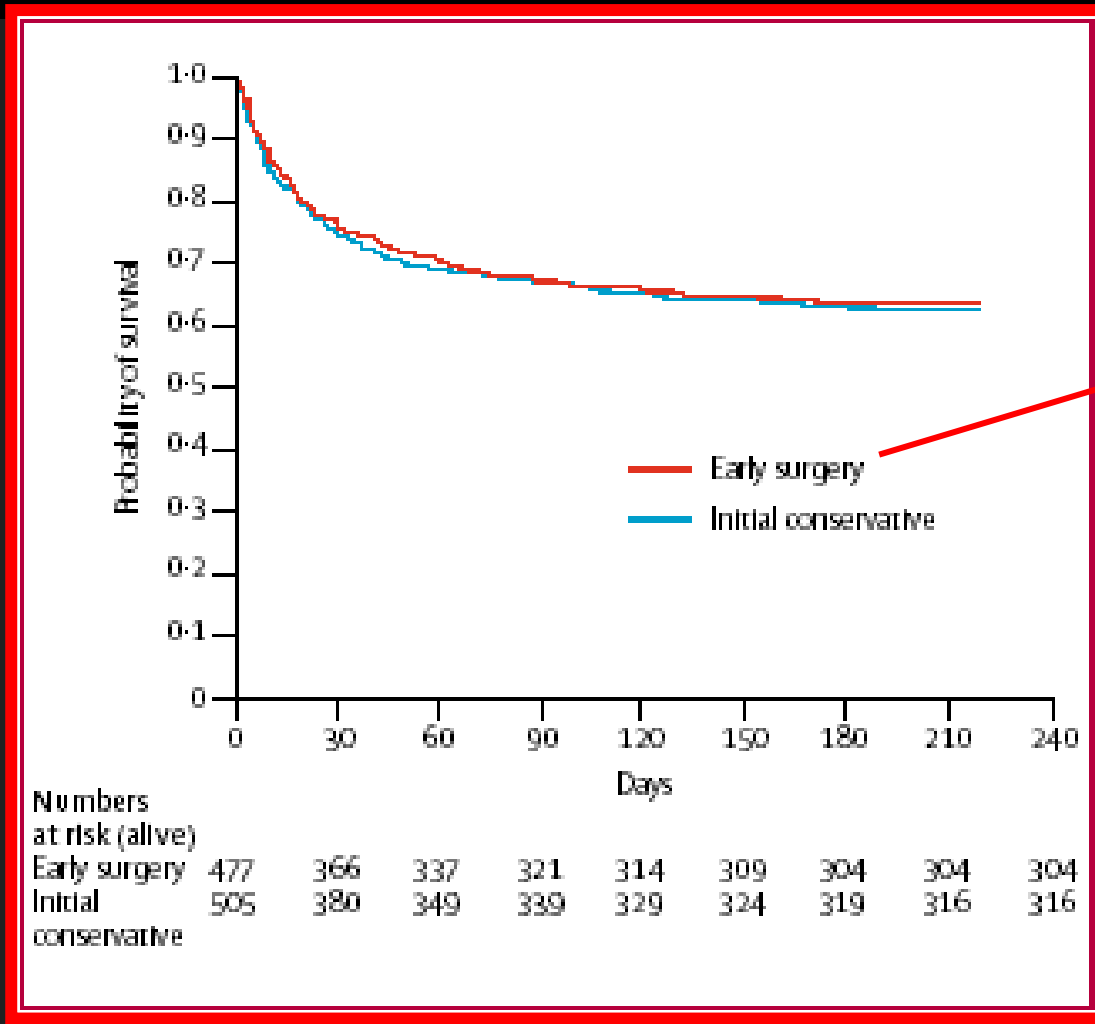
# STICH: CRITERI DI INCLUSIONE

- EMORRAGIE SOVRATENTORIALI SPONTANEE  $\geq 2$  CM
- GCS  $\geq 5$
- TC ENCEFALO ENTRO 72 ORE DALL'ESORDIO CLINICO
- CHIRURGIA ENTRO 24 ORE DALLA RANDOMIZZAZIONE
- "CLINICAL UNCERTAINTY PRINCIPLE":  
IL NCH ERA INDECISO SE OPERARE O NO





# RISULTATI: Nessun beneficio della chirurgia rispetto al trattamento medico



Chirurgia efficace solo per gli ematomi  $\leq 1$  cm dalla corteccia cerebrale

# The STICH Trial

## What Does It Tell Us and Where Do We Go From Here?

Joseph P. Broderick, MD

*(Stroke. 2005;36:1619-1620.)*

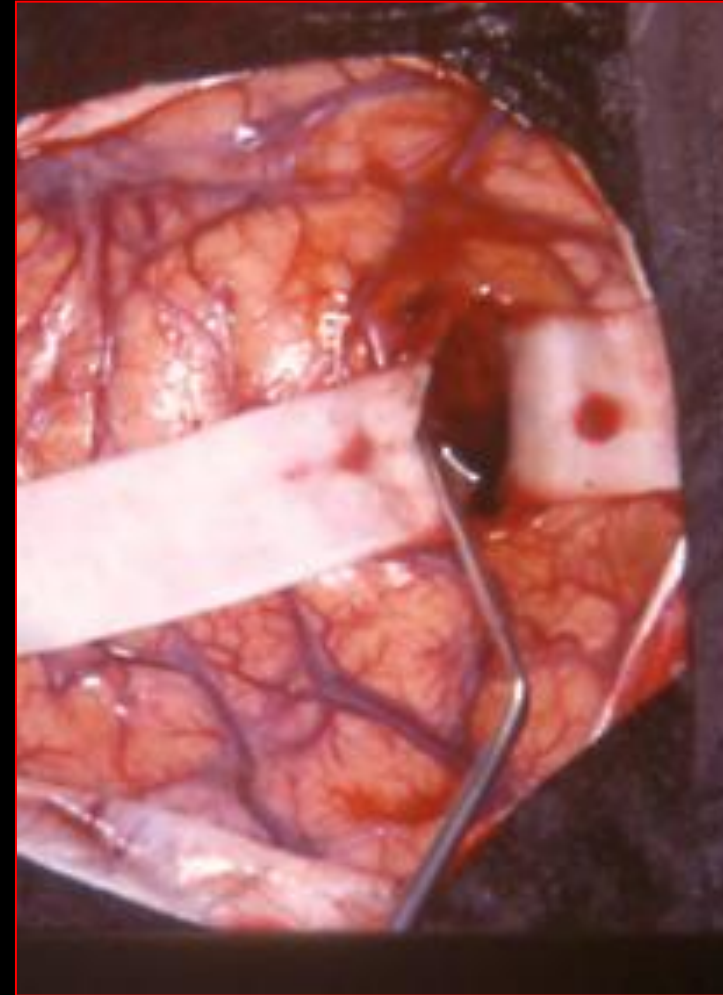
© 2005 American Heart Association, Inc.

LA TERAPIA CHIRURGICA VA RIVISTA IN TERMINI DI :

1. “TECNICHE CHIRURGICHE”
2. “TIMING”

# TECNICA CHIRURGICA STICH: “*CRANIOTOMY TRIAL*”

- Nel 77% dei casi operati, è stata utilizzata la craniotomia.
- 60% operati per ematomi profondi



# TECNICA CHIRURGICA TRADIZIONALE

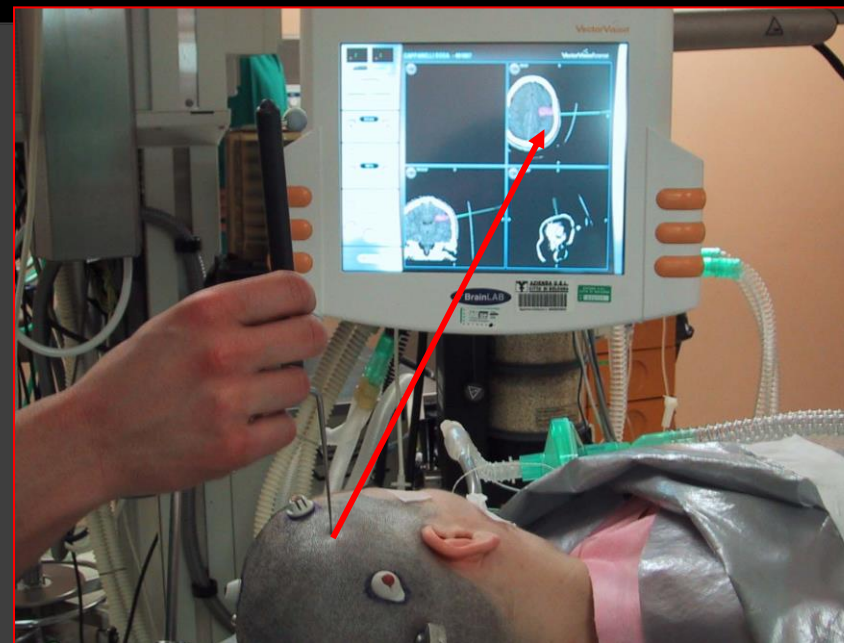
❖ Neuronavigatore

❖ Stereotassi

❖ Endoscopio

- Minima esposizione cerebrale
- Approccio attraverso aree non eloquenti
- Minima retrazione cerebrale

# NEURONAVIGATORE





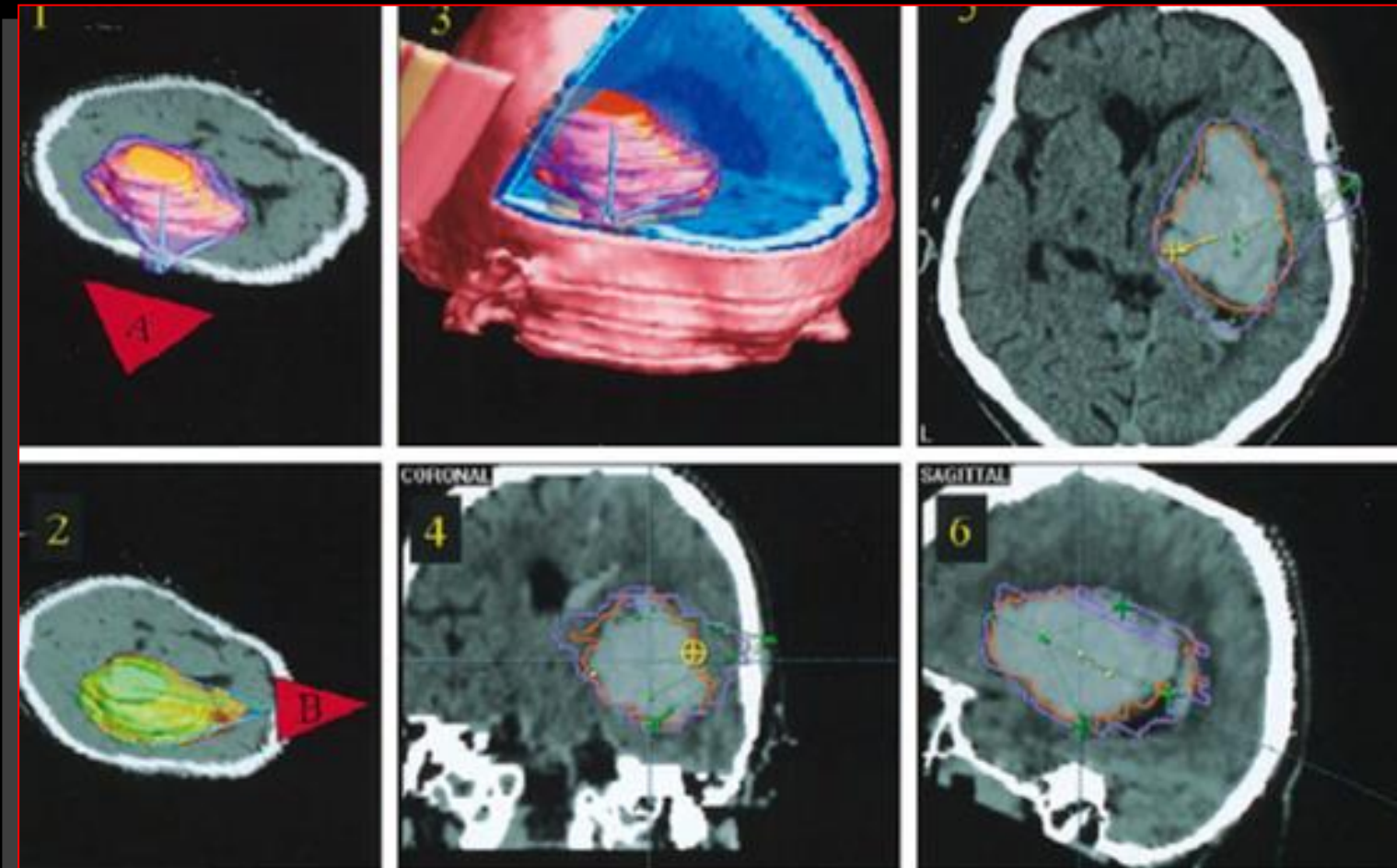
Evaluation of invasiveness and efficacy of 2 different keyhole approaches  
to large basal ganglia hematomas

Mario Carvi y Nievas, MD<sup>a,\*</sup>, Selim Toktamis, MD<sup>b</sup>, Hans-Georg Höllerhage, MD<sup>a</sup>,  
Eberhard Haas, MD<sup>a</sup>, Albert Pöllath, MD<sup>a</sup>

Surgical Neurology 64 (2005) 253–260

30 pts operati entro 6 ore con neuronavigatore:

15 pazienti approccio temporale, 15 pazienti approccio frontale



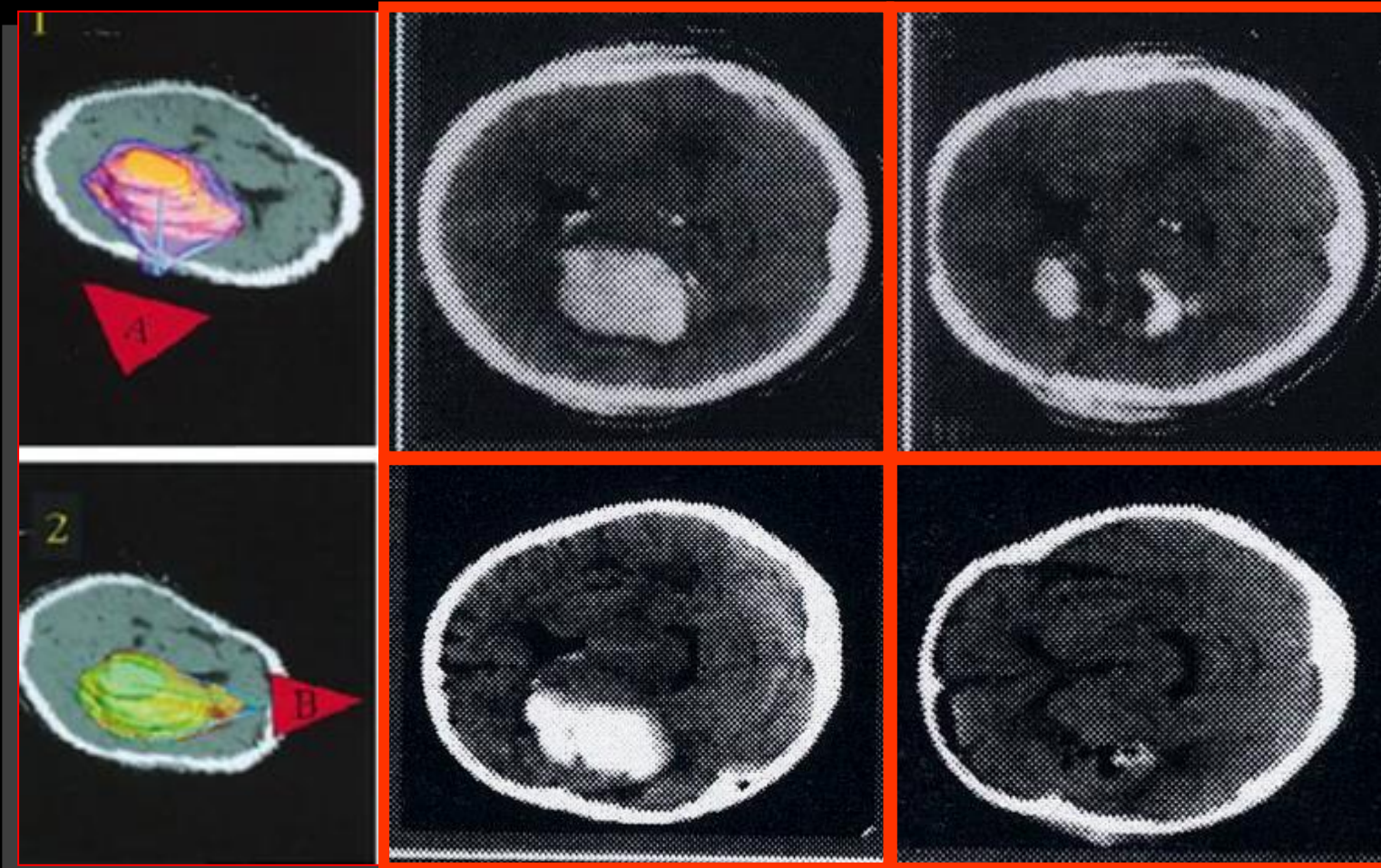
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Surgical Neurology 64 (2005) 253–260

30 pts operati entro 6 ore con neuronavigatore:

15 pazienti approccio temporale, 15 pazienti approccio frontale





## Neuroendoscope-assisted evacuation of large intracerebral hematomas: introduction of a new, minimally invasive technique

Preliminary report

AJAY BAKSHI, M.CH., ASHA BAKSHI, D.N.B., AND AJIT KUMAR BANERJI, M.S.

*Department of Neurosurgery, Vidyasagar Institute of Mental Health and Neurosciences,  
New Delhi, India*

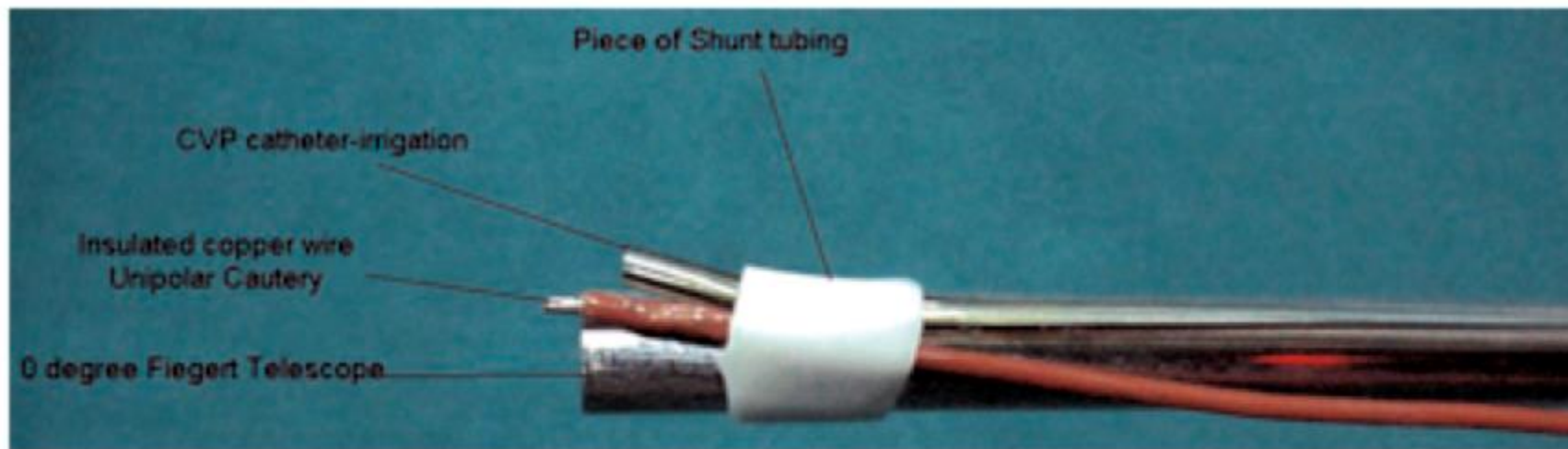


Fig. 1. Photograph depicting the three-in-one device that combines a 0°, 4-mm rigid endoscope, an insulated copper wire used as an electrocautery electrode, and a central venous pressure (CVP) cannula used for irrigation. All three devices are held together with small pieces of shunt tubing.







# Stereotactic Treatment of Intracerebral Hematoma by Means of a Plasminogen Activator

## A Multicenter Randomized Controlled Trial (SICHPA)

O.P.M. Teernstra, MD; S.M.A.A. Evers, PhD; J. Lodder, MD; P. Leffers, MSc;  
C.L. Franke, MD; G. Blaauw, MD

**Background and Purpose**—Treatment of intracerebral hematoma (ICH) is controversial. An advantage of neurosurgical intervention over conservative treatment of ICH has not been established. Recent reports suggest a favorable effect of stereotactic blood clot removal after liquefaction by means of a plasminogen activator. The SICHPA trial was aimed at investigating the efficacy of this treatment.

**Methods**—A stereotactically placed catheter was used to instill urokinase to liquefy and drain the ICH in 6-hour intervals over 48 hours. From 1996 to 1999, 13 centers entered 71 patients into the study. Patients were randomized into a surgical group (n=36) and a nonsurgical group (n=35). Admission criteria were the following: age >45 years, spontaneous supratentorial ICH, Glasgow Eye Motor score ranging from 2 to 10, ICH volume >10 cm<sup>3</sup>, and treatment within 72 hours. The primary end point was death at 6 months. As secondary end points, ICH volume reduction and overall outcome measured by the modified Rankin scale were chosen. The trial was prematurely stopped as a result of slow patient accrual.

**Results**—Seventy patients were analyzed. Overall mortality at day 180 after stroke was 57%; this included 20 of 36 patients (56%) in the surgical group and 20 of 34 patients (59%) in the nonsurgical group. A significant ICH volume reduction was achieved by the intervention (10% to 20%,  $P<0.05$ ). Logistic regression analysis indicated the possibility of efficacy for surgical treatment (odds ratio, 0.23; 95% confidence interval, 0.05 to 1.20;  $P=0.08$ ). The odds ratio of mortality combined with modified Rankin scale score 5 at 180 days was also not statistically significant (odds ratio, 0.52; 95% confidence interval, 1.2 to 2.3;  $P=0.38$ ).

**Conclusions**—Stereotactic aspiration can be performed safely and in a relatively uniform manner; it leads to a modest reduction of 18 mL of hematoma reduction over 7 days when compared with control, which has a 7-mL reduction, and therefore may improve prognosis. (Stroke. 2003;34:968-974.)

**Key Words:** intracerebral hemorrhage ■ randomized controlled trials ■ stereotactic aspiration ■ surgical treatment  
■ thrombolytic therapy



*National Institute of Neurological Disorders and Stroke-Funded  
Minimally Invasive ( stereotactic) Surgery Plus rtPA for ICH Evaluation*

*MISTIE randomized Study*

Confronta i risultati della somministrazione di rt-PA dentro il coagulo entro 24 h dall'esordio vs trattamento medico, in termini di sicurezza del trattamento, riduzione del volume del coagulo e di outcome

Zuccarello M et al.



## TIMING CHIRURGICO

In passato, l'emorragia cerebrale veniva considerata come un evento *monofasico*.



- ▶ Progressione dell'ematoma nel 26 % dei pazienti nella 1^ ora dopo la TC iniziale;  
Un ulteriore 12% entro le 20 ore successive.

*\*Brot et al., Stroke 1997; 28:1-5*

- ▶ Progressione dell'emorragia cerebrale entro 3 ore dall'esordio clinico nel 36% dei casi.

*°Kazui et al., Stroke 1996;27:1783-7*

**Forte razionale per la chirurgia precoce!**



# STICH: TIMING DELLA CHIRURGIA

Early surgery  versus initial conservative treatment

*Lancet 2005; 365: 387-97*

- L'intervallo medio tra l'esordio clinico e la chirurgia è stato di **30 ore** (16-49 ore).
- **Nel 26%** dei pz trattati inizialmente con terapia medica e successivamente operati: timing chirurgico di **60 ore** (27-99 ore).

# Rebleeding leads to poor outcome in ultra-early craniotomy for intracerebral hemorrhage

L.B. Morgenstern, MD; A.M. Demchuk, MD, FRCPC; D.H. Kim, MD; R.F. Frankowski, PhD;  
and J.C. Grotta, MD

La rimozione chirurgica entro 4 ore dall'esordio dei  
sintomi è complicata da risanguinamento,  
correlato ad emostasi difficoltosa!

Article  
of intra  
patient  
evacua  
at 6 mo  
surgica  
4-hour  
NIH Stro

score was 75 in survivors. Postoperative rebleeding occurred in four patients. The relationship between  
postoperative rebleeding and mortality was apparent ( $p = 0.03$ ). Rebleeding occurred in 12% of the patients treated within  
4 hours, compared with 12% of the patients treated within 12 hours ( $p = 0.11$ ). There was a clear correlation between  
improved outcome and smaller postsurgical hematoma volume ( $p = 0.04$ ). **Conclusions:** Surgical hematoma evacuation  
within 4 hours of symptom onset is complicated by rebleeding, indicating difficulty with hemostasis. Maximum removal of  
blood remains a predictor of good outcome.

NEUROLOGY 2001;56:1294-1299

**NovoSeven**<sup>®</sup>  
Coagulation Factor VIIa  
(Recombinant)





# Recombinant Activated Factor VII for Acute Intracerebral Hemorrhage

Stephan A. Mayer, M.D., Nikolai C. Brun, M.D., Ph.D., Kamilla Begtrup, M.Sc.,  
Joseph Broderick, M.D., Stephen Davis, M.D., Michael N. Diringer, M.D.,  
Brett E. Skolnick, Ph.D., and Thorsten Steiner, M.D., for the Recombinant  
Activated Factor VII Intracerebral Hemorrhage Trial Investigators\*

N ENGL J MED 352;8 WWW.NEJM.ORG FEBRUARY 24, 2005

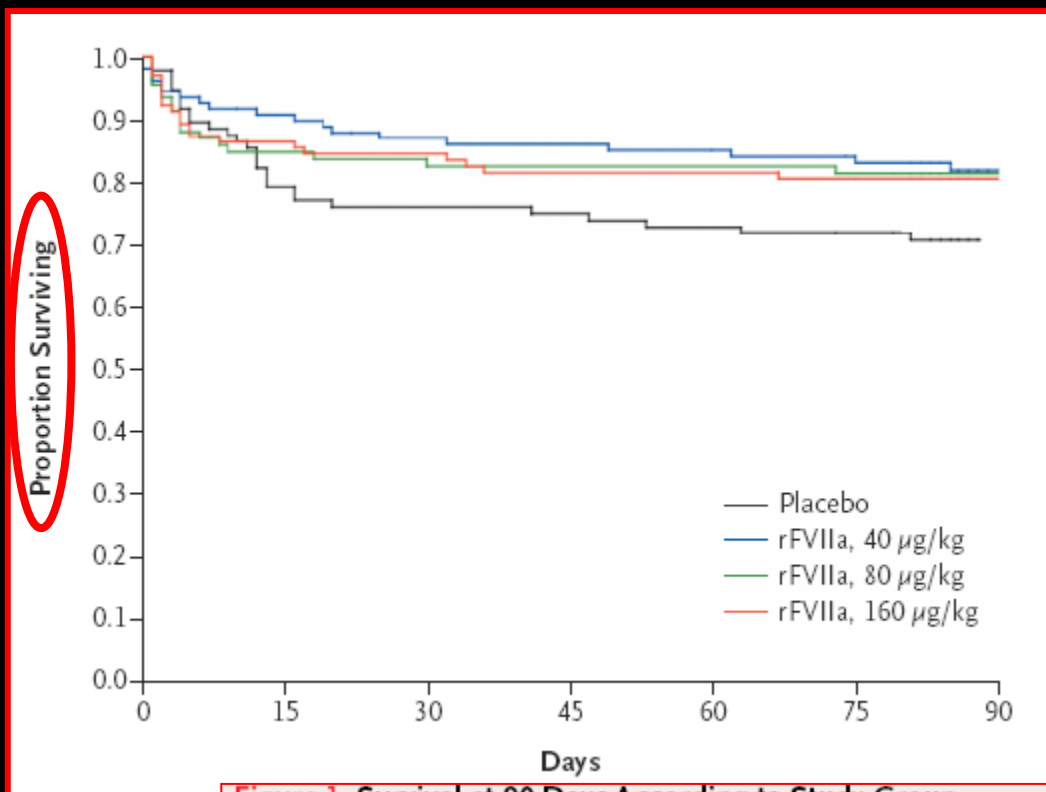


Figure 1. Survival at 90 Days According to Study Group.

- ✓ Limita la crescita dell'ematoma
- ✓ Riduzione della mortalità
- ✓ Migliora l'outcome
- ✓ *Eventi tromboembolici avversi: 7% vs 2% del placebo*

# Ematomi Intracerebrali Spontanei

## Disturbi della Coagulazione

- **Coagulopatie da farmaci:**
  - A Antiaggreganti  
( aspirina, clopidogrel, GPi IIb/IIIa)
  - B Anticoagulanti ( eparina, warfarin)
  - C Terapia fibrinolitica ( rtPA,.. )

## Quadro Clinico dei Pazienti con ICH da Farmaci Anticoagulanti

- \* Evoluzione clinica graduale e spesso insidiosa
- \* L'ematoma può aumentare anche dopo alcuni giorni , quindi attento monitoraggio clinico e neuroradiologico del paziente nei giorni seguenti la diagnosi
- \* Mortalità attorno all'60% nei primi 30 giorni

✓ Uomo      ✓ 59 anni

✓ Tp con coumadin per FA      ✓ INR 4.0

*Ore 20:00 Esordio ictale: Emiparesi dx - Nausea e vomito*

*GCS 15/15*

TC Urgente



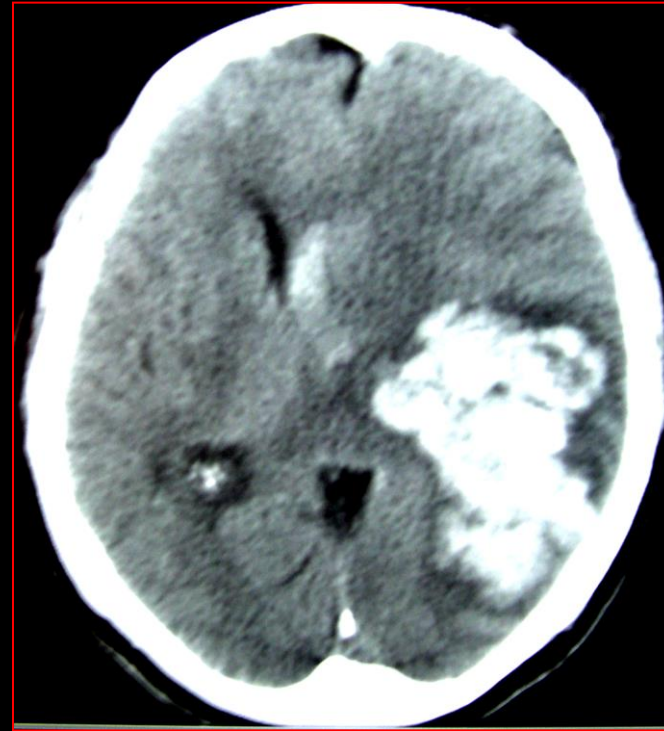


CASO 3

✓ Ore 02:30

Deterioramento dello stato di coscienza:  
GCS 7/15

TC di Controllo



Intervento Chirurgico



# TC CONTROLLO POST-OPERATORIO



*tuttavia...*

***Cattivo Risultato Clinico!***

# RECOMBINANT ACTIVATED FACTOR VII FOR THE RAPID CORRECTION OF COAGULOPATHY IN NONHEMOPHILIC NEUROSURGICAL PATIENTS

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Received, January 27, 2003.

Accepted, March 11, 2003.

**OBJECTIVE:** Coagulopathy is a significant contraindication for neurosurgery. Unfortunately, many coagulopathic patients require urgent neurosurgical intervention. Standard use of blood products, including fresh-frozen plasma or prothrombin complexes, to correct the coagulopathy often leads to significant delays in treatment. Recombinant activated factor VII (rFVIIa) is a medication originally designed to treat bleeding in hemophiliacs but also seems to correct a wide variety of coagulopathies rapidly and safely in nonhemophilic patients.

**METHODS:** The medical records of nine patients with coagulopathy requiring urgent neurosurgical intervention were reviewed retrospectively. Each patient was given a dose ranging from 40 to 90  $\mu\text{g}/\text{kg}$  of rFVIIa before undergoing surgery. Pre-rFVIIa coagulation and post-rFVIIa coagulation parameters were obtained. Once correction of the coagulopathy was verified, each patient underwent the appropriate neurosurgical procedure.

**RESULTS:** The average age of the patients was 40.9 years; six were women. The causes of the coagulopathy included anticoagulant medication, liver dysfunction, and dilutional coagulopathy after traumatic hemorrhage. Neurosurgical indications included intraparenchymal/intraventricular hemorrhage, hydrocephalus, diffuse cerebral edema, and epidural hematoma. Post-rFVIIa coagulation parameters obtained as early as 20 minutes after infusion of the medication showed normalization of values. There were no procedural or operative complications and no postoperative hemorrhagic complications. No associated thromboembolic or other complications with the use of rFVIIa were observed.

**CONCLUSION:** The use of rFVIIa for the urgent surgical treatment of coagulopathic patients is quite promising. Further studies, including randomized, prospective trials using rFVIIa to address issues such as optimal dosing, efficacy, surgical indications, cost-effectiveness, morbidity, and mortality are needed.

**KEY WORDS:** Coagulopathy, Hemostasis, NovoSeven, Recombinant activated factor VII

TABLE 1. Patient characteristics, diagnosis, procedure, blood coagulation parameters, dose, and complications<sup>a</sup>

Patient no.	Age (yr)/sex	Cause of coagulopathy	Indication for surgery	Procedure	Pre-rFVIIa PT (INR)/PTT <sup>b</sup>	Dose (μg/kg)	Post-rFVIIa PT (INR)/PTT	Procedure-related complications
1	78/M	Coumadin for arial fibrillation	Right temporoparietal intraparenchymal hemorrhage	Craniotomy	28.0 (2.8)/36.0	90	9.6 (0.9)/32.0	None
2	84/F	Coumadin for arial fibrillation	Subarachnoid hemorrhage with hydrocephalus	Ventriculostomy	38.0 (3.8)/35.6	90	9.7 (0.9)/27.5	None <sup>c</sup>
3	75/F	Coumadin for arial fibrillation	Intraventricular hemorrhage with hydrocephalus	Ventriculostomy	23.7 (2.4)/37.2	90	10.6 (1.0)/35.1	None <sup>c</sup>
4	5 mo/F	Dilutional coagulopathy after trauma	Right epidural hematoma	Craniotomy	19.4 (1.9)/35.5	90 <sup>d</sup>	10.8 (1.0)/46.6	None
5	8/F	Dilutional coagulopathy after trauma	Left epidural hematoma	Craniotomy	15.6 (1.5)/57.3	40	10.3 (0.9)/29.2	None
6	45/F	End-stage liver disease	Cerebral edema, Grade IV encephalopathy	ICP monitor	24.2 (2.4)/27.1	80	11.0 (1.0)/27.3	None
7	20/M	End-stage liver disease	Cerebral edema, Grade IV encephalopathy	ICP monitor	19.4 (1.9)/26.3	80	9.3 (0.9)/23.5	None
8	17/M	End-stage liver disease	Cerebral edema, Grade IV encephalopathy	ICP monitor	26.2 (2.6)/34.0	80	12.7 (1.2)/37.0	None
9	41/F	End-stage liver disease	Right frontoparietal intraparenchymal hemorrhage	Craniotomy	16.2 (1.6)/36.9	40	12.4 (1.2)/33.7	None

<sup>a</sup>rFVIIa, recombinant activated factor VII; PT, prothrombin time; INR, international normalized ratio; aPTT, activated partial thromboplastin time; ICP, intracranial pressure.

<sup>b</sup>Normal values: PT, 10.1–11.6; aPTT, 25.0–32.6.

<sup>c</sup>No postprocedure imaging obtained.

<sup>d</sup>A second dose was given intraoperatively for excessive bleeding.

20 minuti dopo l'infusione del rFVIII



# NAO

- DABIGATRAN (PRADAXA) → IDARUCIZUMAB
- APIXABAN (ELIQUIS) O RIVAROXABAN (XARELTO) → ANDEXANET



Conclusioni:

Conoscenze più Approfondite sugli Ematomi Intracerebrali Spontanei!

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## Guidelines for the Management of Spontaneous Intracerebral Hemorrhage:

### A Scientific Statement

### from the Stroke Council of the American Heart Association


2005 Update

*Joseph Broderick, MD, FAHA, Chair; E. Sander Connolly, Jr. MD, FAHA, Vice-Chair; Edward Feldmann, MD, FAHA; Daniel Hanley, MD, FAHA; Carlos Kase, MD, AHA; Derk Krieger, MD; Marc Mayberg, MD, FAHA; Lewis Morgenstern, MD, FAHA; Chris Ogilvy, MD; Michael Sayre, MD, Paul Vespa, MD; **Mario Zuccarello, MD***

Stroke, 2006

## Recommendations:

- ❖ The routine evacuation of supratentorial ICH by standard craniotomy within 96 hours of ictus is not recommended (*Class III, Level B*).
- ❖ However patients presenting with lobar clots within 1cm of the surface may represent an exception. (*Class IIb, Level B*).

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- ❖ Operative removal **within 12 hours** particularly when performed **by less-invasive methods** has the most supportive evidence but the number of subjects treated within this window is very small (*Class IIb, Level of Evidence B*).

❖ There is no clear evidence at present that ultra-early craniotomy improves outcome or mortality (Class IIb, Level B).

Very early surgery may be associated with increased risk of ongoing bleeding.

*Further study of very early surgery with pro-thrombotic therapies such as Factor VIIa is needed.*





GRAZIE