

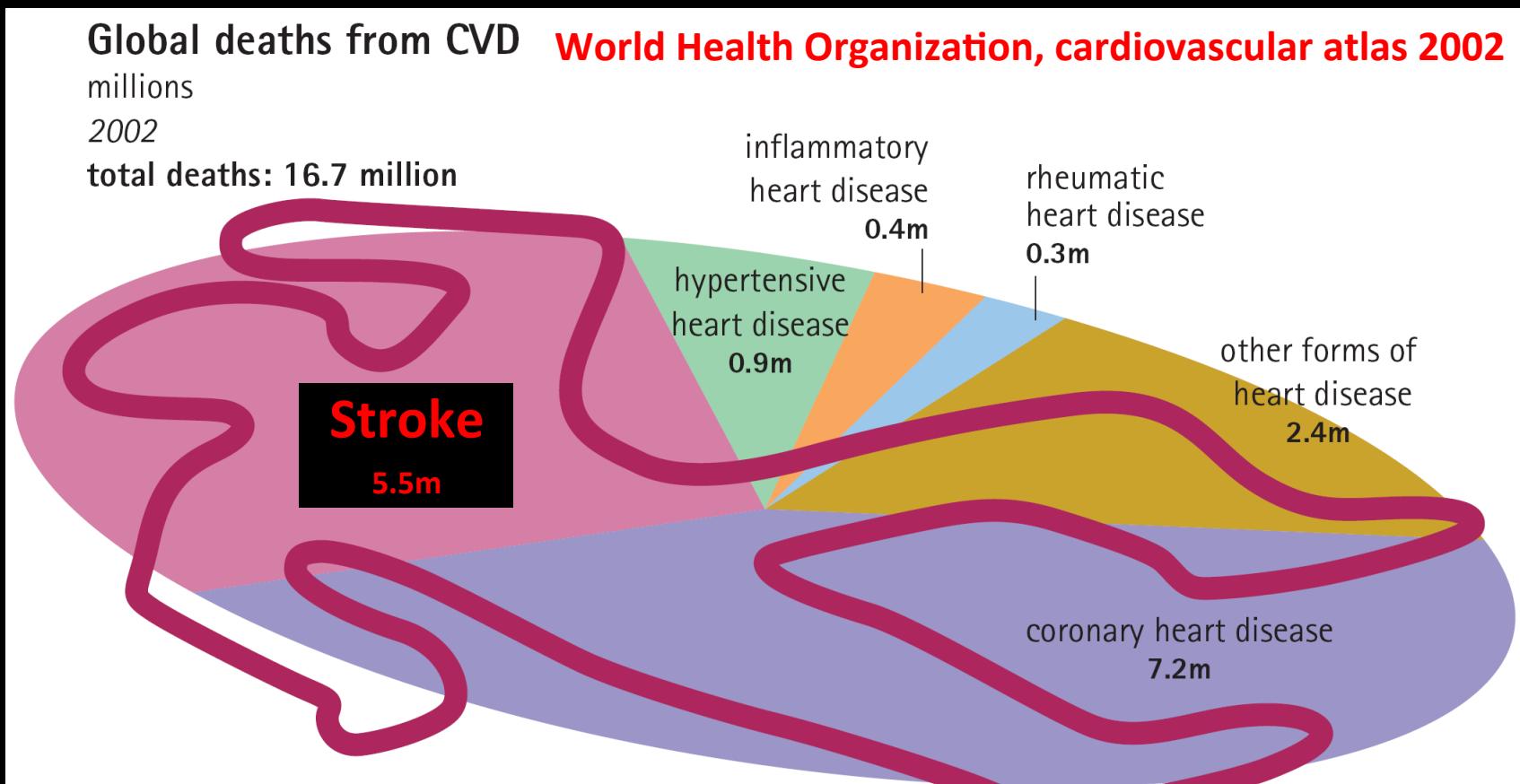
# **Comment j'explore un AVC**

**Y Berthezène**

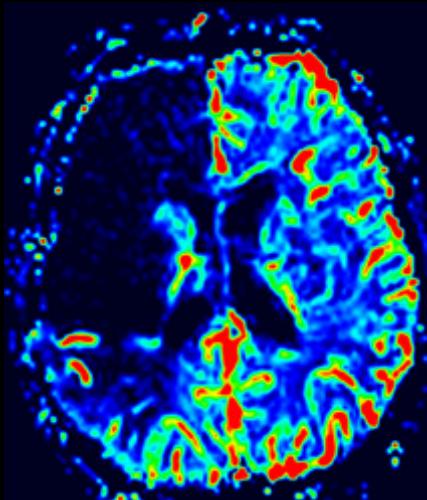
Hôpital Neurologique – Lyon

UMR CNRS 5220 - INSERM U1044

# The burden of stroke



- ✓ Second leading cause of death worldwide
- ✓ Leading cause of significant disability
- ✓ 3-5% of total health care costs in Europe
- ✓ France, 2008: 8.3 billion euros / year (~4% total healthcare costs)



**Stroke**

Ischemic 80%

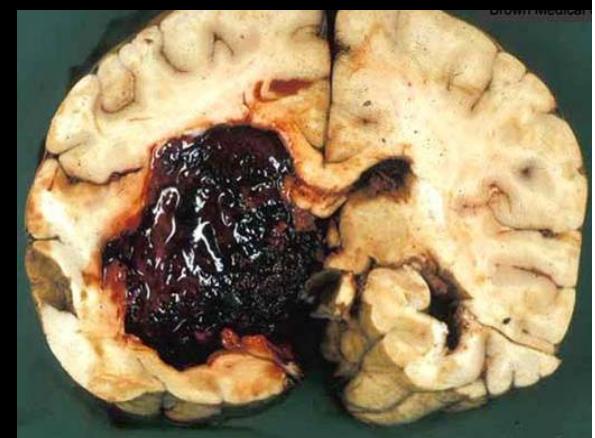
Hemorrhagic 20%

# THE WAR ON STROKES

They strike out of the blue, insidious and deadly, killing brain cells, destroying lives. Now a new wave of research offers hope to millions. Inside the search for treatments that work.

BY JERRY ADLER

UNTIL THE DAY HE COLLAPSED, John Kelly, 57—an exceptionally fit, non-smoking, retired Marine officer from Kansas City, Kans.—had never given a moment's thought to strokes. His cholesterol was low; he worked out six days a week; no one in his family had ever had one. One morning in January he sat down on the edge of his bed, bent over to tie his shoes, and, he says, "kept right on going" until he toppled to the floor. A blood clot had cut circulation to a large region on the right side of his brain, which instantly began



# Time is brain !!!



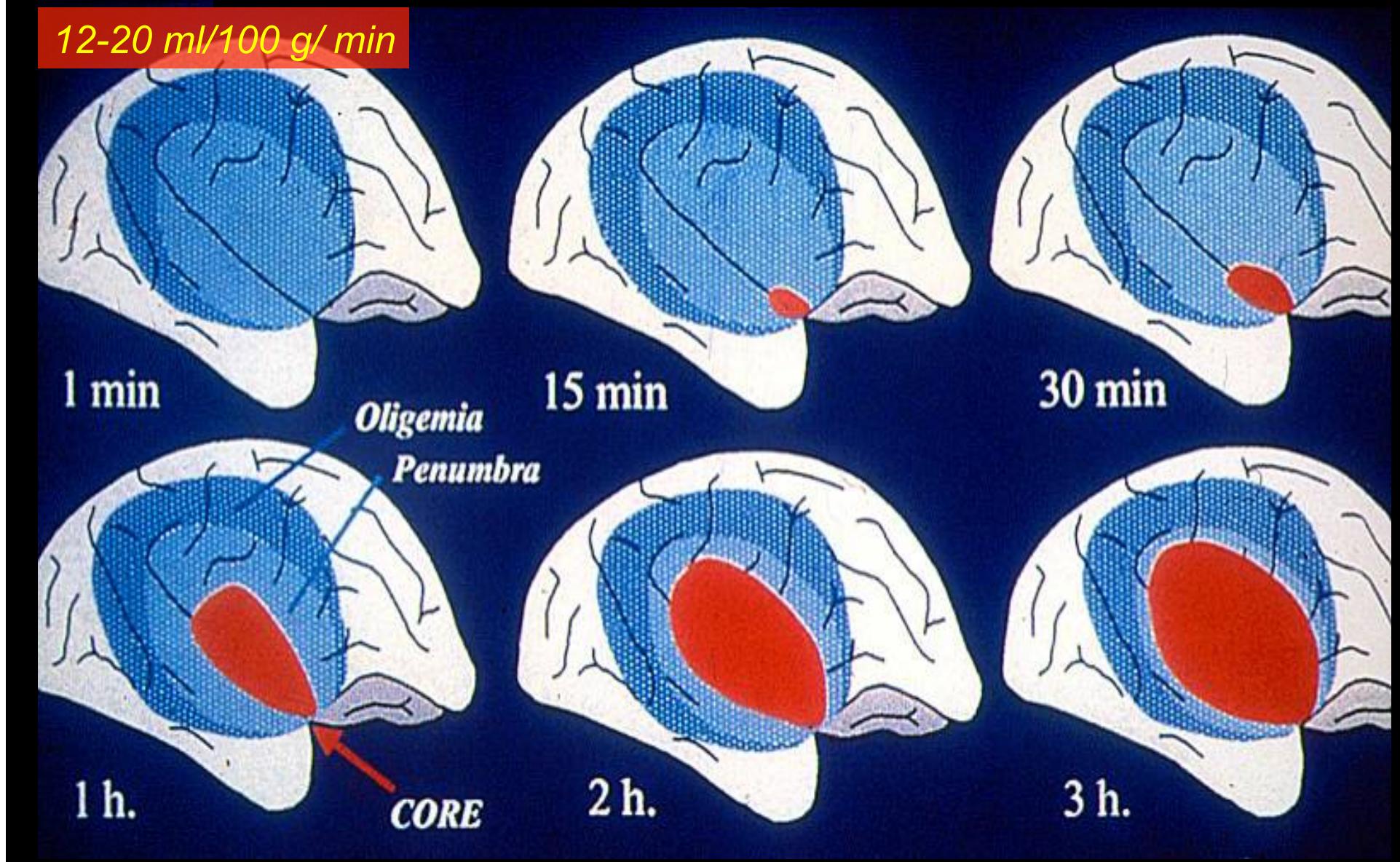
## Estimated Pace of Neural Circuitry Loss in Typical Large Vessel, Supratentorial Acute Ischemic Stroke

	Neurons Lost	Synapses Lost	Myelinated Fibers Lost	Accelerated Aging
Per Stroke	1.2 billion	8.3 trillion	7140 km/4470 miles	36 y
Per Hour	120 million	830 billion	714 km/447 miles	3.6 y
Per Minute	1.9 million	14 billion	12 km/7.5 miles	3.1 wk
Per Second	32 000	230 million	200 meters/218 yards	8.7 h

$\sim 2 \times 10^6$  neurons / minute

*Saver, Stroke 2006*

# The ischemic penumbra: a dynamic [time + space] concept



# Therapeutic strategies

Reperfusion +++



Thrombolysis-  
Thrombectomy

tPA

Primary Neuroprotection

Glu-Ca<sup>++</sup> antag., Free radical scavengers



Recovery of function

Growth factors, promoters of plasticity



Secondary Neuroprotection

Anti-inflammatory and anti-apoptotic agents

Min

Hours

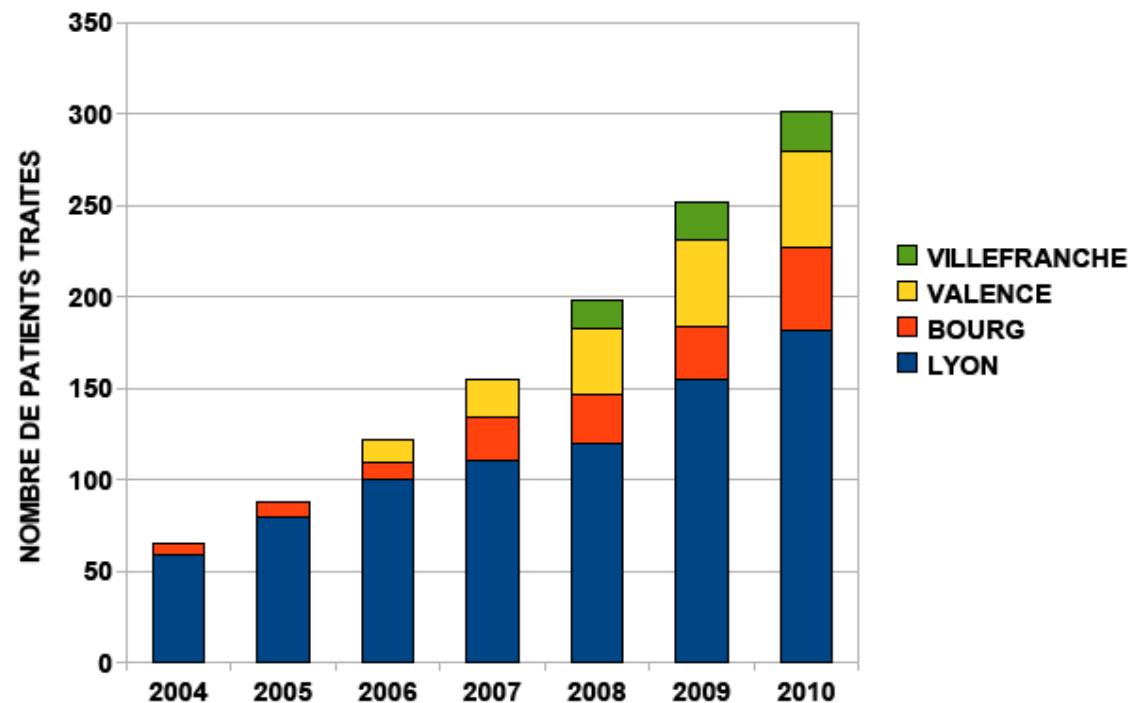
Days

Weeks

# Activité thrombolyse: évolution annuelle

## THROMBOLYSES DANS RESUVAL

EVOLUTION ANNUELLE ET DISTRIBUTION SELON LES CENTRES



# **Stroke MRI:**

## Current practice

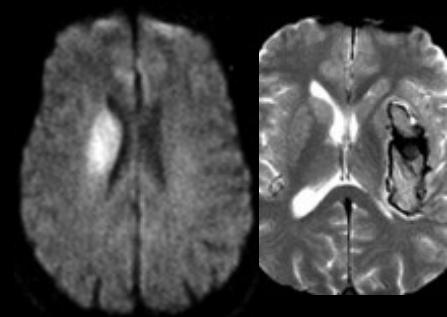
# Acute stroke: aims of imaging

- Confirm diagnosis of ischemic stroke (*stroke mimics !!*)
  - Occlusion site (**proximal vs distal**)
  - Extent of already lost tissue (**necrosis**)
  - Extent of tissue still at risk (**penumbra**)
  - Risk of intracranial **hemorrhage**
- Method of reperfusion (I.V. tPA and/or thrombectomy)
- Benefit/risk ratio assessment

# Multiparametric MRI

Ischemic vs  
hemorrhagic  
stroke

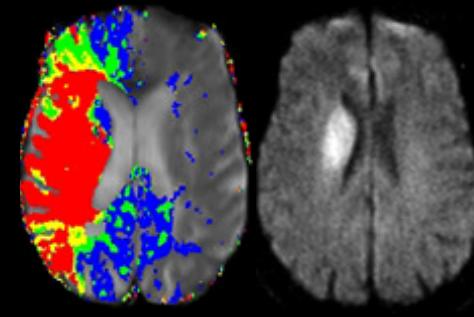
DWI/T2\*



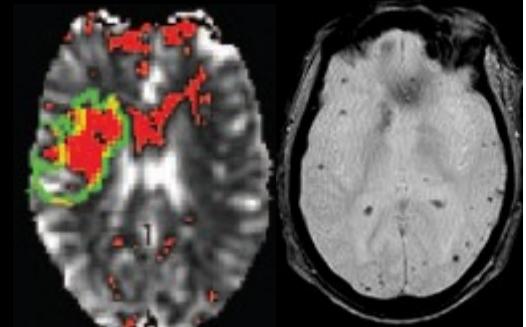
MR  
angiography



Ischemic  
penumbra  
DWI/PWI



Risk of  
intracranial  
hemorrhage  
DWI, PWI, T2\*



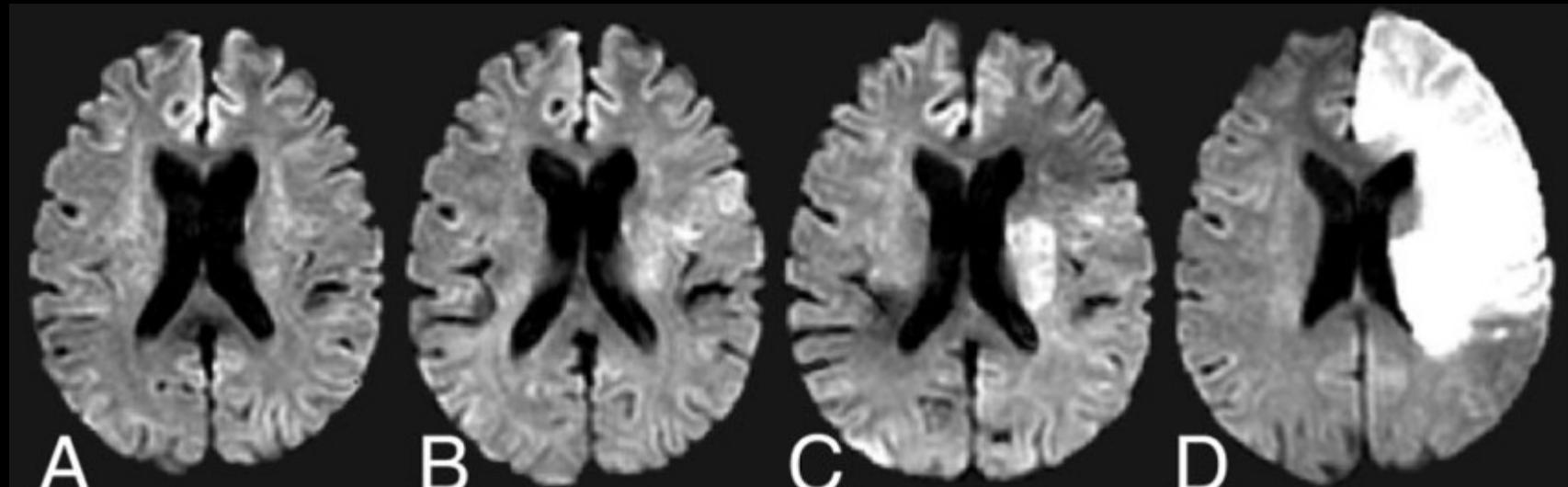
# Diffusion

- Intérêt majeur :

**Diagnostic PRECOCE**

Anomalies dès les premières minutes

# Diffusion MRI



Before deficit

+ 11 min

C

+ 3 hrs

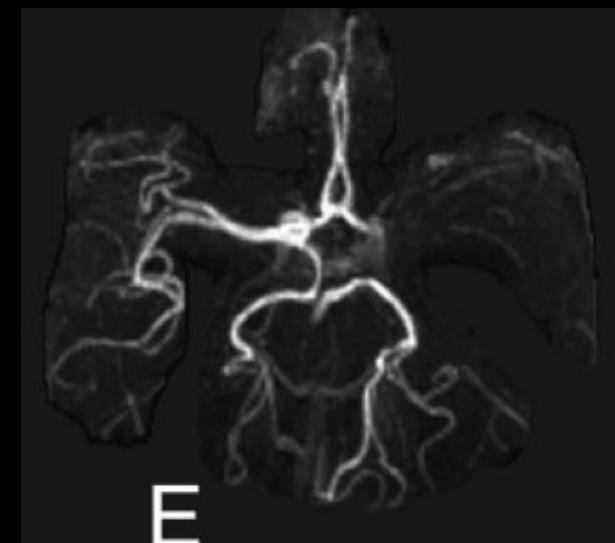
D

+ 24 hrs

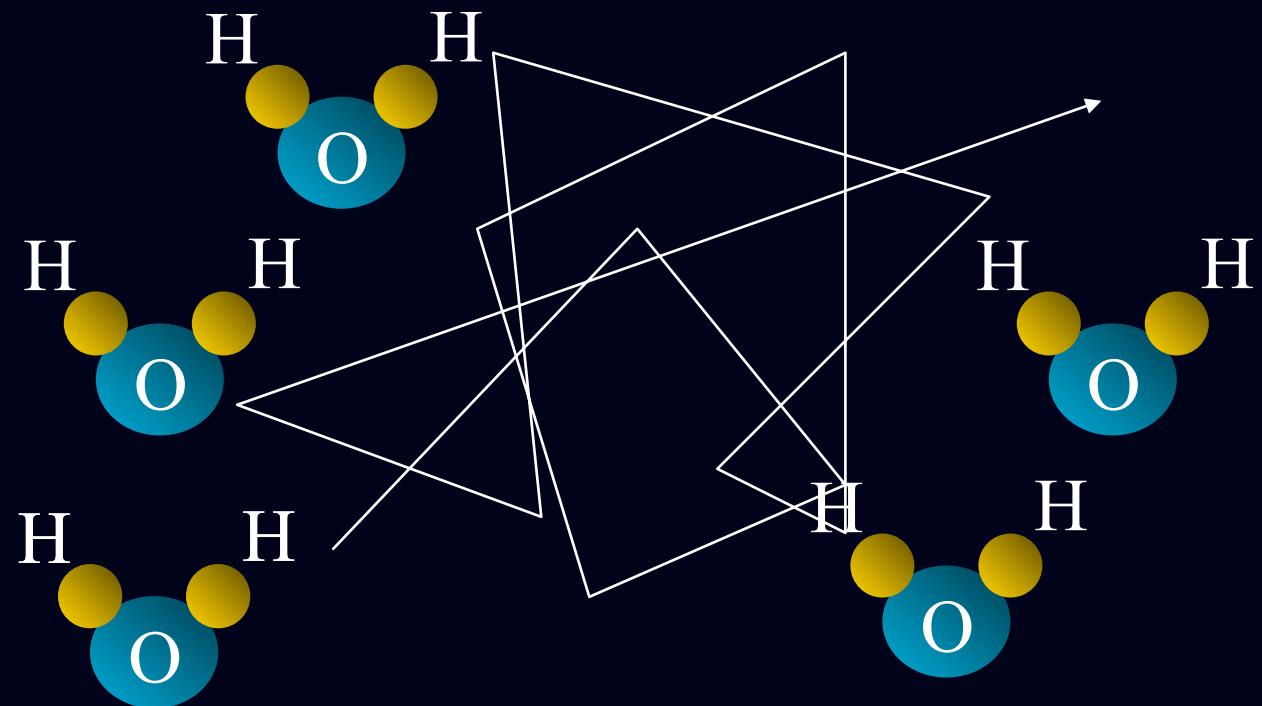
Ischemic Injury Detected by  
Diffusion Imaging 11  
Minutes after Stroke

Niels Hjort, MD,<sup>1,2</sup> Søren Christensen, MSc,<sup>1</sup>  
Christine Sølling, MD,<sup>1</sup> Mahmoud Ashkanian, MD,<sup>1</sup>  
Ona Wu, PhD,<sup>1</sup> Lisbeth Røhl, MD, PhD,<sup>1</sup>  
Carsten Gyldensted, MD, PhD,<sup>1</sup>  
Grethe Andersen, MD, PhD,<sup>2</sup>  
and Leif Østergaard, MD, PhD<sup>1</sup>

Ann Neurol 2005;58:462–465



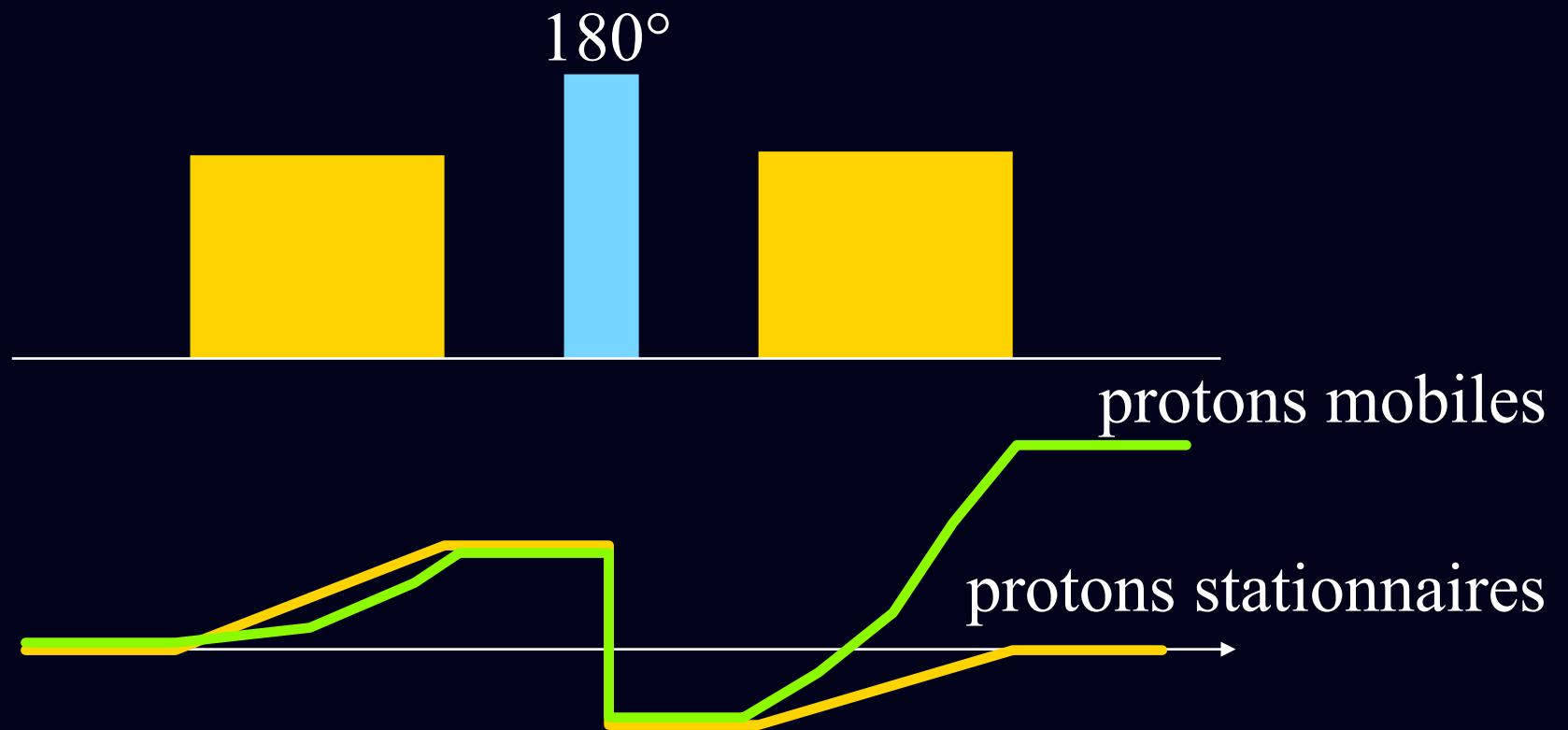
# L'IRM est la technique la plus sensible aux mouvements



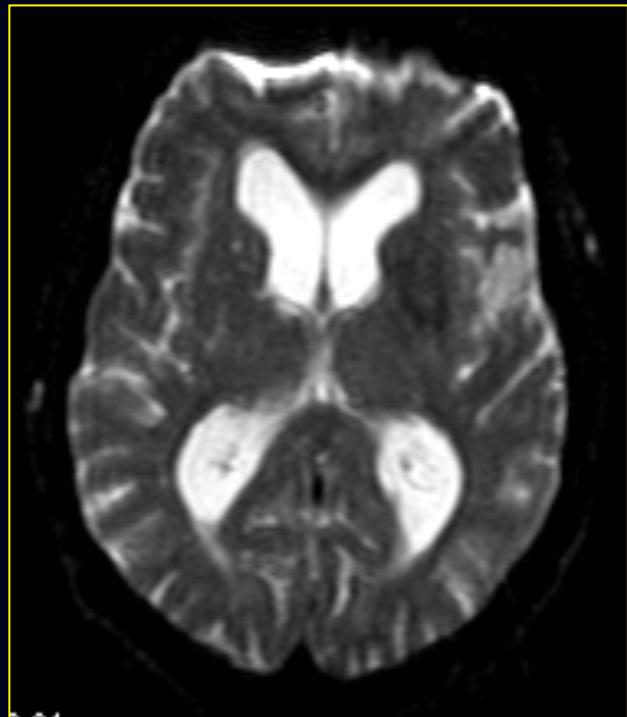
La diffusion mesure les mouvements microscopiques de l'eau dans un tissu

# PULSES DE GRADIENTS BIPOLAires

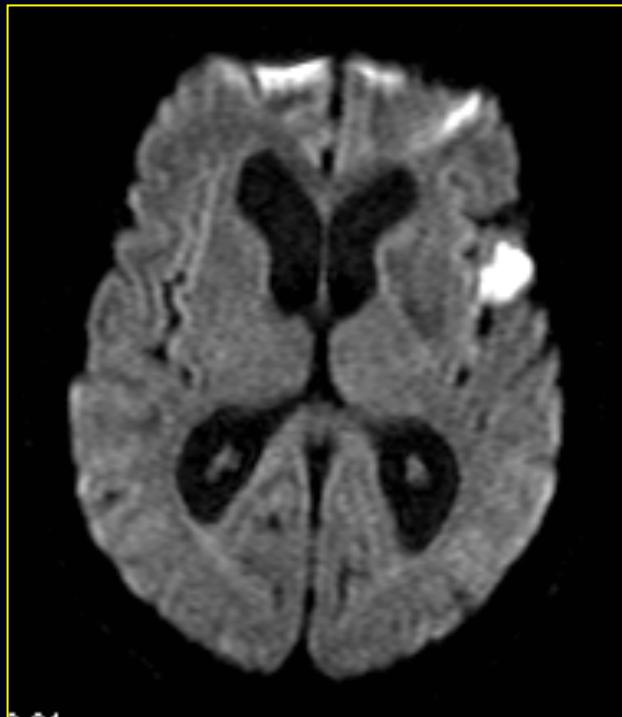
La diffusion est mise en évidence par la différence de phase entre les protons mobiles et stationnaires en présence de gradients.



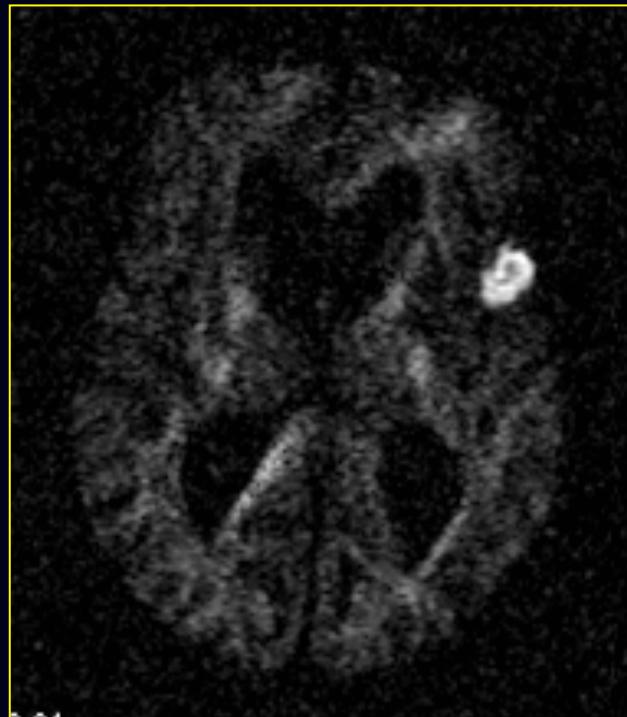
# Pondération en diffusion



$b = 0$

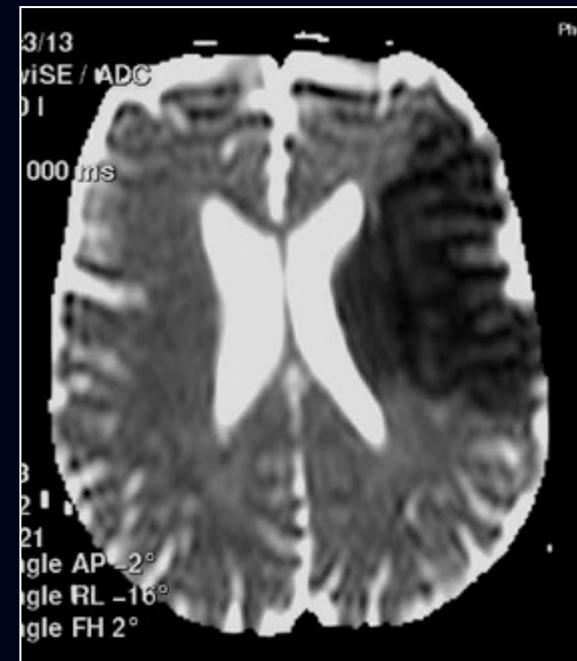
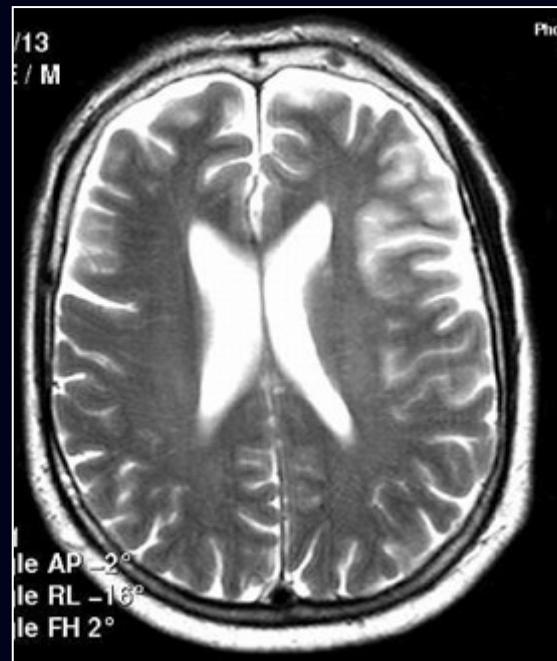


$b = 1000 \text{ s/mm}^2$



$b = 4000 \text{ s/mm}^2$

# Diffusion → Dg précoce

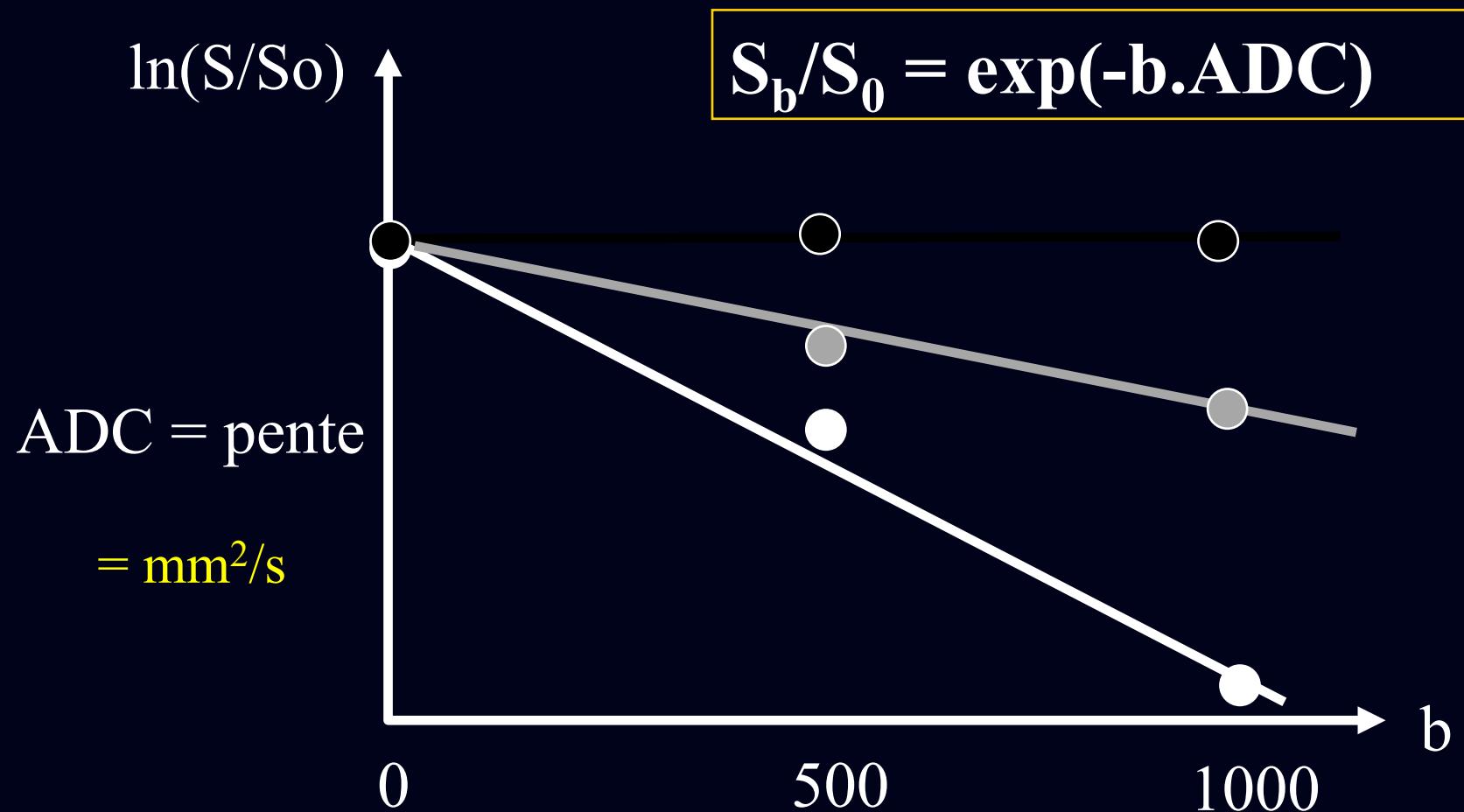


T2

Trace b= 1000

ADC

# Coefficient Apparent de Diffusion



# Intérêt de la mesure de l' ADC

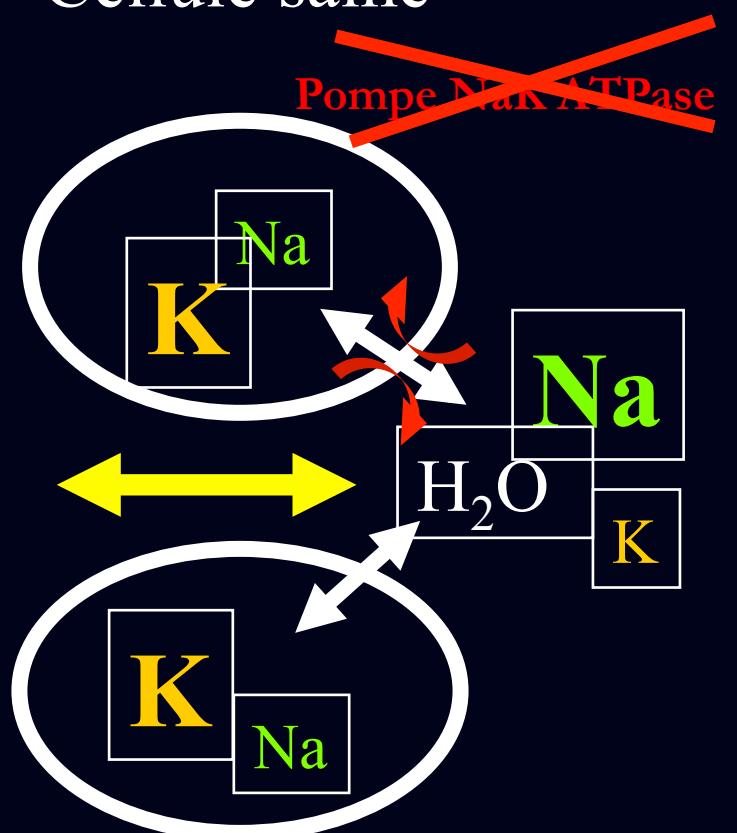
Elle permet de s' affranchir de l' effet T2 engendré par l' augmentation du volume d' eau en rapport avec la constitution de l' œdème.



distinction œdème **cytotoxique / vasogénique**

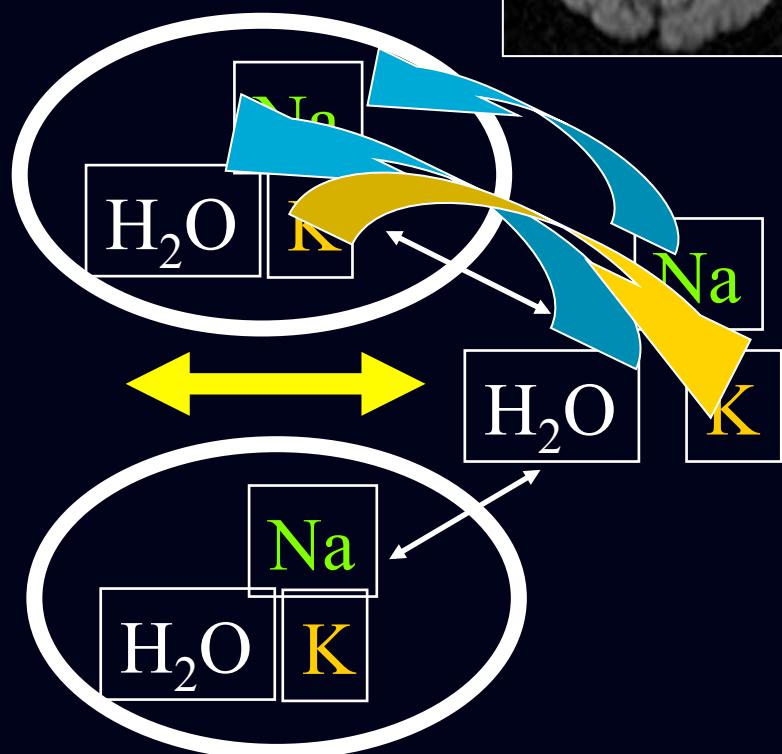
# Modification de la diffusion lors d'un AIC

Cellule saine



Equilibre actif

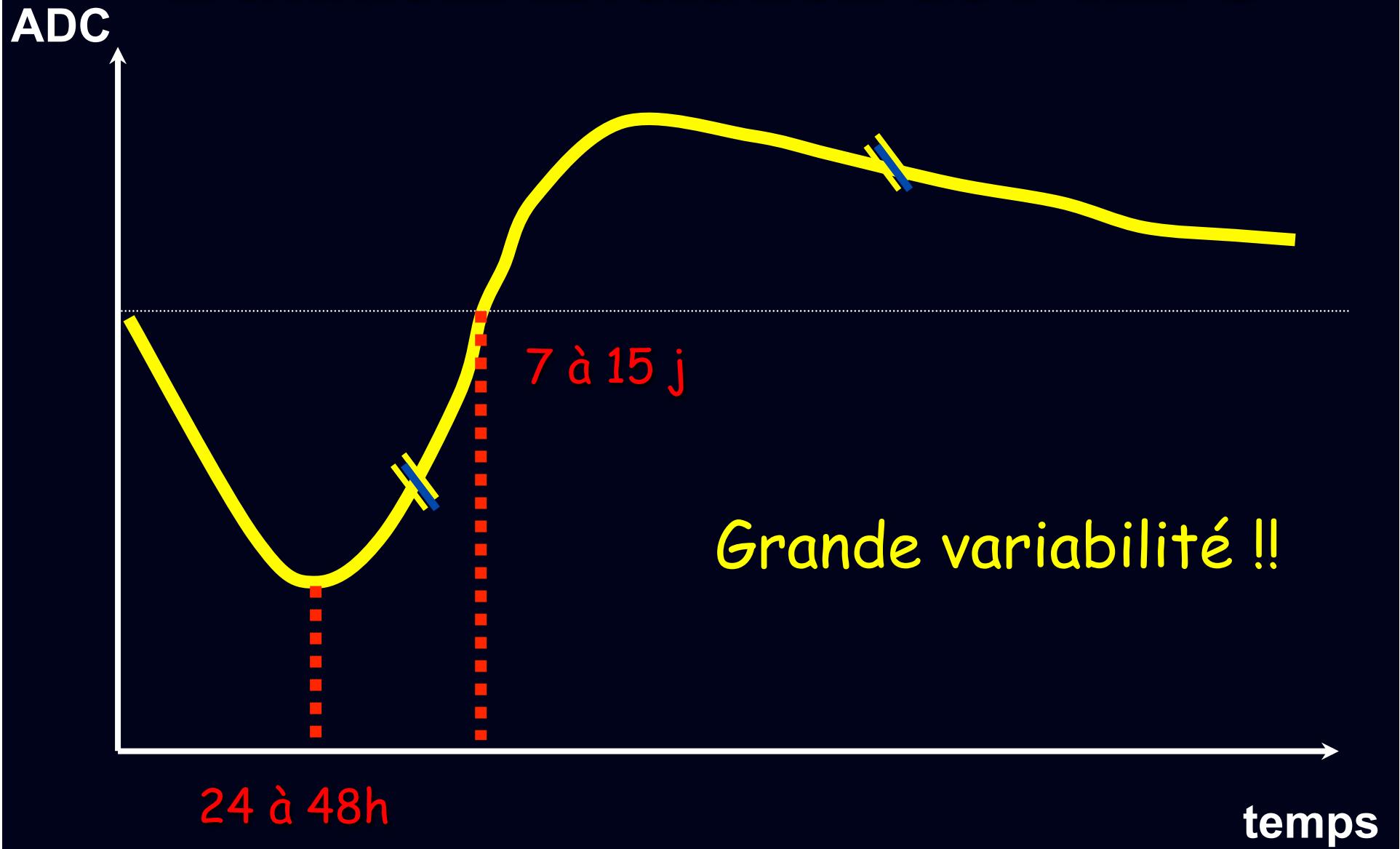
Cellule lésée



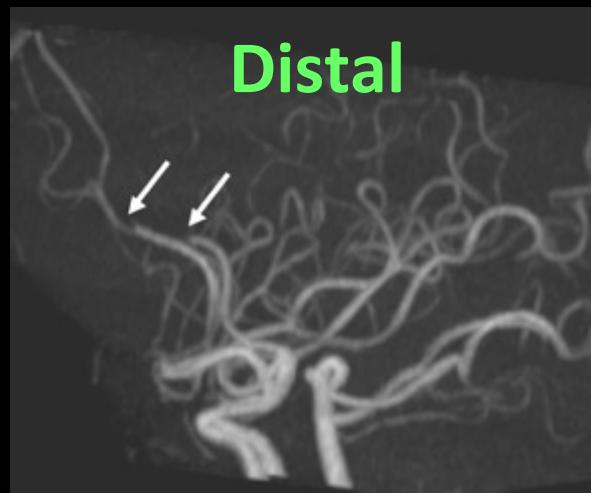
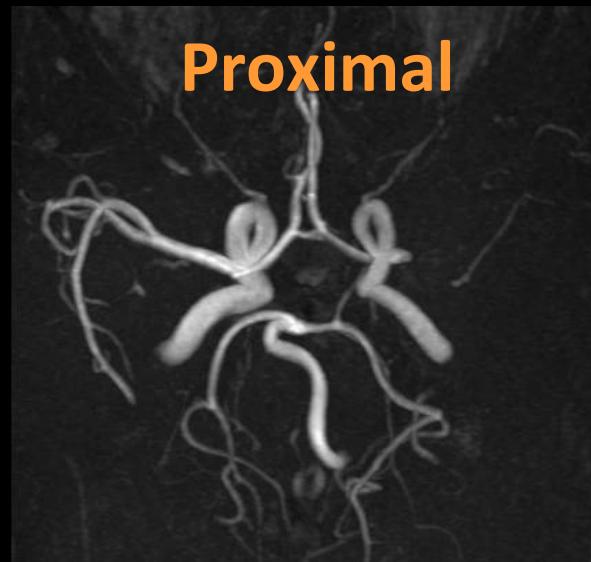
Equilibre osmotique passif  
**Edème intracellulaire**



# Datation: Evolution de l' ADC



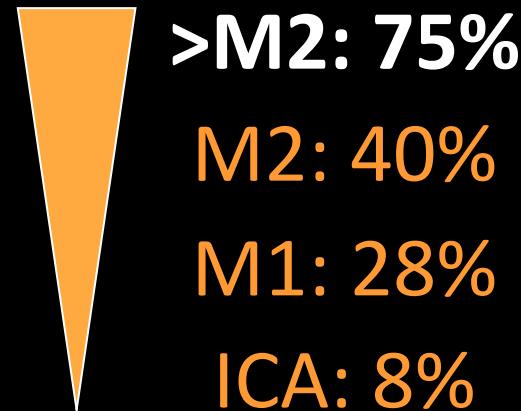
# Occlusion level



# Low efficiency of I.V. thrombolysis for large vessel occlusions

Recanalization rates

1 hr after IV rt-PA:

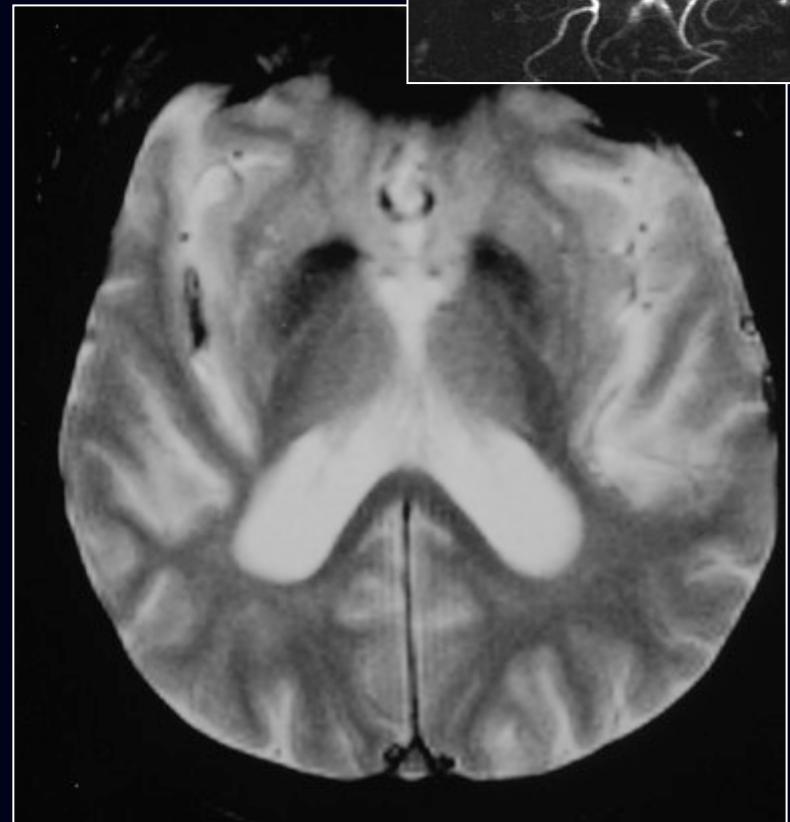
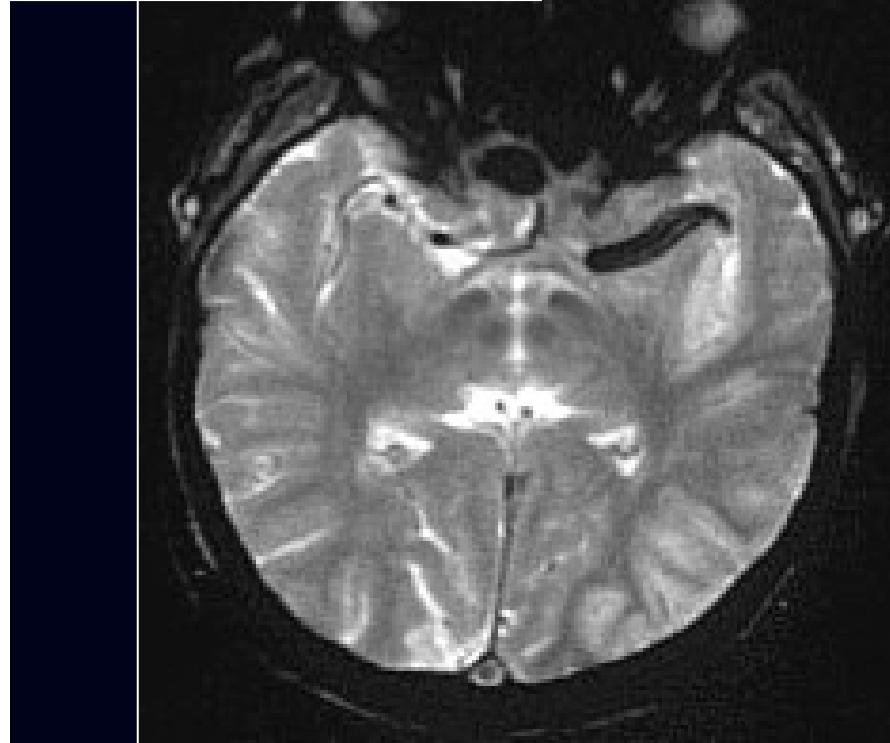


Del Zoppo et al. Ann Neurol. 1992; 32: 78-86.

Wolpert et al. AJNR Am J Neuroradiol. 1993; 14: 3-13.



T2\*



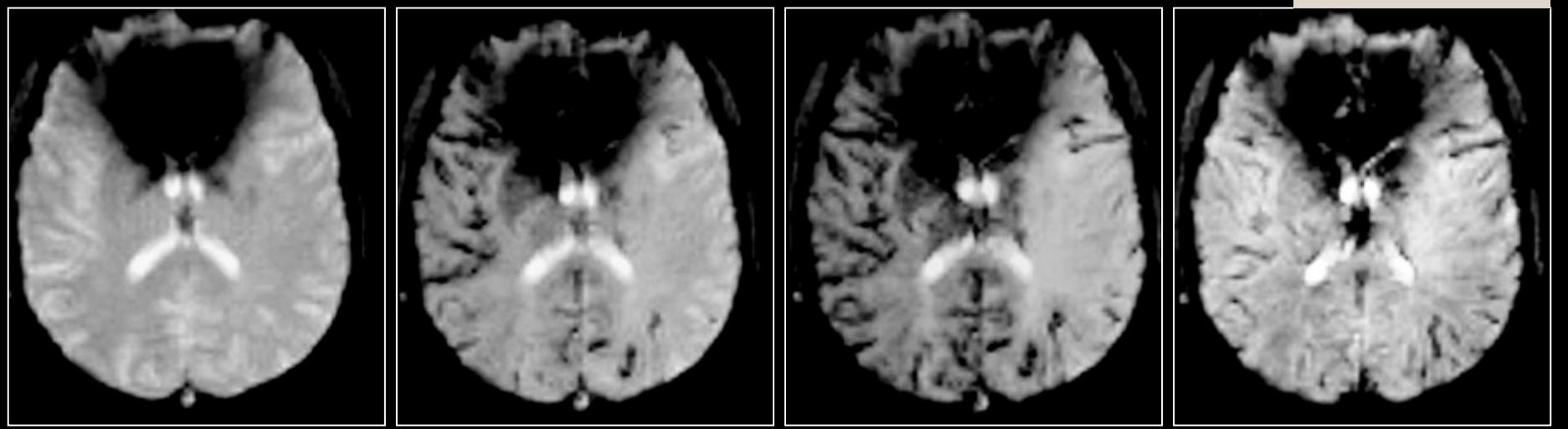
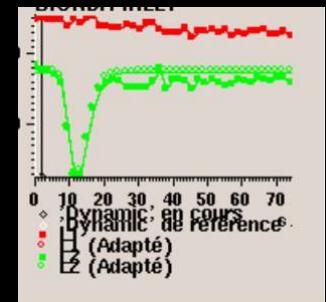
Visualisation directe du **thrombus** artériel  
(mauvais pronostic Kimura et al Stroke 2011)

# Perfusion MRI

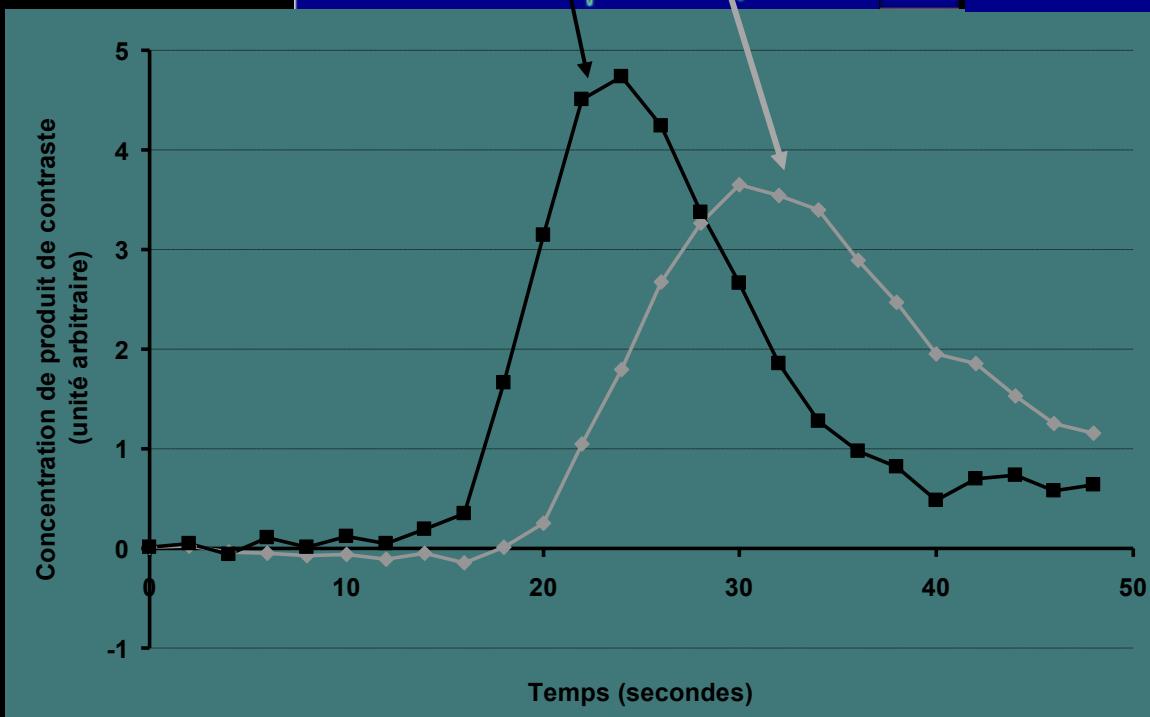
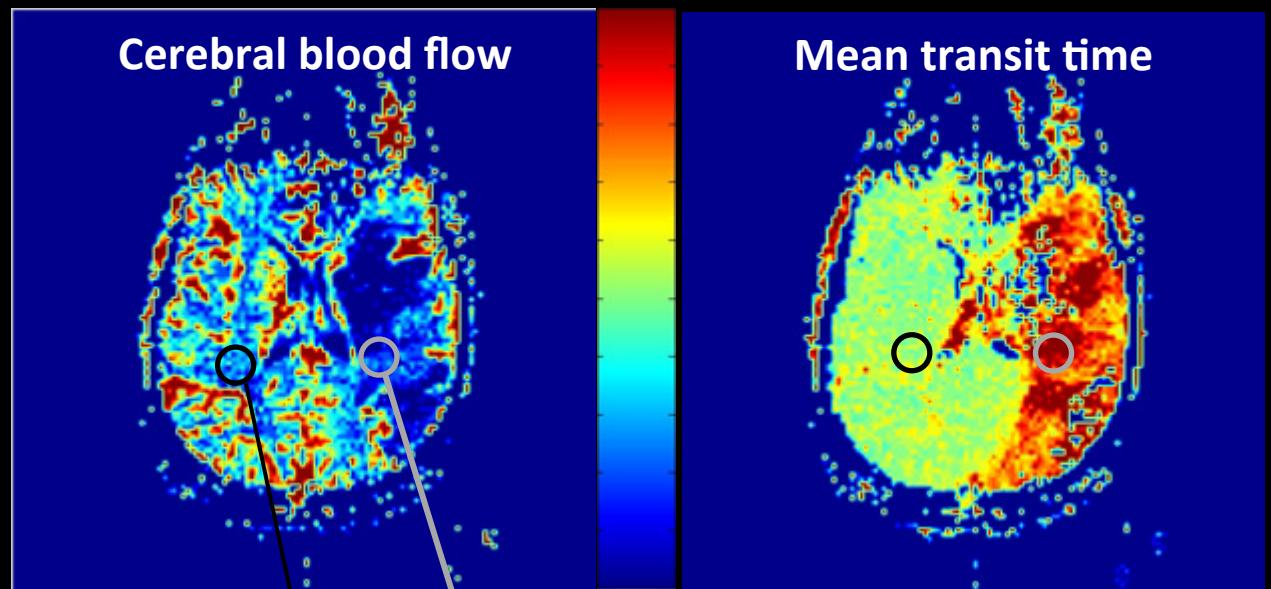
MR signal-time curve after an intravenous injection of a gadolinium-based contrast agent

MR signal evolution related to magnetic susceptibility effects induced by the intravascular contrast agent

→ MR signal drop in T2\* weighted sequences

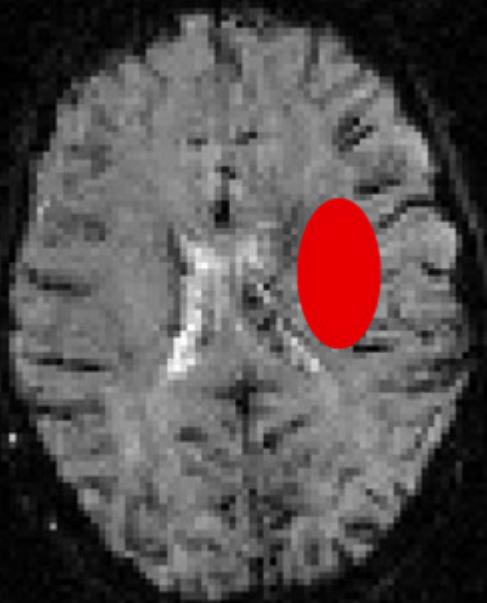
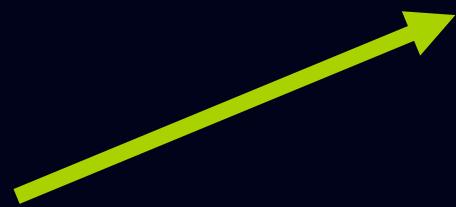
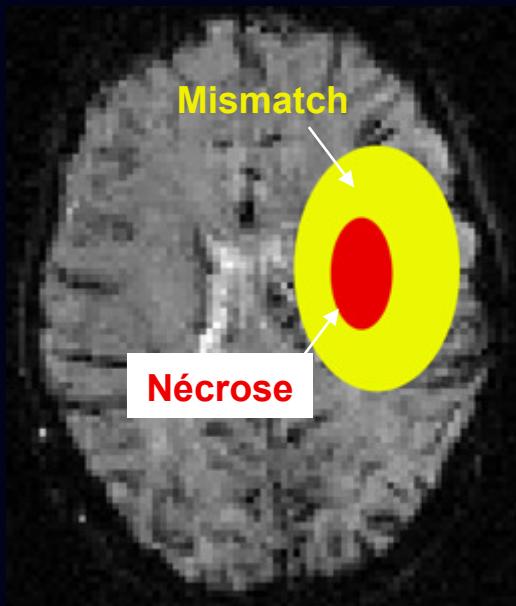


# Perfusion maps



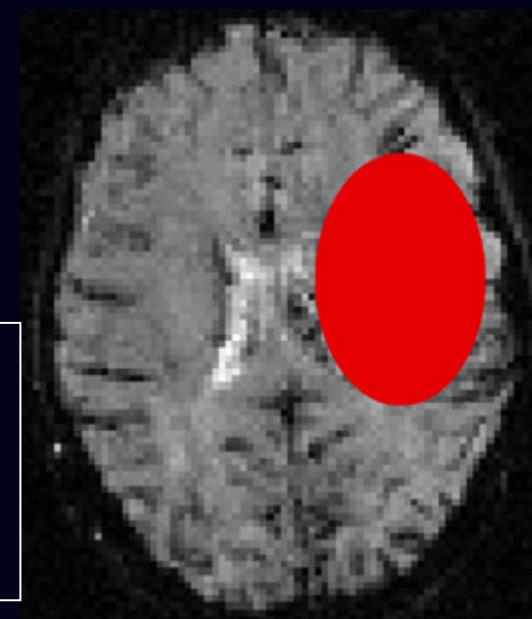
**Recanalisation précoce:**

**Limitation de volume  
De la nécrose finale**

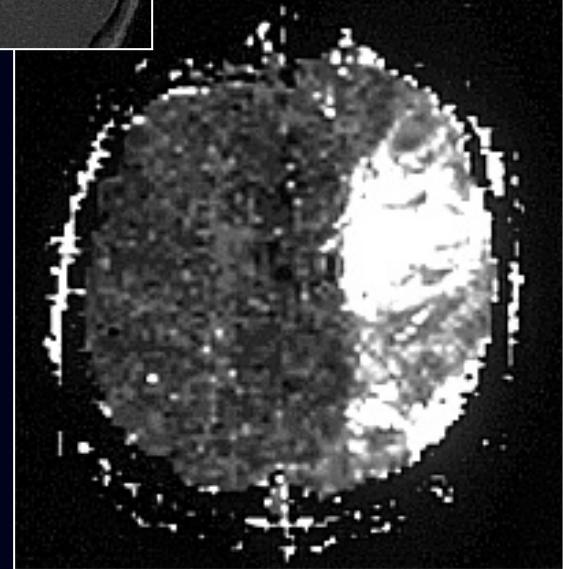


**Pas de recanalisation :**

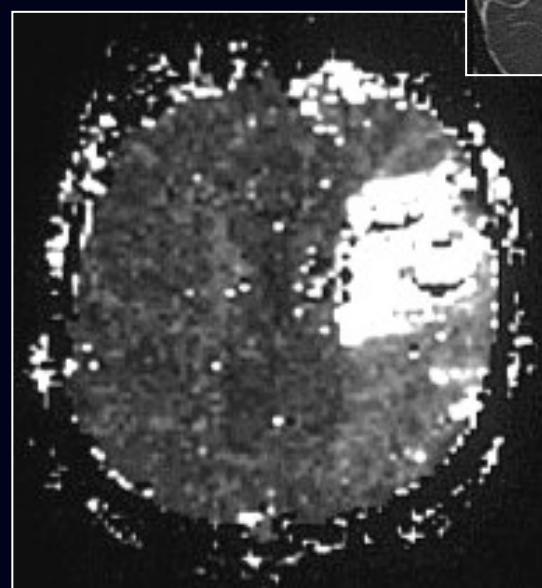
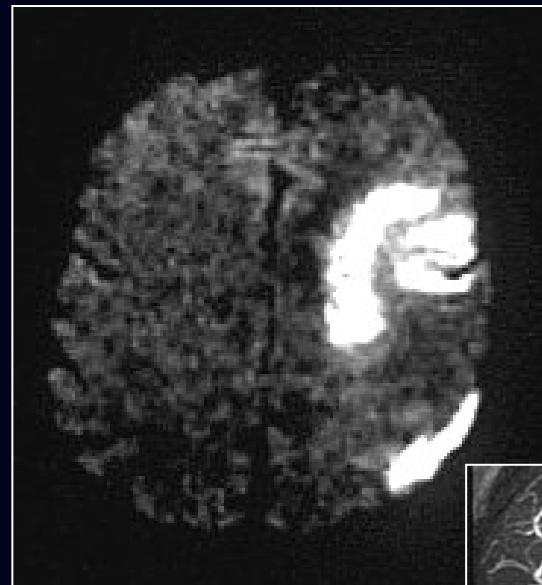
**Extension de la nécrose sur  
toute la zone de mismatch**

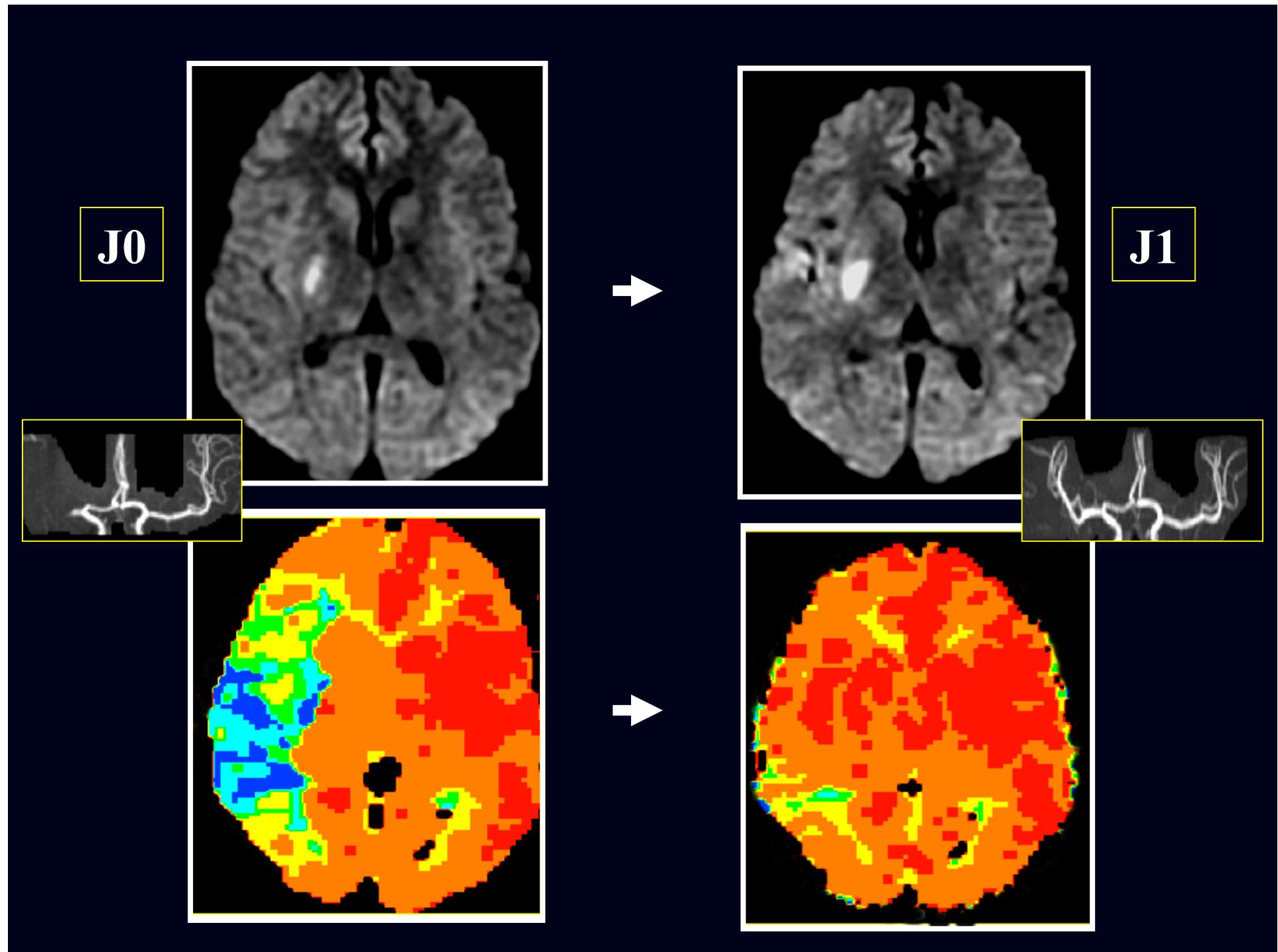


J0

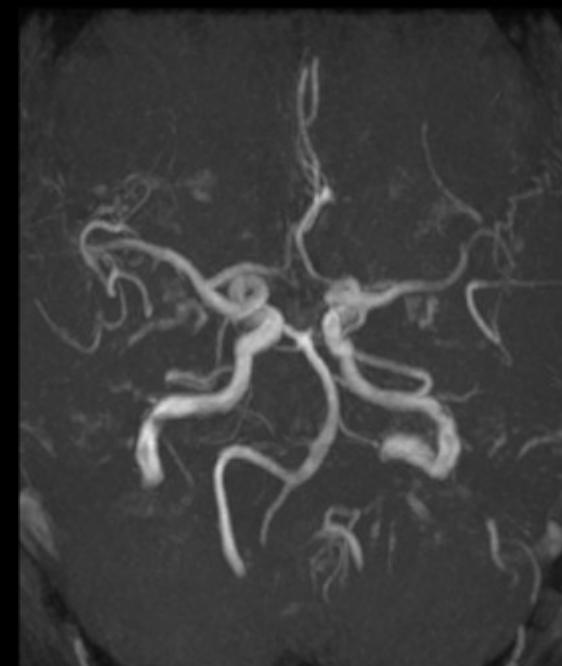
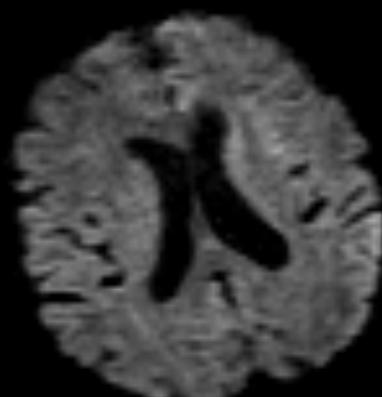
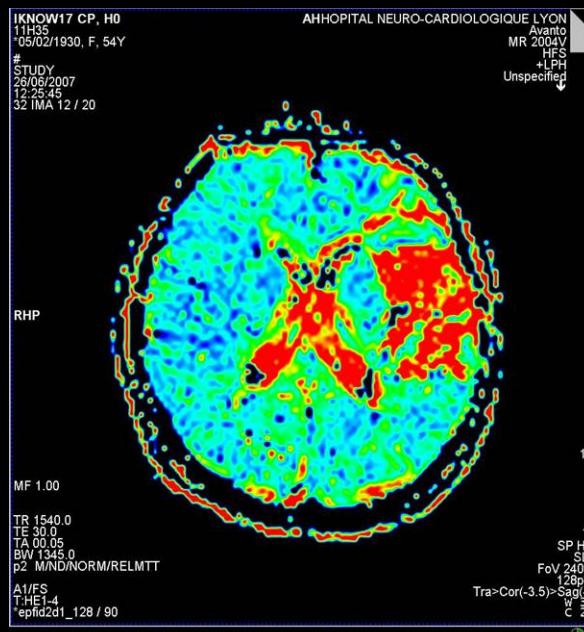


J1





# Aide au diagnostic d'occlusion distale

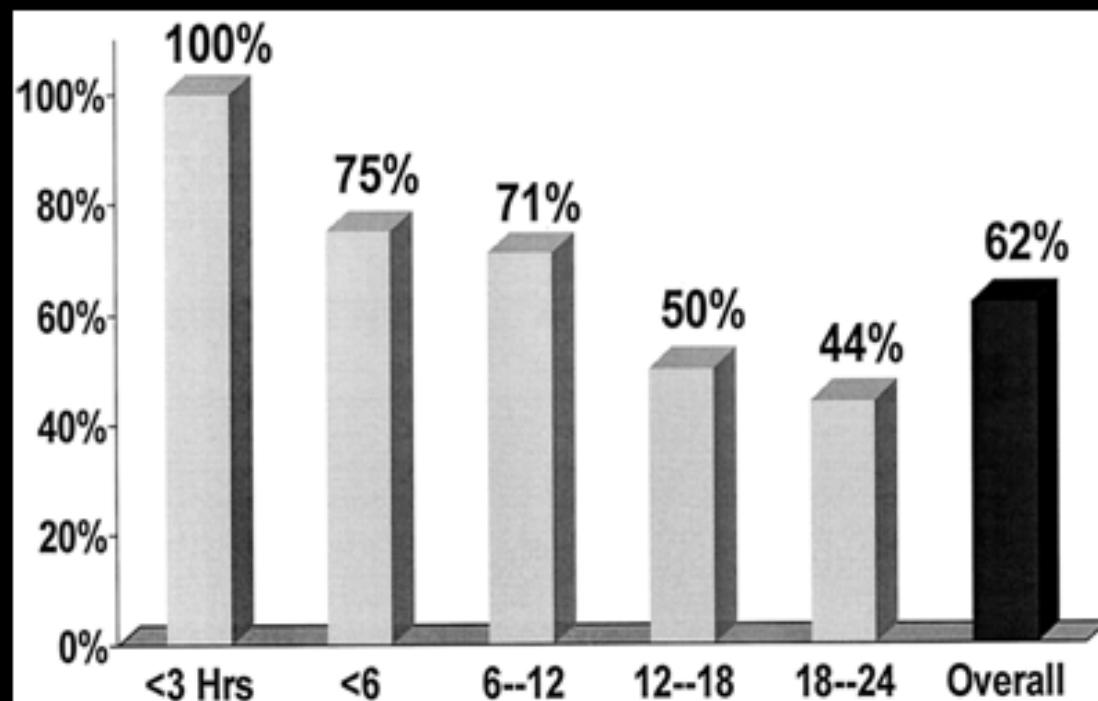


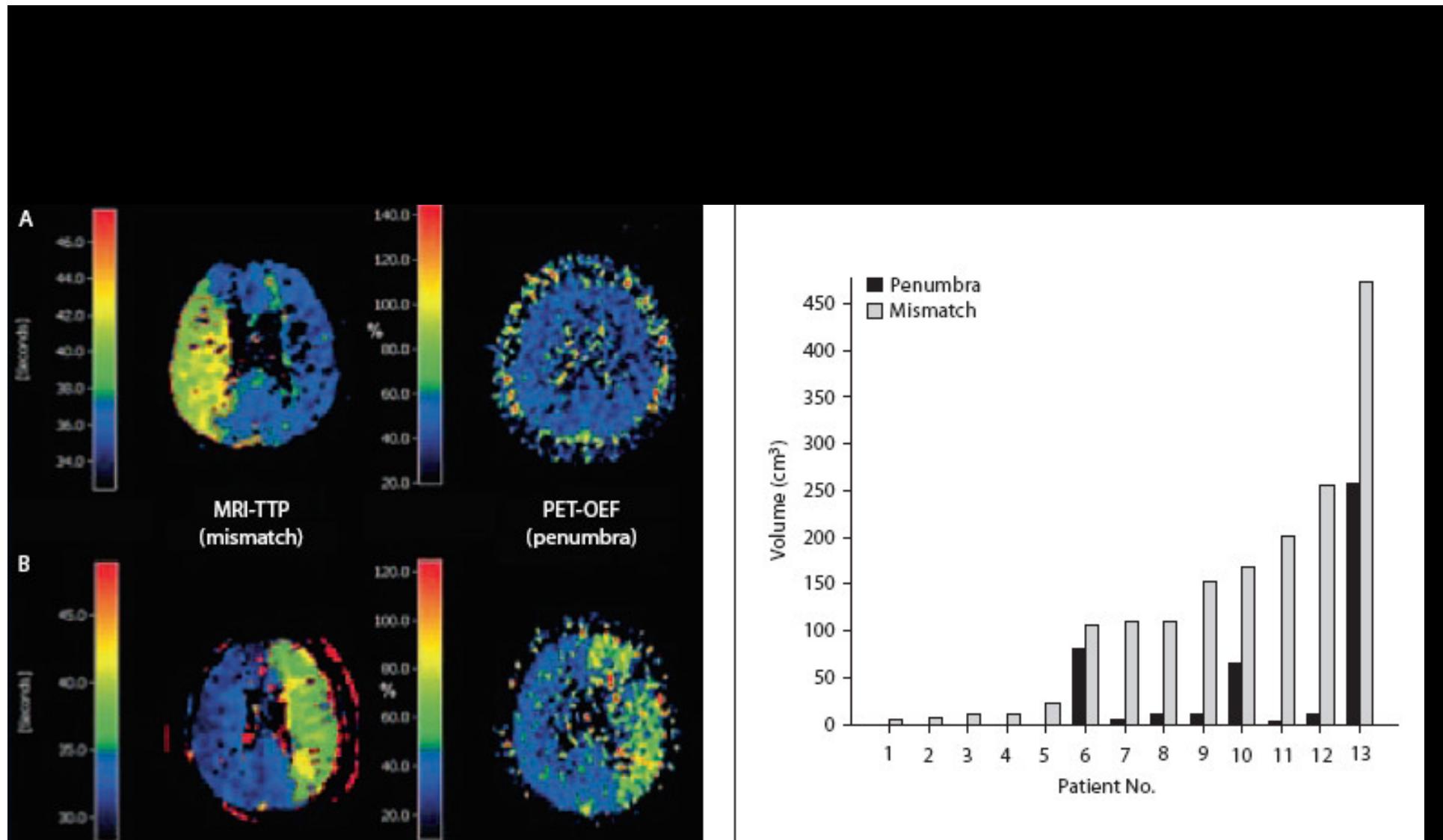
# MRI Guided Therapy

## Time window versus MRI Clock

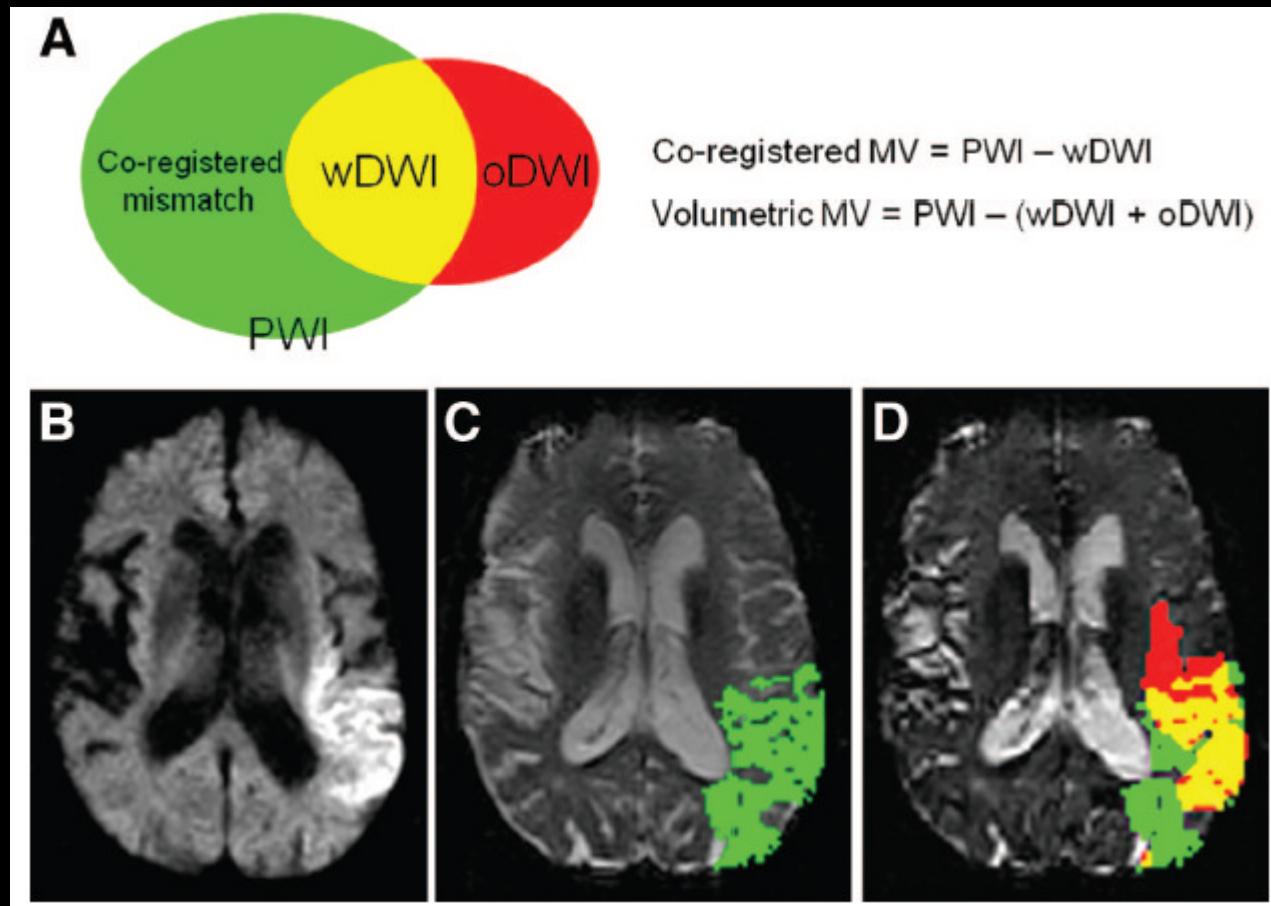
CS Kidwell, Stroke 2003 : % de patients  
avec mismatch de 3 à 24h

Brain Clock / Time Clock





*Sobesky et al Stroke , 2005;36:980*



*Nagakane et al Stroke 2011;42:59-64*

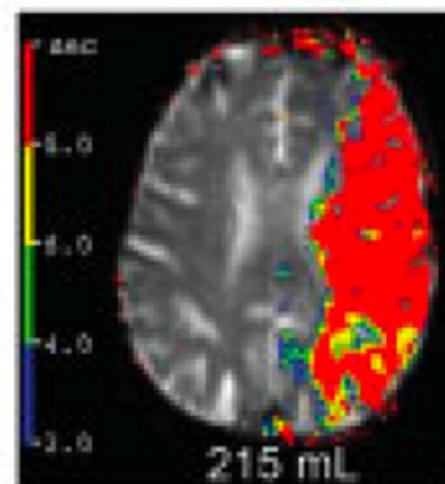
Profil infarctus malin : aucun bénéfice de la recanalisation après t-PA  
DEFUSE, Albers Ann Neurol, 2006

**Malignant Profile**

4 hr 36 min after  
stroke onset:  
NIHSS 26



105 mL

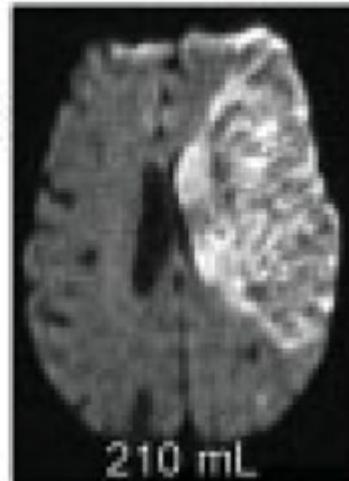


215 mL

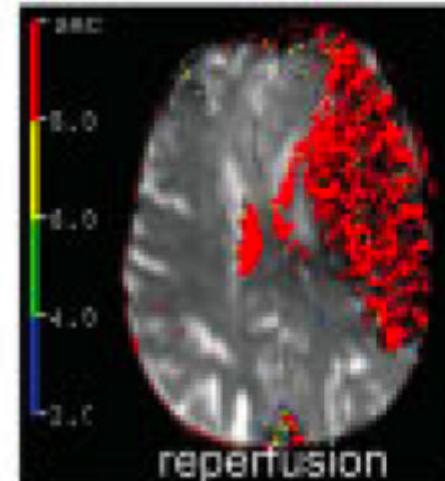


MCA occlusion

4 hrs after tPA  
bolus: NIHSS 27



210 mL



reperfusion

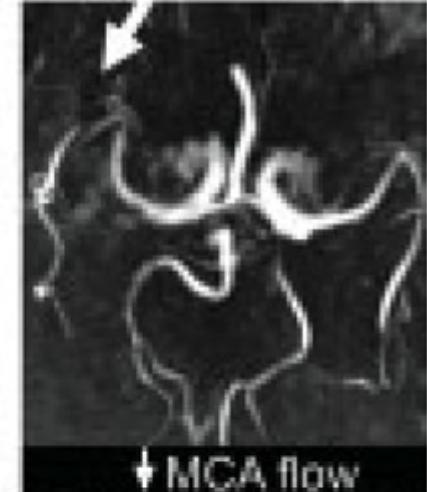
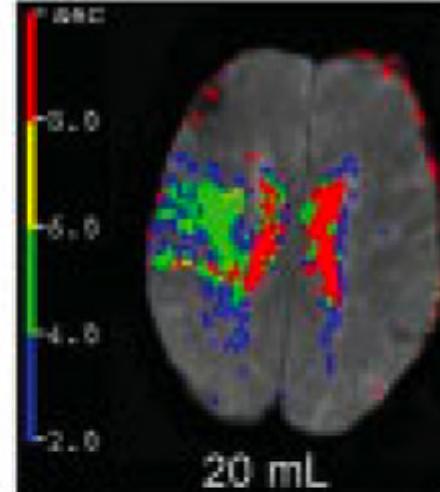
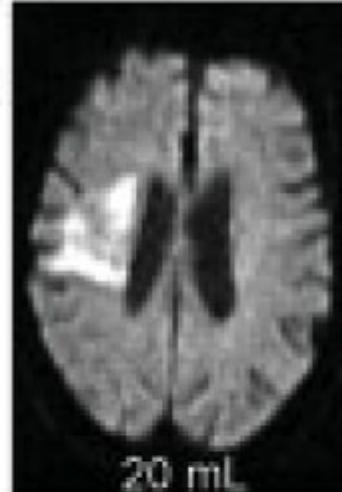


recanalization

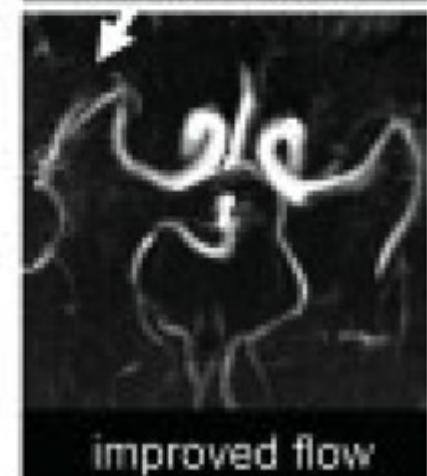
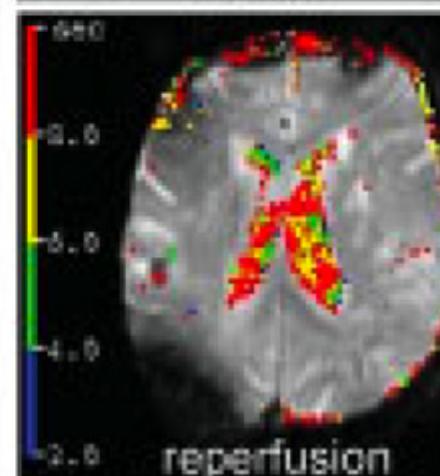
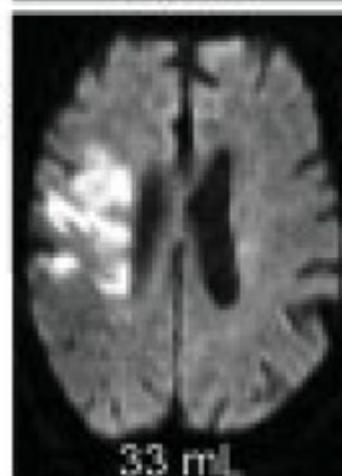
Absence de Mismatch mais volume lésionnel modéré:  
Bénéfice possible de la recanalisation par rt-PA  
DEFUSE, Albers Ann Neurol. 2006

**No Mismatch Profile**

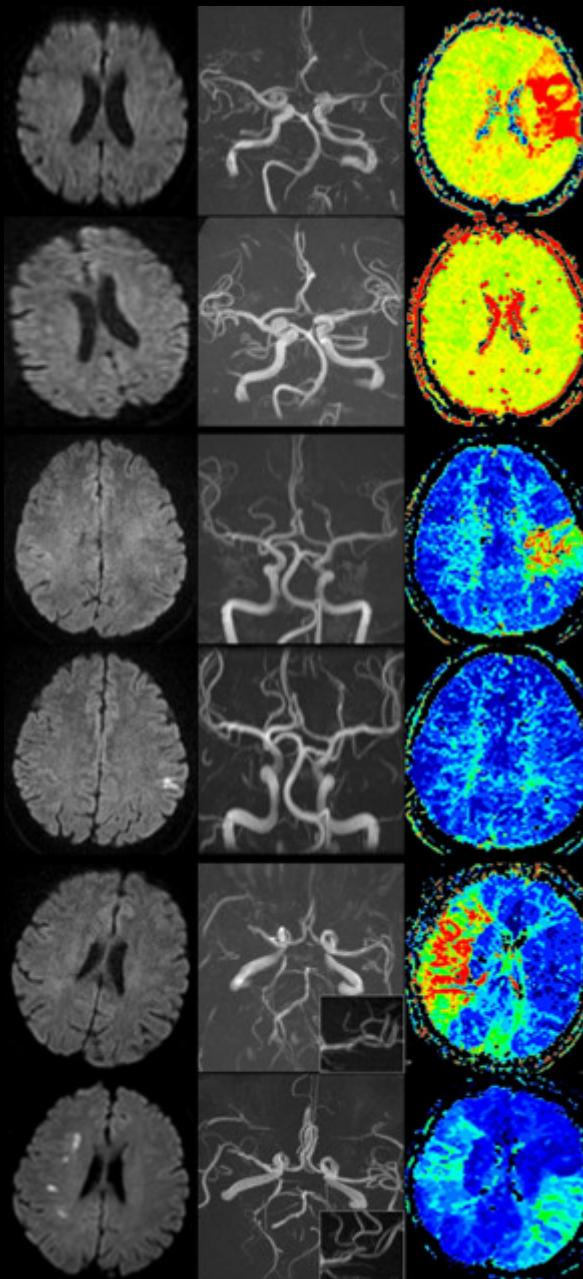
5 hr 15 min after  
stroke onset:  
NIHSS 14



6.5 hrs after tPA  
bolus: NIHSS 11

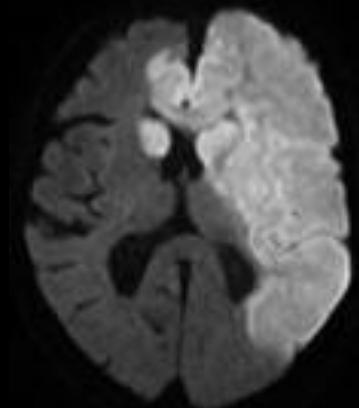
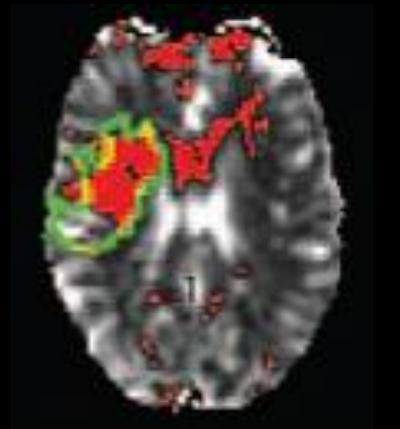
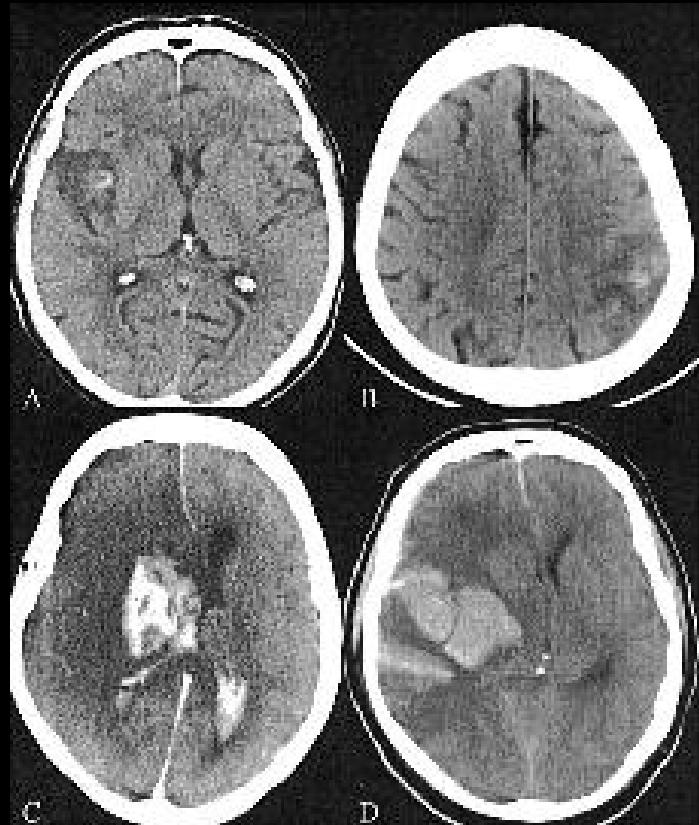


PWI defect without DWI damage (3- 5% of patients) CHO et al Stroke 2009

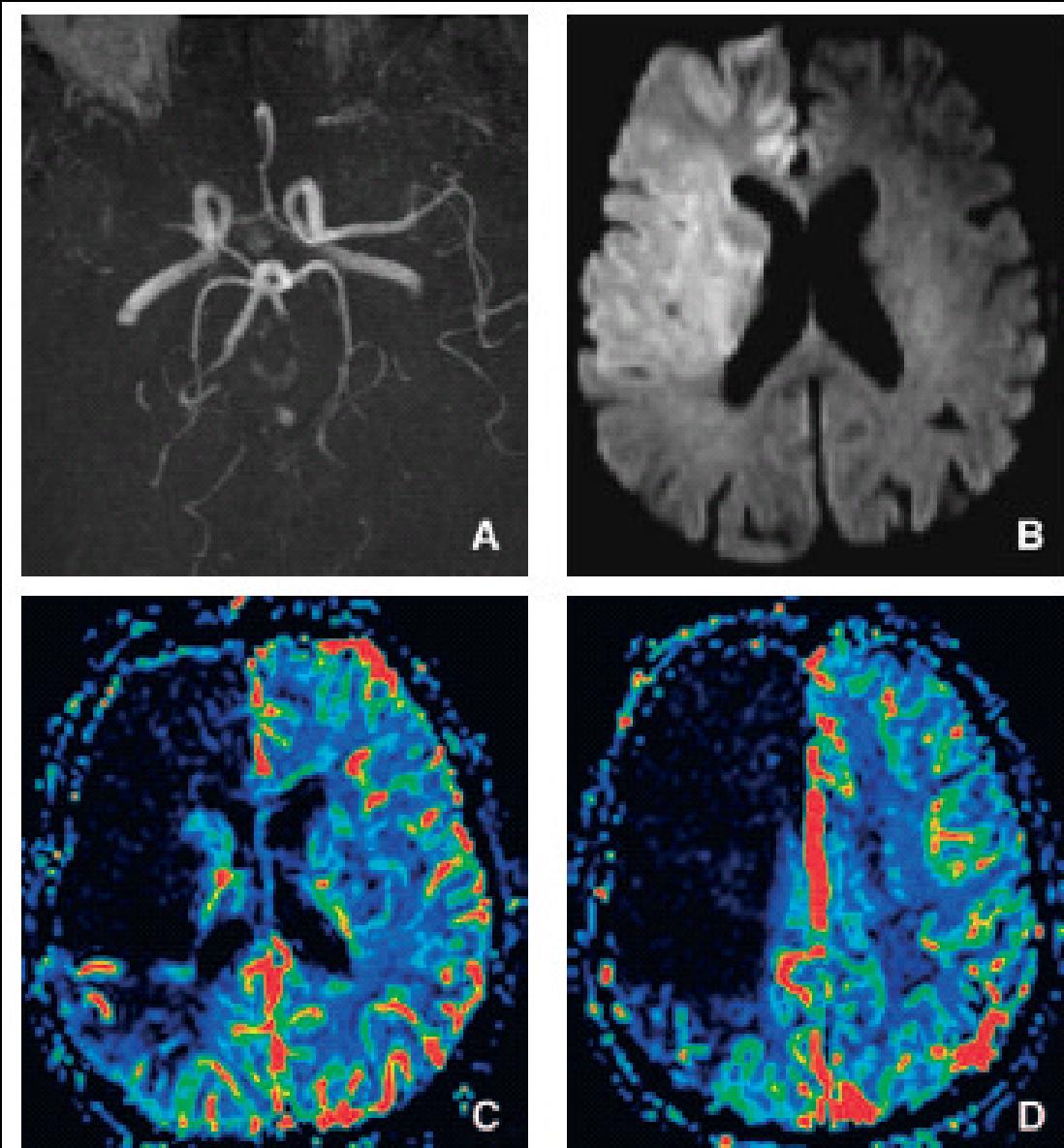


# Predictors of intracranial hemorrhage

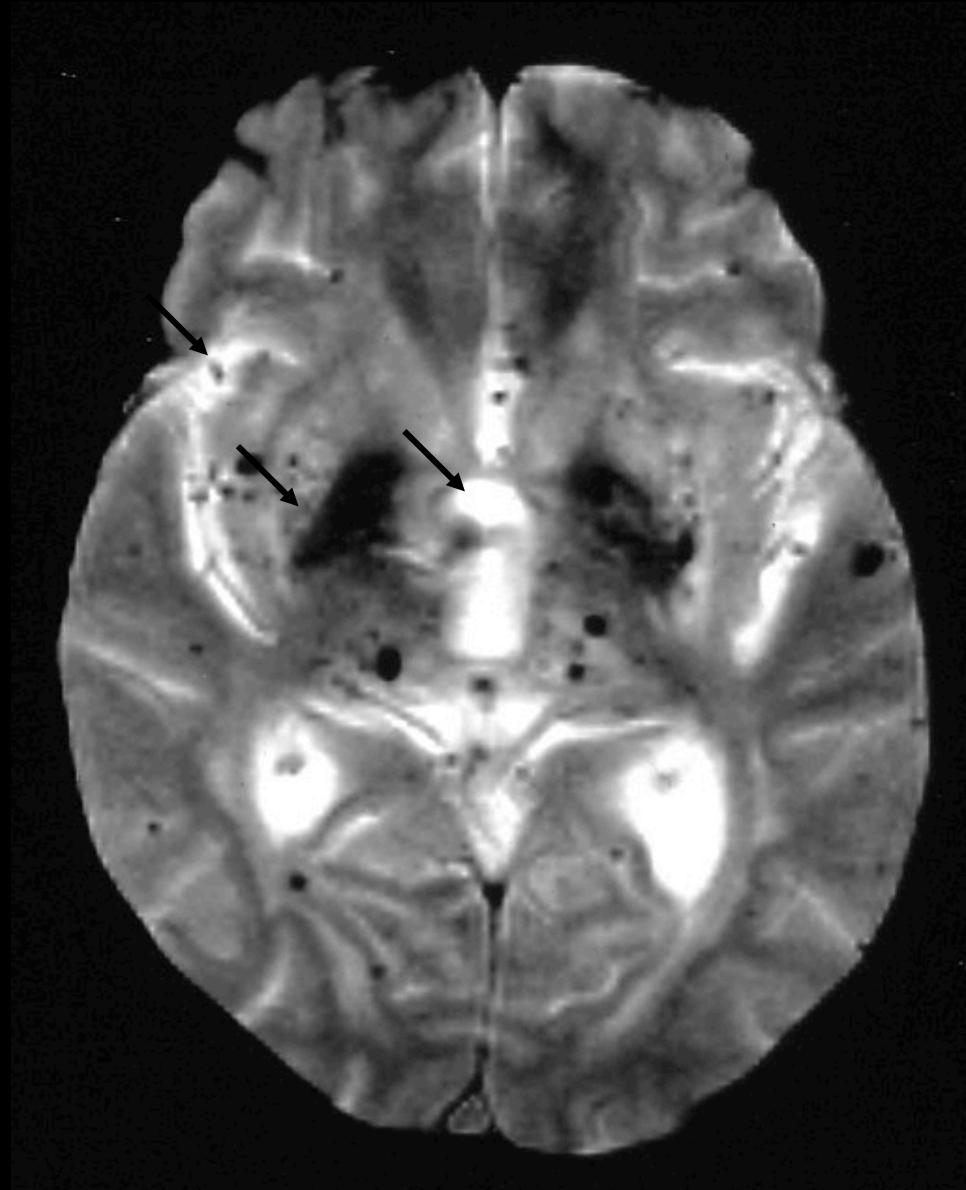
- Large lesions on baseline diffusion MRI
- Extensive areas of very low CBV

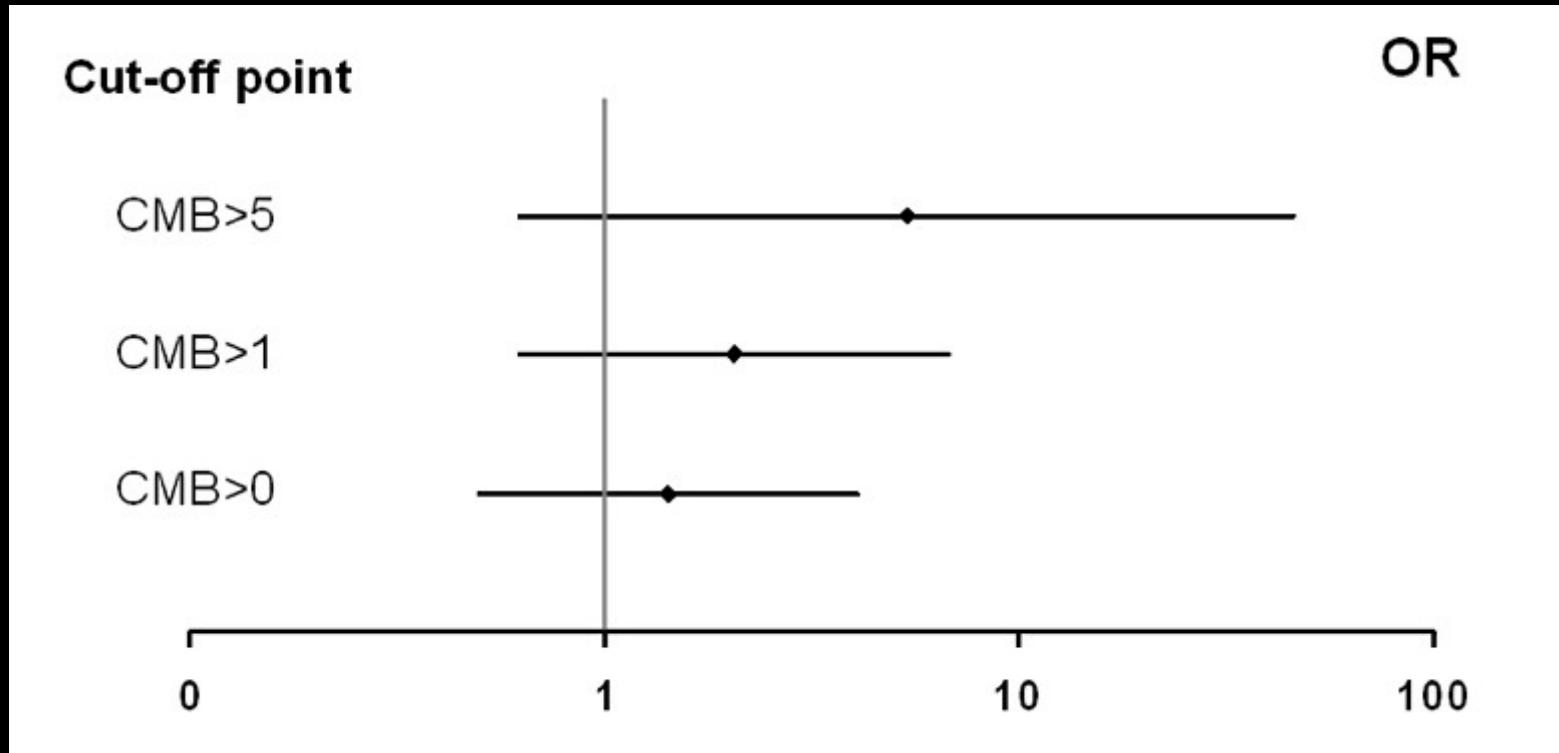


H2. MRI may predict malignant infarct  
Large area on DWI (B) with acute MCA occlusion  
With low CBF c and decreased CBV d



## Foyers de microsaignements





Microbleeds et risque d'hémorragie symptomatique après t-PA  
535 Patients IRM avant et après Thrombolyse  
Absence d'augmentation significative du risque même chez les patients avec 5 Mbs ( $P = 0.13$ ).

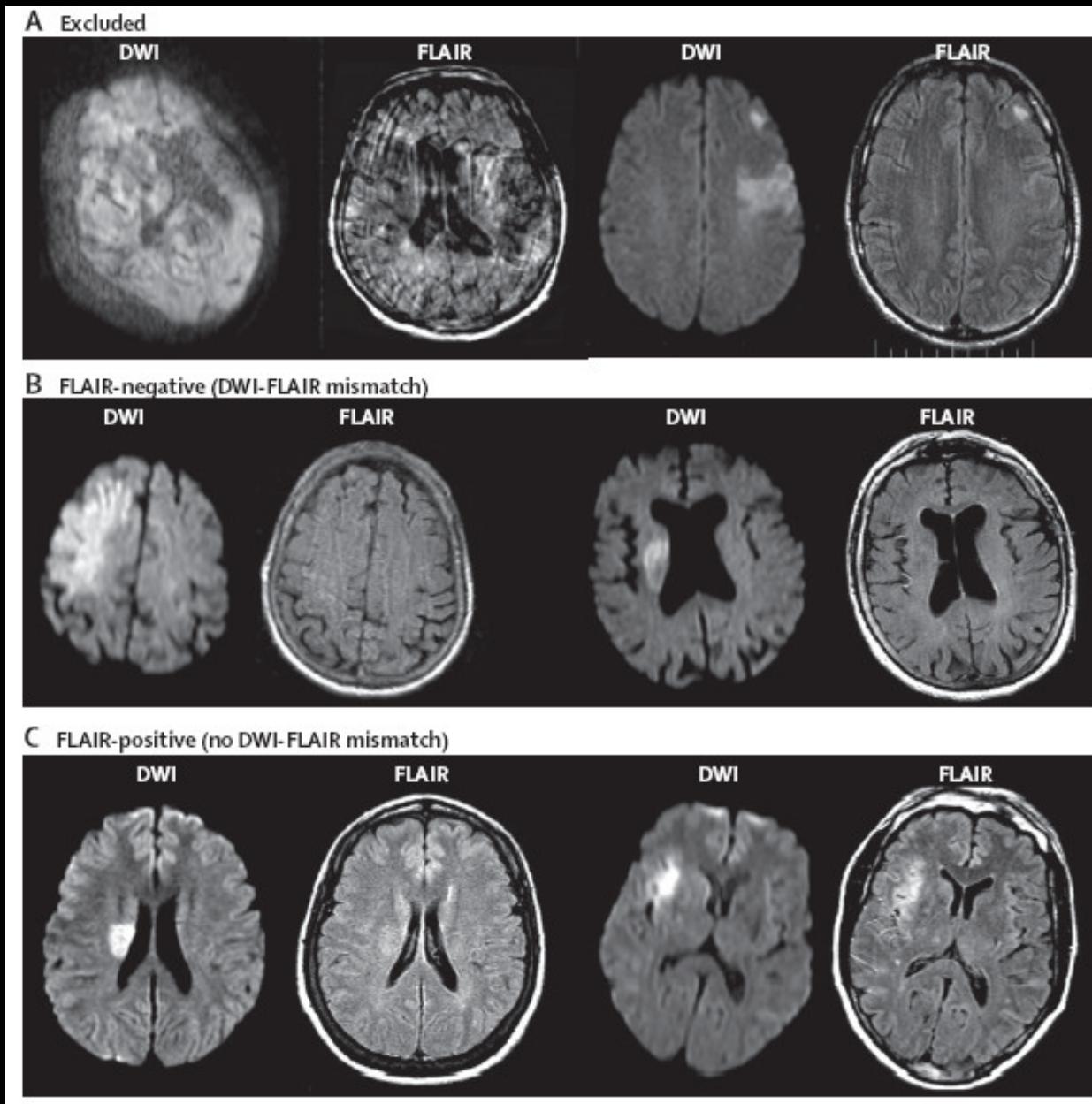
Brasil Study. MRI Collaborative Group, J Fiehler STROKE 2007

# Horaire imprécis: « AVC du réveil »

## Utilité du FLAIR ?

- < 3h: T2/FLAIR normaux (?) : thrombolyse ?
- > 6h: hypersignal FLAIR/T2: contre-indication potentielle à la thrombolyse ?

Gotz T et al Lancet Neurol. 2011 Nov;10(11):978-86



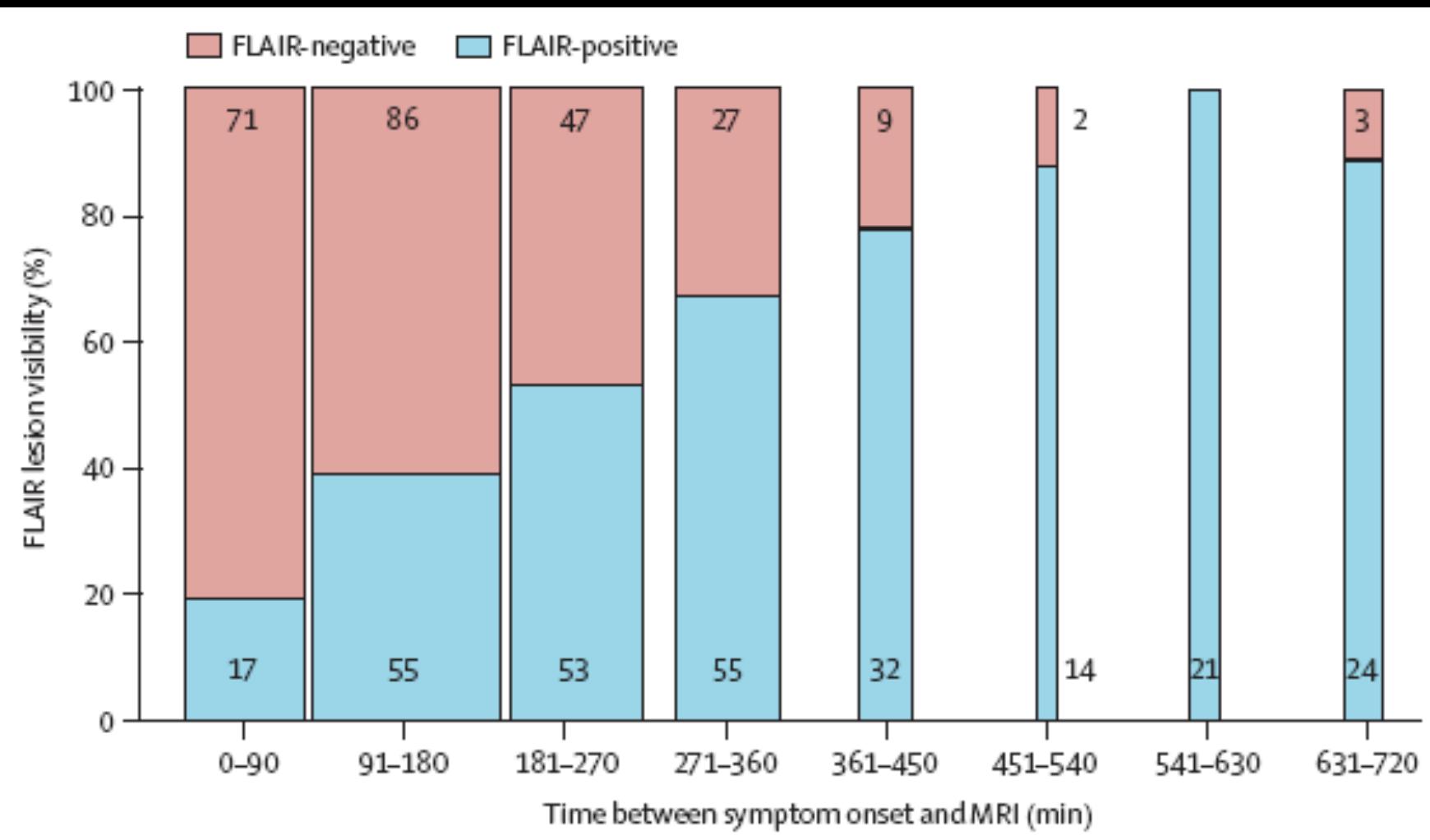
## Mismatch Diffusion/Flair (identification AVC < 4h30):

- Spécificité élevée Sensibilité faible

	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
<b>Identification of patients within 4·5 h of symptom onset</b>				
DWI-positive (n=516)	62% (57–67)	78% (72–84)	83% (79–88)	54% (48–60)
MCA (n=469)	63% (57–68)	79% (37–86)	85% (80–90)	53% (47–60)
MCA+NIHSS >3 (n=408)	64% (58–70)	81% (74–87)	87% (81–91)	53% (46–60)
MCA+DWI lesion >5 mL (n=280)	58% (51–66)	84% (75–90)	86% (78–91)	55% (47–63)
<b>Identification of patients within 6 h of symptom onset</b>				
DWI-positive (n=516)	56% (51–61)	87% (80–93)	93% (91–97)	34% (28–39)
MCA (n=469)	56% (51–61)	87% (80–94)	95% (92–98)	33% (27–39)
MCA+NIHSS >3 (n=408)	57% (52–62)	88% (78–94)	95% (92–98)	32% (25–39)
MCA+DWI lesion >5 mL (n=280)	52% (45–59)	92% (82–97)	96% (90–99)	34% (27–42)
DWI=diffusion-weighted imaging. PPV=positive predictive value. NPV=negative predictive value. MCA=middle cerebral artery. NIHSS=National Institutes of Health Stroke Scale.				

- Taille de la lésion

Gotz T et al Lancet Neurol. 2011 Nov;10(11):978-86



# Scanner

# Signes précoces d'ischémie

- Signes artériels: vaisseau dense
  - Sylvienne dense
  - Insulaire
  - Tronc basilaire...
- Signes parenchymateux
  - Effacement du noyau lenticulaire, du noyau caudé
  - Effacement du ruban insulaire
  - Indistinction gris/blanc
  - Discret effet de masse





Hémiplégie droite et aphasicie  
2H10 après le début des symptômes

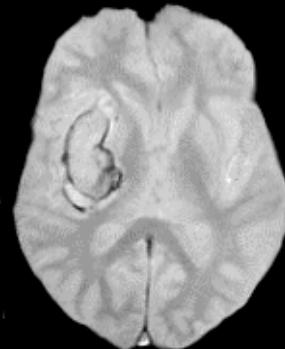
## Scanner:

- Disponible et rapide
- Sans et avec iodé (angiographie & perfusion)
- ↘ CBF, CBV et ↗ MTT # nécrose
- ↘ CBF et CBV normal # pénombre

# MRI Stroke Imaging

GRE

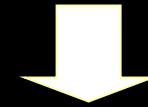
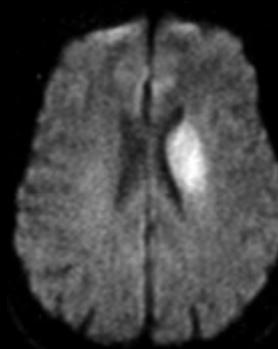
Hemorrhage



Hemorrhage

DWI

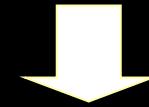
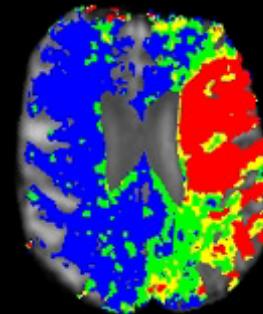
Ischemic  
Injury



Infarct Core

PWI

Perfusion  
Status



Mismatch

MRA

Vessel  
Status

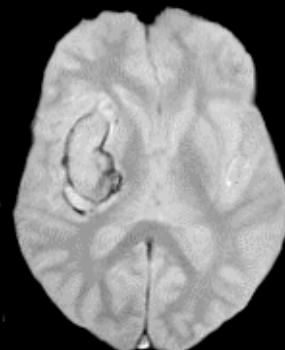


Large Vessel  
Occlusions

# CT Stroke Imaging

GRE

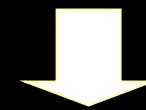
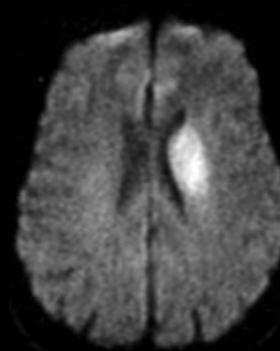
Hemorrhage



Hemorrhage

DWI

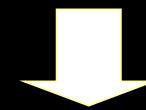
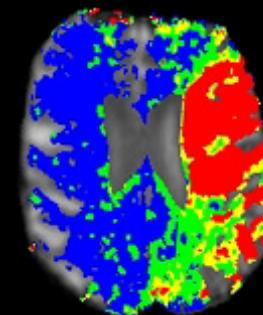
Ischemic  
Injury



Infarct Core

PWI

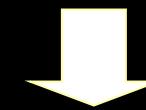
Perfusion  
Status



Mismatch

MRA

Vessel  
Status



Large Vessel  
Occlusions

# CT Stroke Imaging

GRE

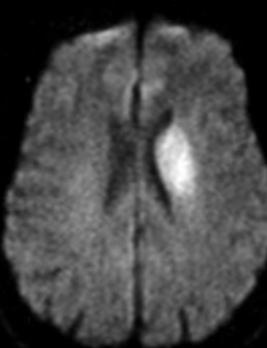
Hemorrhage



Hemorrhage

DWI

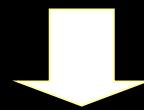
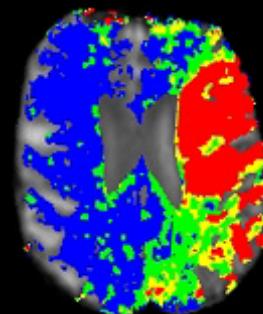
Ischemic Injury



Infarct Core

PWI

Perfusion Status



Mismatch

CTA

Vessel Status



Large Vessel Occlusions

# CT Stroke Imaging

NCT

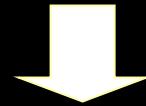
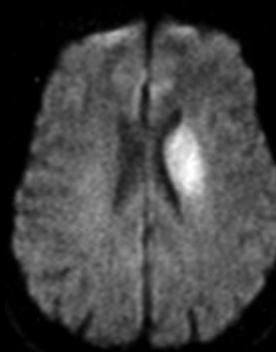
Hemorrhage



Hemorrhage

DWI

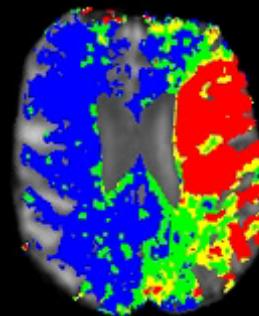
Ischemic  
Injury



Infarct Core

PWI

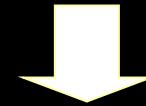
Perfusion  
Status



Mismatch

CTA

Vessel  
Status



Large Vessel  
Occlusions

# CT Stroke Imaging

NCT

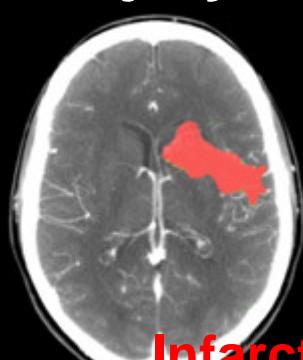
Hemorrhage



Hemorrhage

PCT

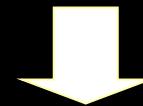
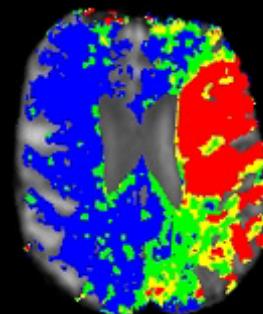
Ischemic Injury



Infarct Core

PWI

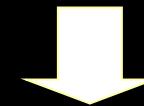
Perfusion Status



Mismatch

CTA

Vessel Status



Large Vessel Occlusions

# CT Stroke Imaging

NCT

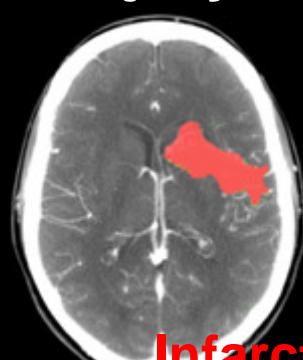
Hemorrhage



Hemorrhage

PCT

Ischemic Injury



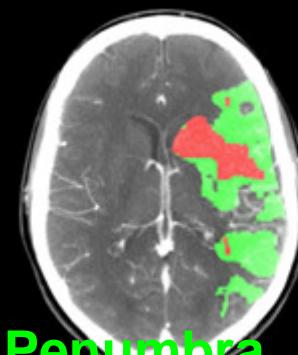
Infarct



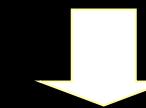
Infarct Core

PCT

Perfusion Status



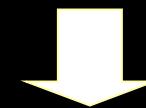
Penumbra



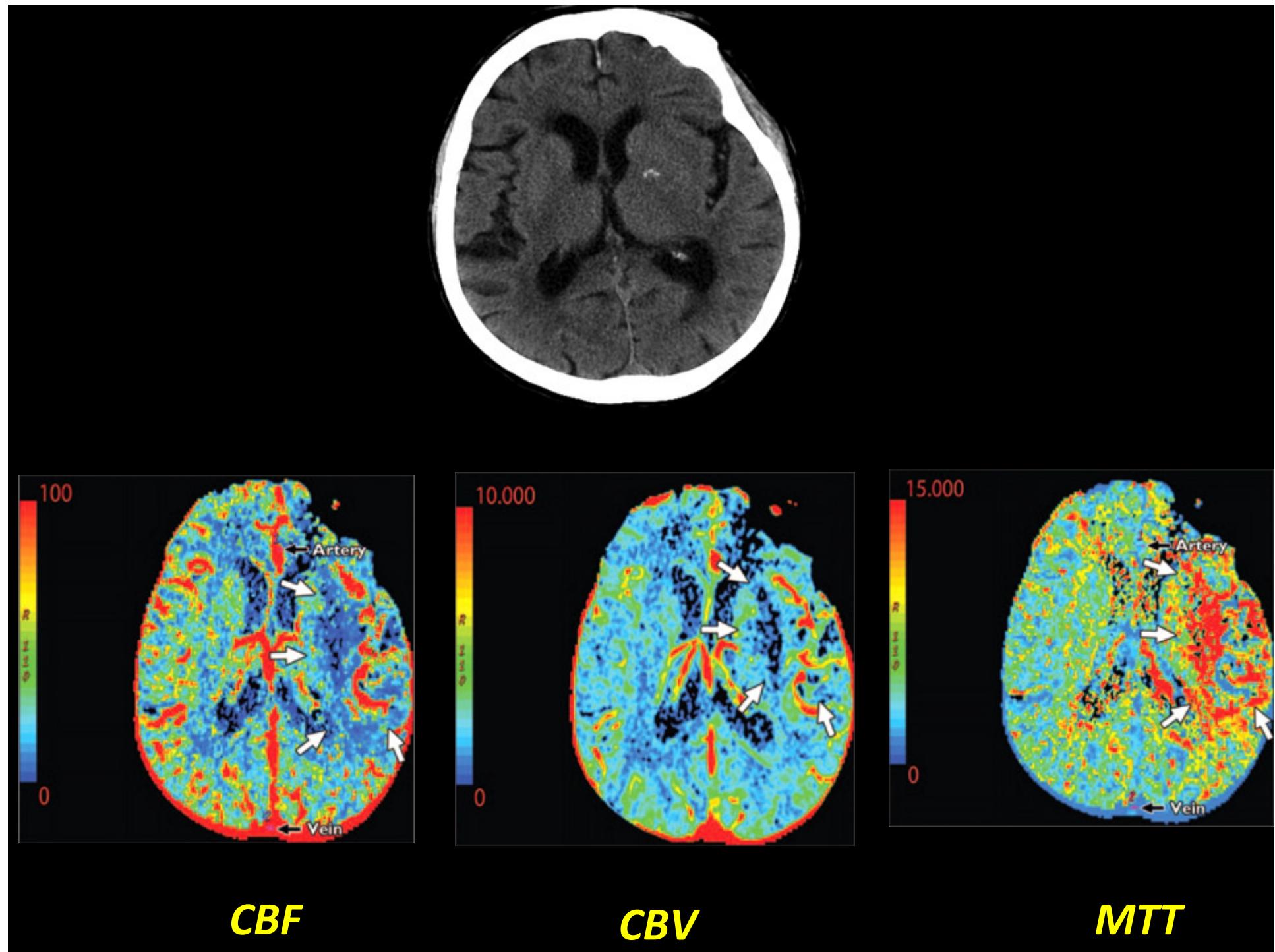
Mismatch

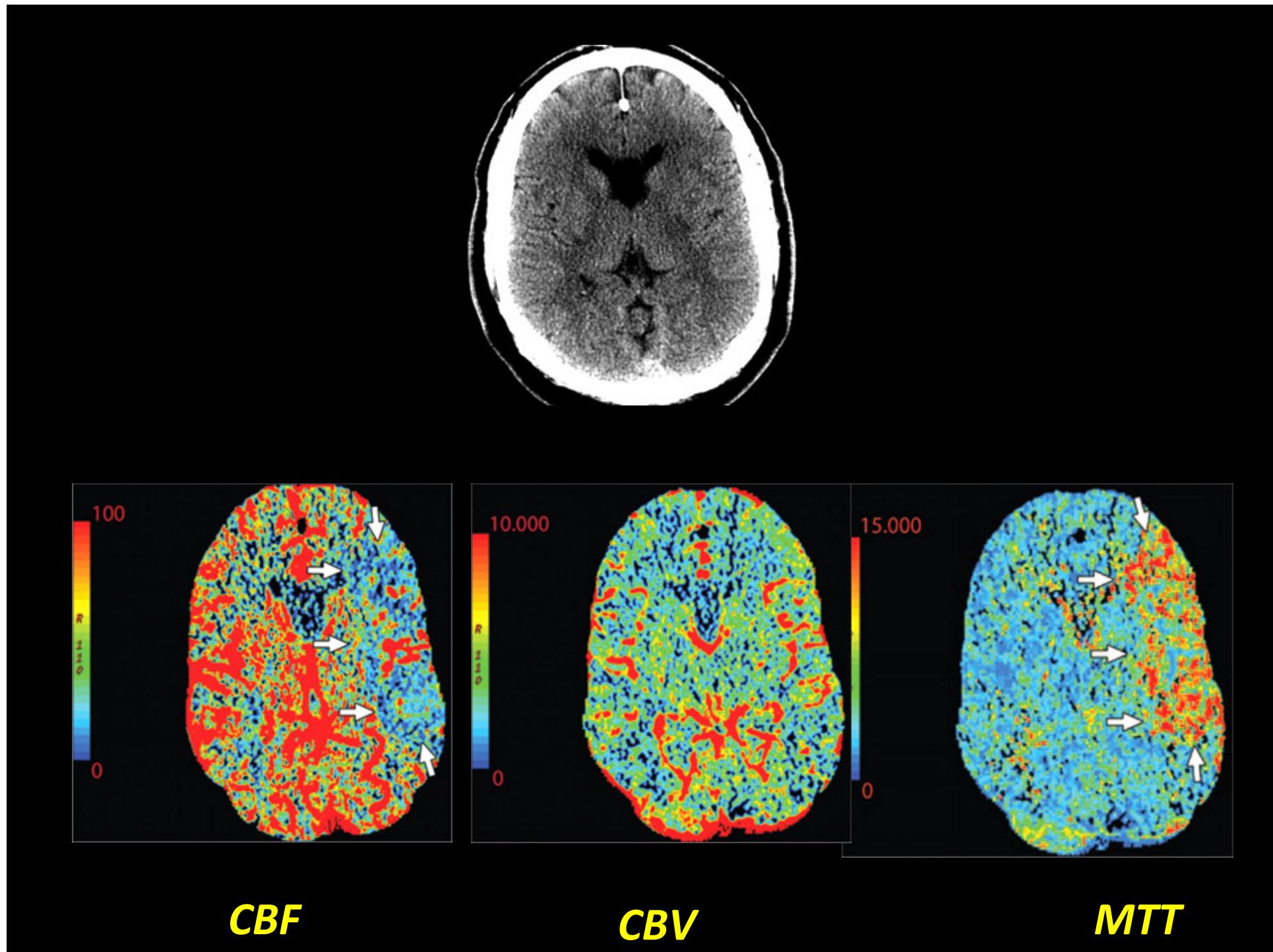
CTA

Vessel Status

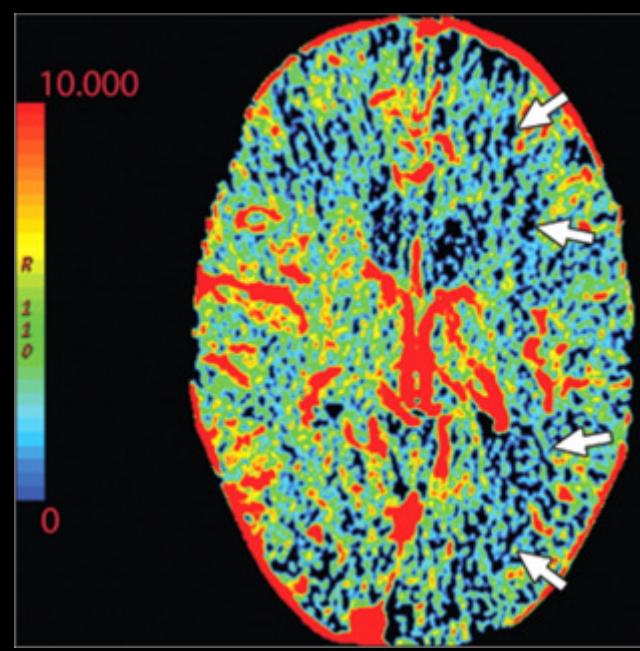
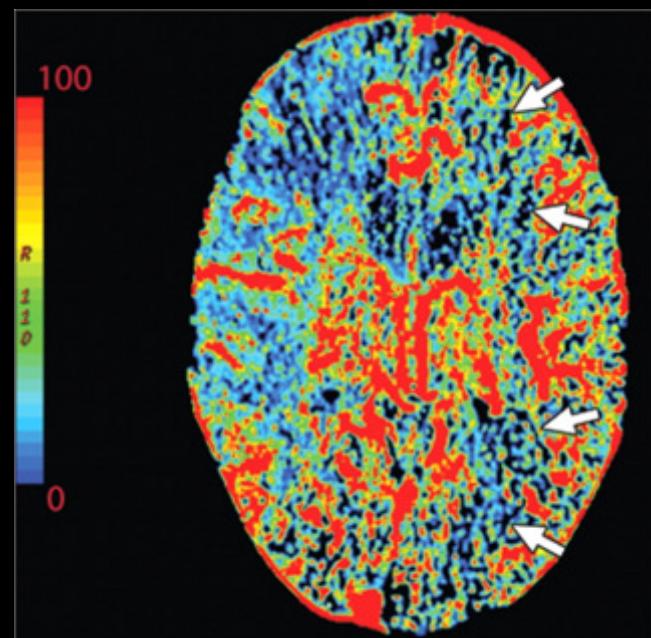


Large Vessel Occlusions

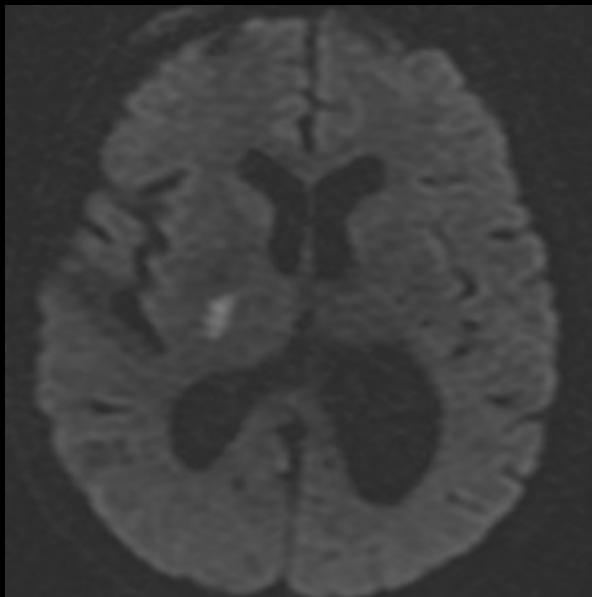
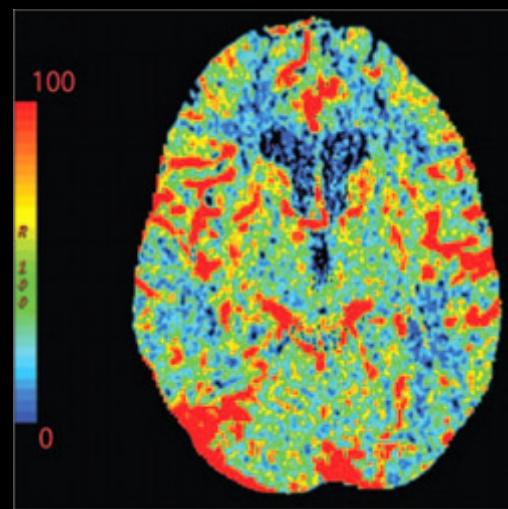




## *Leucoarrose*



*Petites lésions*

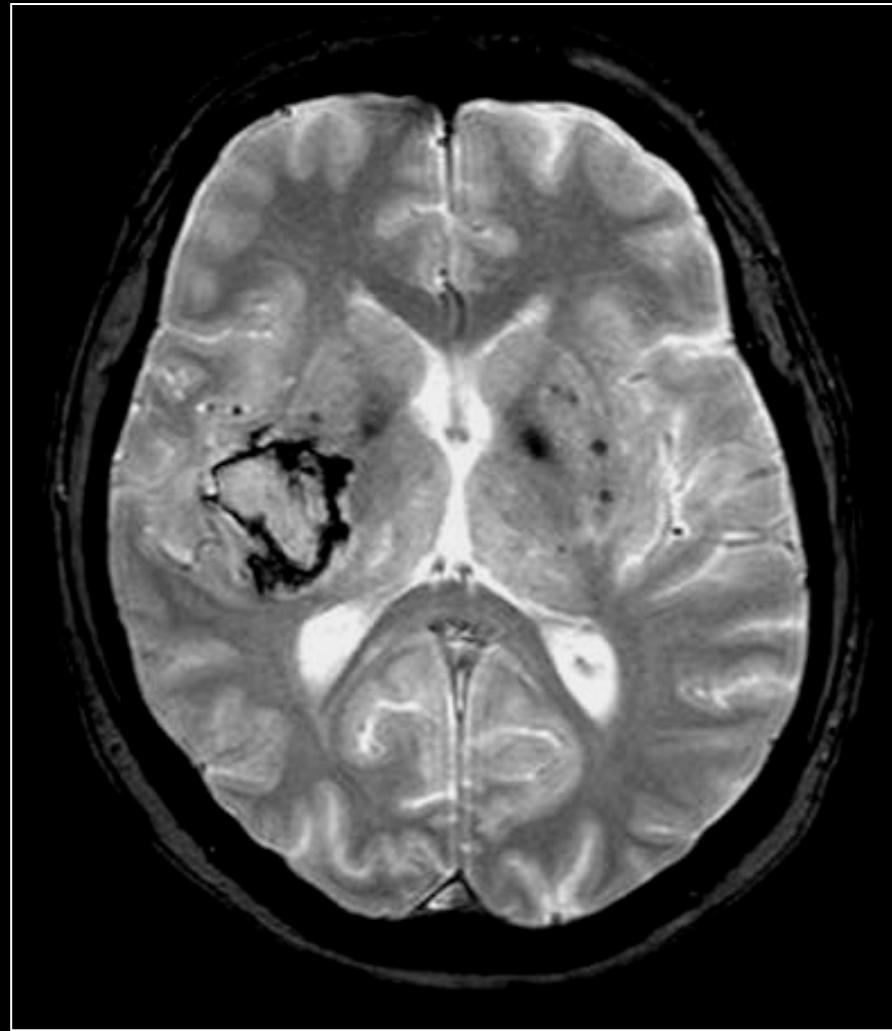


## Détection du sang: T2\*

- Distinction ischémie/hématome:  
IRM au moins équivalente au scanner

Fiebach JB et al. Stroke 2004; 35: 502-6

Kidwell CS et al. JAMA 2004; 292: 1883-5



## ***En pratique***

### Patient agité, vomissement...: TDM

#### tableau clinique “simple”

Déficit neurologique **stable, modéré à sévère** (e.g. NIHSS>5),  
avec un **horaire de début clair <4h30**.

**DWI**

**T2\***

**3D TOF crâne “rapide”**

#### tableau clinique “ambigu”

Déficit neurologique *instable* (e.g. fluctuations neurologiques),  
symptômes “mineurs” (e.g. symptôme isolé sensitif, visuel ou aphasique),  
*horaire de début douteux ou >4h30*, ou tout autre situation clinique faisant douter  
du diagnostic d’ischémie cérébrale aiguë

**DWI**

**T2\***

**+/- FLAIR (si horaire incertain)**

**3D TOF “standard”**

**PWI**

**+/- ARM TSA Gd selon contexte clinique (e.g. confirmation d’une occlusion du tronc basilaire)**

**La majorité des patients avec une occlusion proximale ont un déficit neurologique faible à modéré**

