SALA POLISSENA B

EMERGENZE NEUROLOGICHE

Moderatori: **Rosa Intermite– Vincenzo Natale**

Maurizio Paciaroni

La prima ora del sospetto ictus

XII congresso nazionale
simeu
RICCIONE 13-15 MAGGIO 2022

La prima ora del sospetto ictus

Maurizio Paciaroni

Stroke Unit – Internal and Cardiovascular Medicine

Azienda Ospedaliero-Universitaria of Perugia - Italy

XII congresso nazionale

simeu

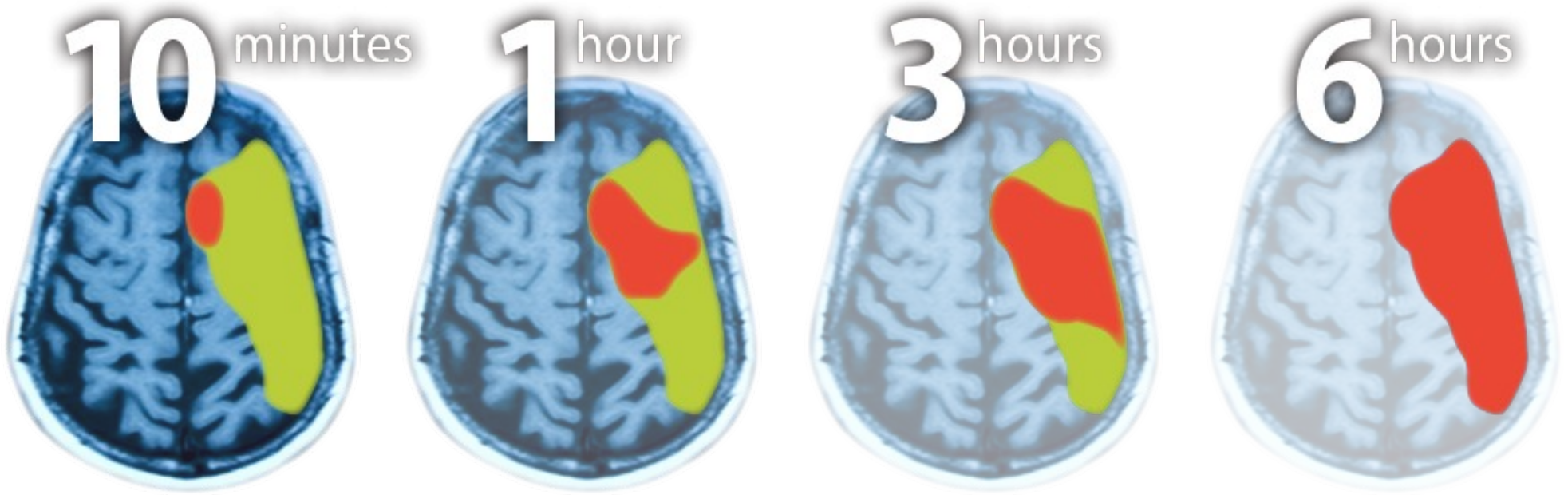
RICCIONE 13-15 MAGGIO 2022

DISCLOSURES

Maurizio Paciaroni has served in the last 5 years on the speakers' bureaus of:

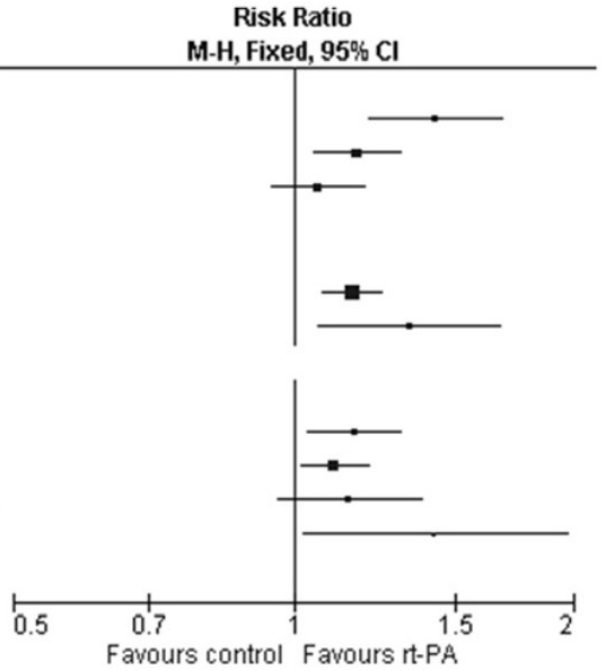
- Aspen
- Bayer
- Boehringer Ingelheim
- Bristol-Myers Squibb
- Daiichi Sankyo
- Medtronic
- Pfizer
- Sanofi Aventis

Reperfusion therapy



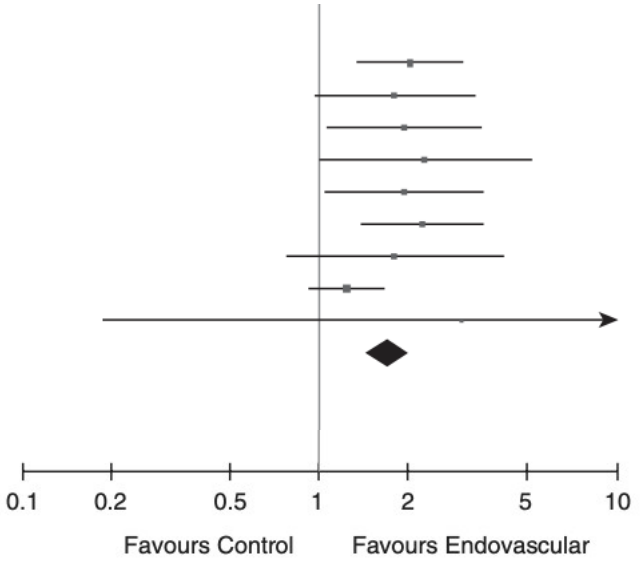
rtPA (<4.5 h) vs. control mRS 0-1 at 3-6 months
0.9 mg/Kg (10% bolus → 90% in 1 h)

Study or Subgroup	rt-PA Events	rt-PA Total	Control Events	Control Total	Risk Ratio M-H, Fixed, 95% CI
Treatment time					
1-3.0 h	259	787	176	762	1.42 [1.21, 1.68]
3.01 - 4.5 h	485	1375	432	1437	1.17 [1.05, 1.31]
More than 4.5 h	401	1229	357	1166	1.07 [0.95, 1.20]
Heterogeneity: $Chi^2 = 7.98$, df = 2 (P = 0.02); $I^2 = 75\%$					
Age					
18-80	990	2512	853	2515	1.16 [1.08, 1.25]
81 and over	155	879	112	850	1.34 [1.07, 1.67]
Heterogeneity: $Chi^2 = 1.39$, df = 1 (P = 0.24); $I^2 = 28\%$					
0-4	237	345	189	321	1.17 [1.04, 1.31]
5-10	611	1281	538	1252	1.11 [1.02, 1.21]
11-15	198	794	175	808	1.15 [0.96, 1.38]
16-21	77	662	55	671	1.42 [1.02, 1.97]
Heterogeneity: $Chi^2 = 7.15$, df = 4 (P = 0.13); $I^2 = 44\%$					



Thrombectomy (<6 h) vs. control mRS 0-1 at 3 months

1.1.4 Highly effective mechanical thrombectomy (HiEf-MT) versus control, early window inclusive						
ESCAPE	58	165	26	150	9.8%	2.03 [1.35, 3.04]
EXTEND-IA	18	35	10	35	5.9%	1.80 [0.97, 3.33]
MR CLEAN	27	233	16	267	6.2%	1.93 [1.07, 3.50]
PISTE	14	33	6	32	3.8%	2.26 [0.99, 5.16]
REVASCAT	25	103	13	103	6.0%	1.92 [1.04, 3.55]
SWIFT PRIME	42	98	18	93	8.3%	2.21 [1.38, 3.56]
THERAPY	13	55	7	53	3.7%	1.79 [0.77, 4.14]
THRACE	70	200	57	202	13.0%	1.24 [0.93, 1.66]
THRILL	1	2	0	2	0.4%	3.00 [0.19, 47.96]
Subtotal (95% CI)		**924**		**937**	**57.2%**	**1.70 [1.43, 2.01]**
Total events	268		153			
Heterogeneity: $Tau^2 = 0.00$, $Chi^2 = 7.47$, $df = 8$ ($P = 0.49$); $I^2 = 0\%$						
Test for overall effect: $Z = 6.00$ ($P < 0.00001$)						

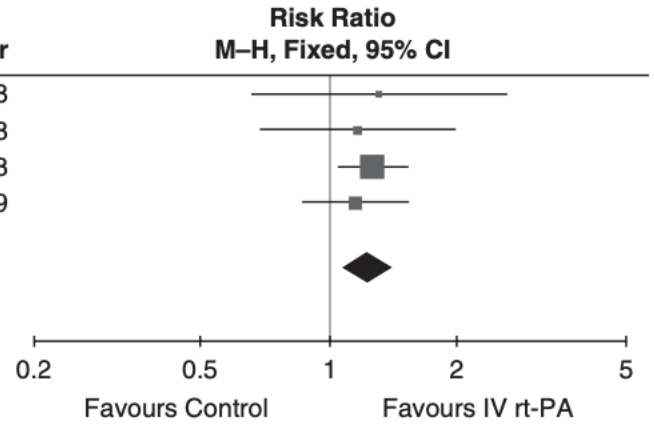


rtPA (4.5-9 h) vs. control mRS 0-1 at 3-6 months
0.9 mg/Kg (10% bolus → 90% in 1 h)

Study or Subgroup	IV rt-PA Events	Total	Control Events	Total	Weight	Risk Ratio M–H, Fixed, 95% CI	Year
EPITHET 4.5–6h 2008	13	33	9	30	5.3%	1.31 [0.66, 2.62]	2008
ECASS 4 2018	21	61	17	58	9.8%	1.17 [0.69, 1.99]	2018
WAKE-UP 2018	131	246	102	244	57.7%	1.27 [1.05, 1.54]	2018
EXTEND 2019	56	113	48	112	27.2%	1.16 [0.87, 1.54]	2019
Total (95% CI)		**453**		**444**	**100.0%**	**1.23 [1.06, 1.43]**	
Total events	221		176				

Heterogeneity: $Chi^2 = 0.38$, $df = 3$ ($P = 0.95$); $I^2 = 0\%$

Test for overall effect: $Z = 2.79$ ($P = 0.005$)

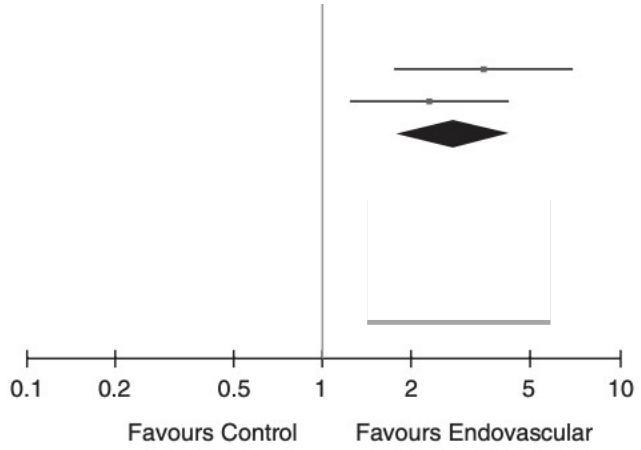


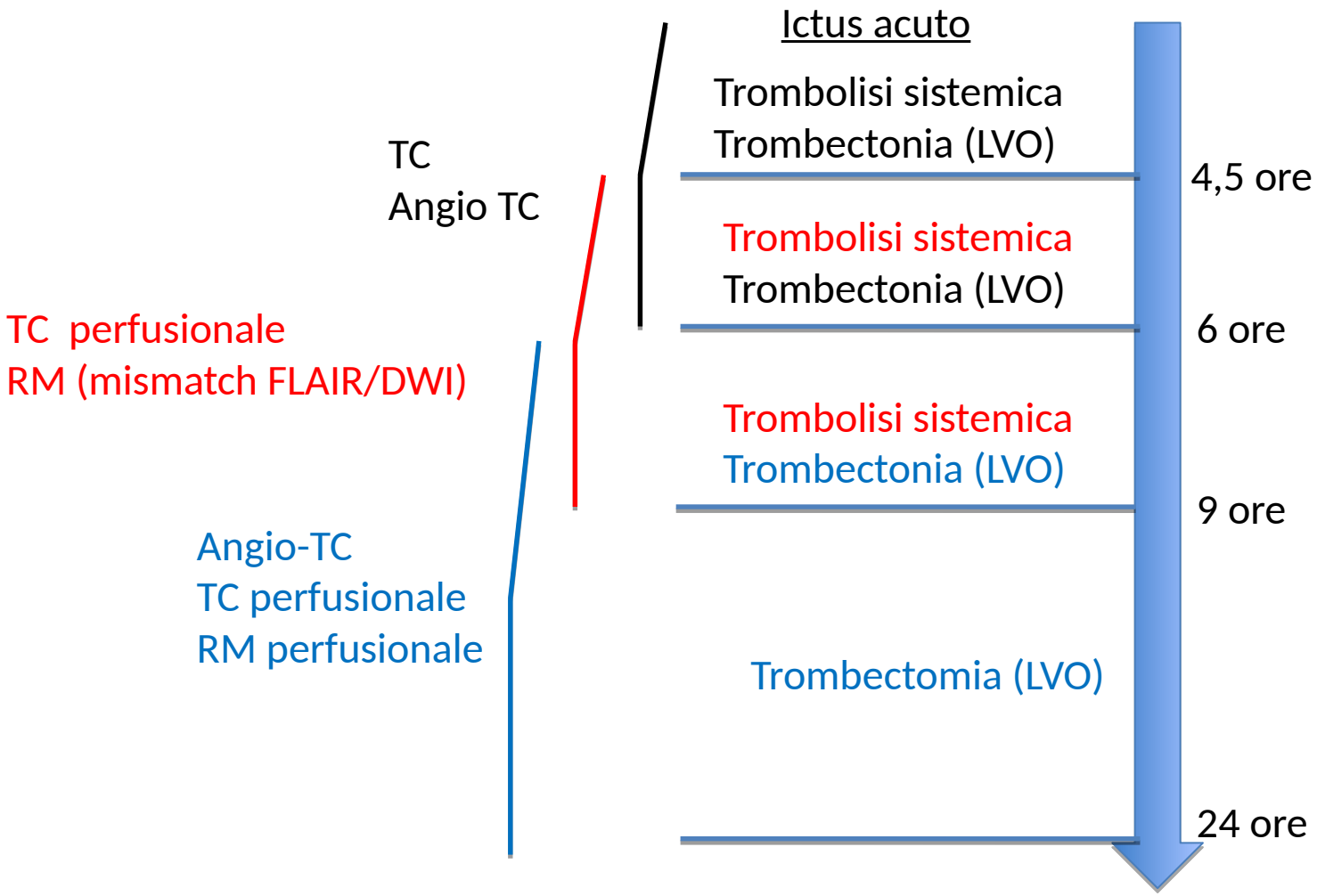
Thrombectomy (<24 h) vs. control mRS 0-1 at 3 months

1.1.5 Highly effective mechanical thrombectomy (HiEf-MT) versus control late window only						
DAWN	34	107	9	99	5.1%	3.50 [1.77, 6.91]
DEFUSE 3	28	92	12	90	6.0%	2.28 [1.24, 4.20]
Subtotal (95% CI)		**199**		**189**	**11.1%**	**2.76 [1.75, 4.35]**
Total events	62		21			

Heterogeneity: $Tau^2 = 0.00$, $Chi^2 = 0.83$, $df = 1$ ($P = 0.36$); $I^2 = 0\%$

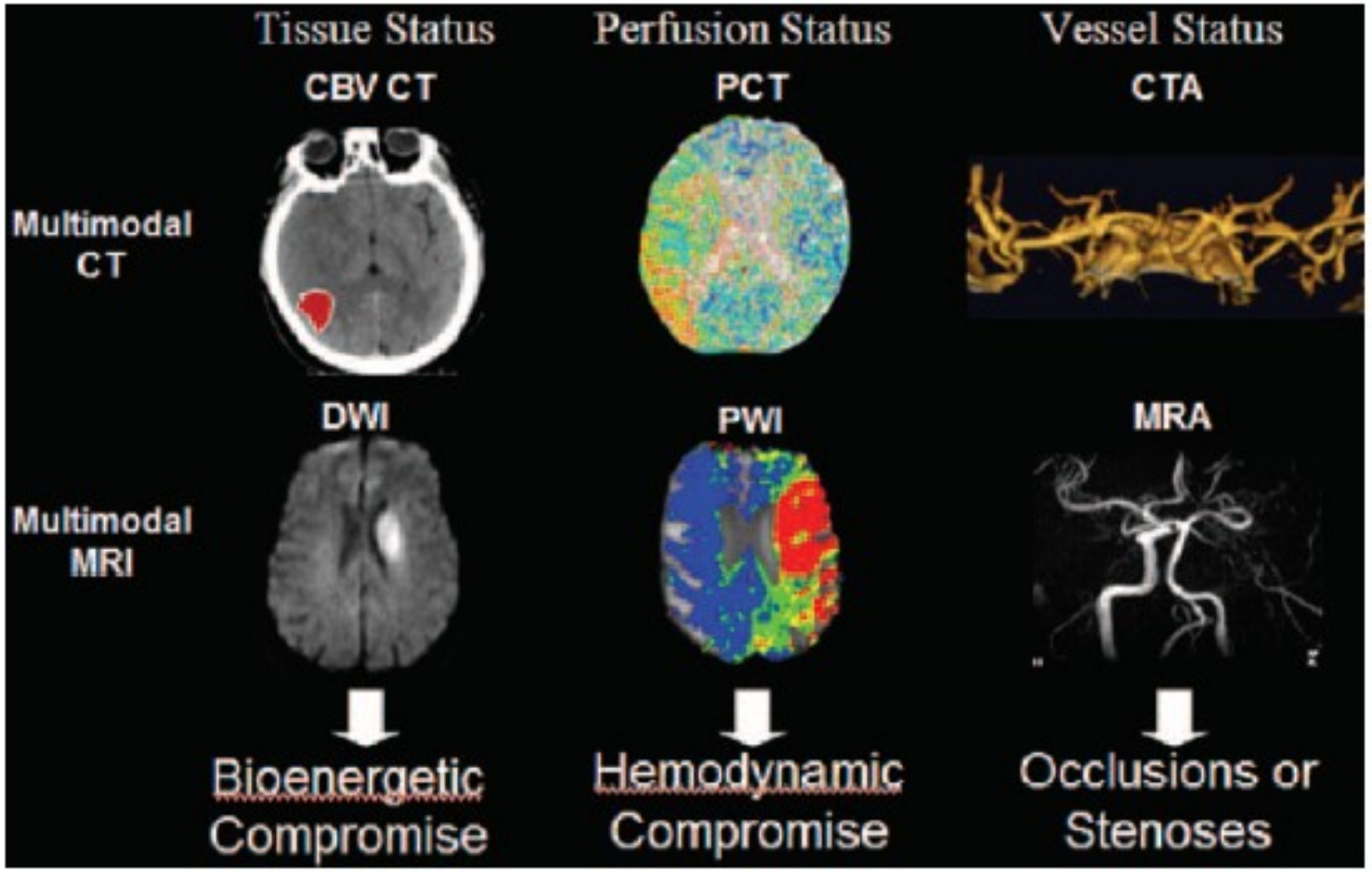
Test for overall effect: $Z = 4.37$ ($P < 0.0001$)



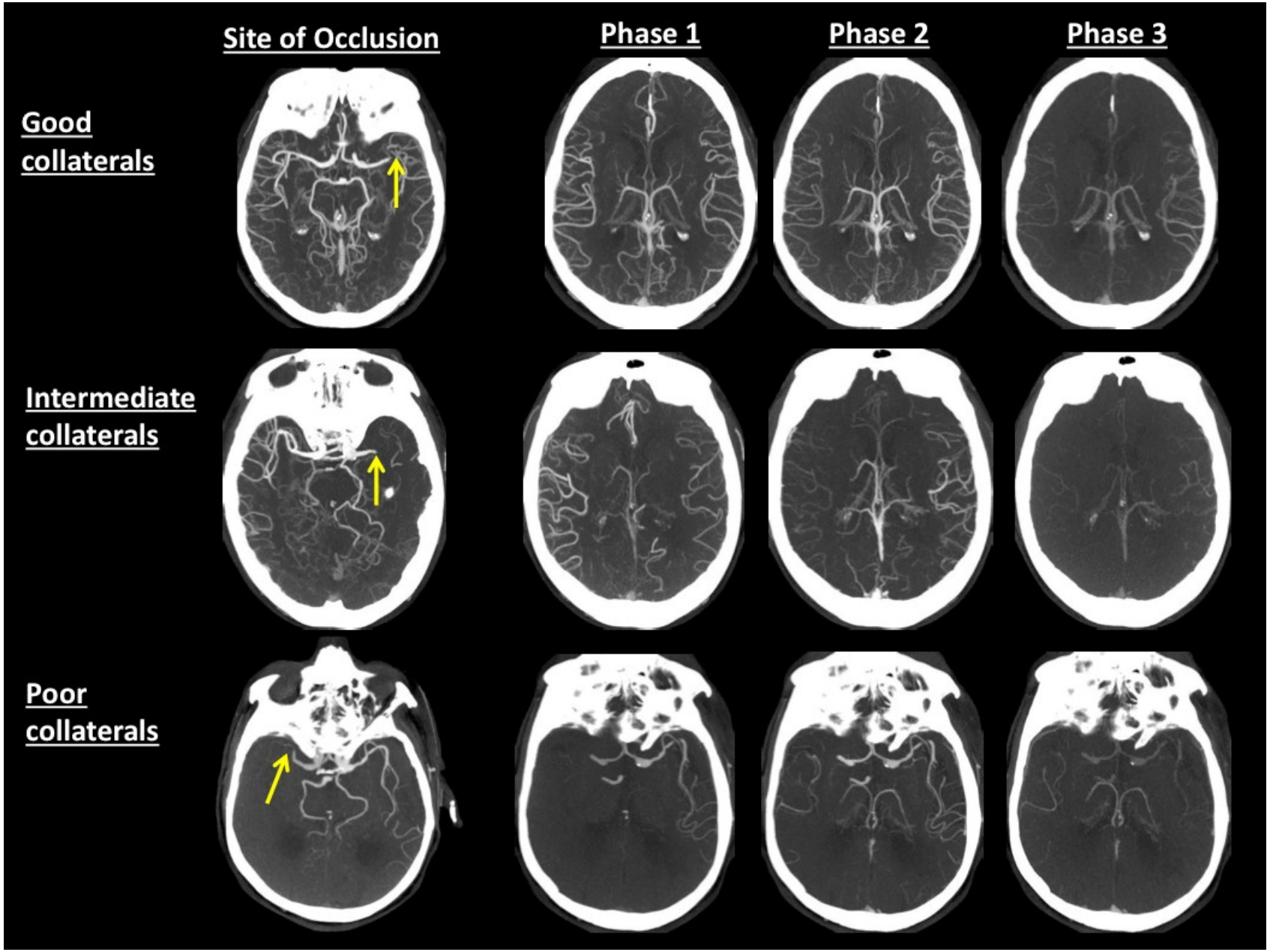

Ictus acuto
TC
Angio TC
Trombolisi sistemica
Trombectonia (LVO)
4,5 ore
TC perfusionale
RM (mismatch FLAIR/DWI)
Trombolisi sistemica
Trombectonia (LVO)
6 ore
Trombolisi sistemica
Trombectonia (LVO)
9 ore
Angio-TC
TC perfusionale
RM perfusionale
Trombectomia (LVO)
24 ore

		NINDS	EUSI
Arrival	→ Neurological diagnosis	15 min	15 min
Arrival	→ Start of brain imaging	25 min	30 min
Arrival	→ Diagnosis of brain imaging	45 min	45 min
Arrival	→ Thrombolysis	60 min	60 min

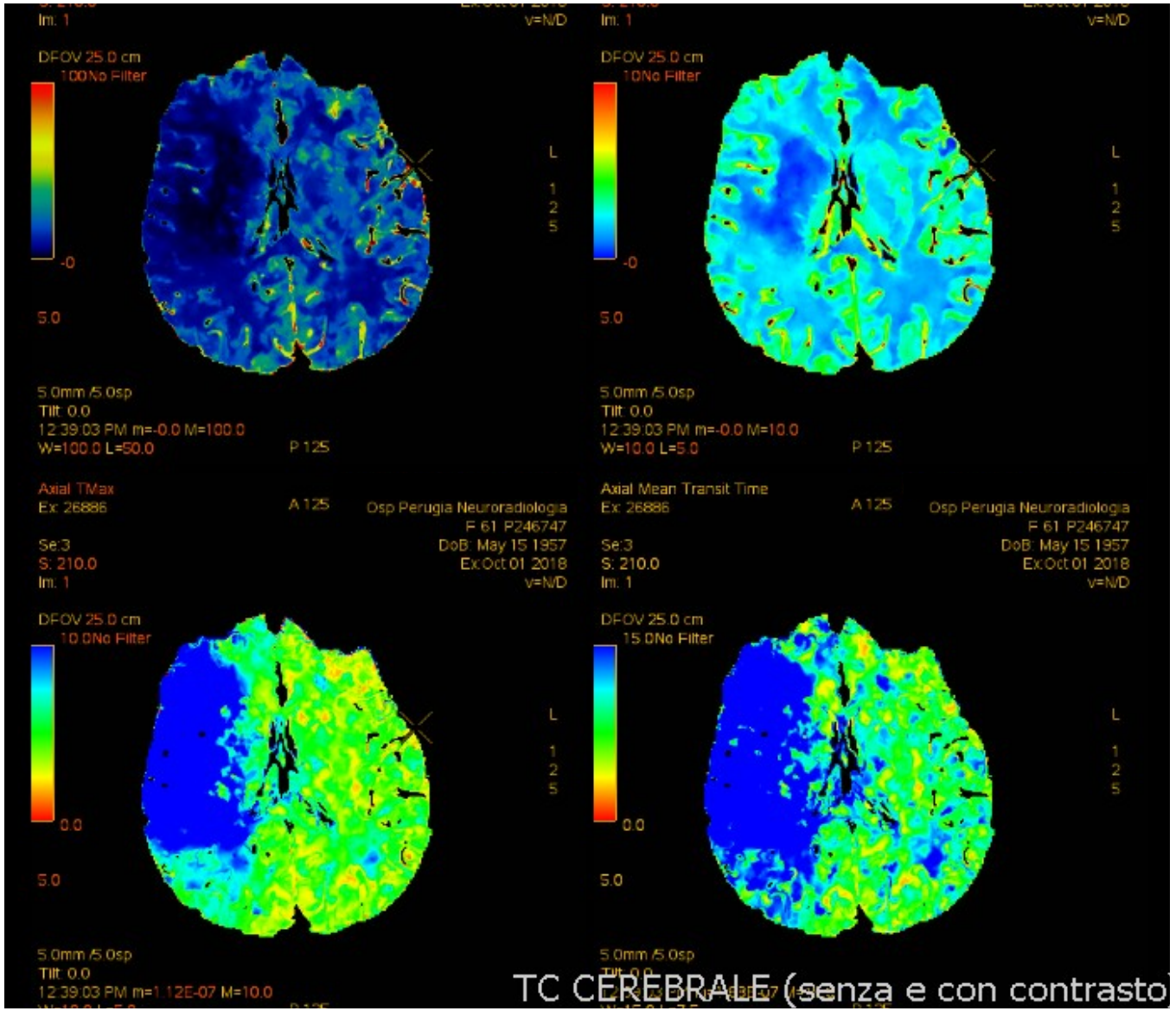
The ideal situation for a clinician:



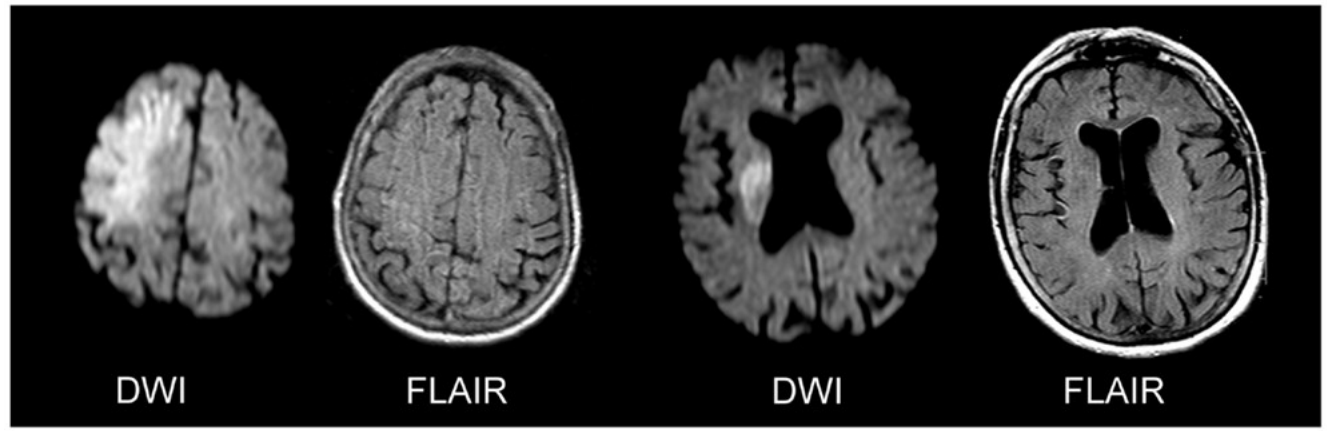
Angio-CT scan



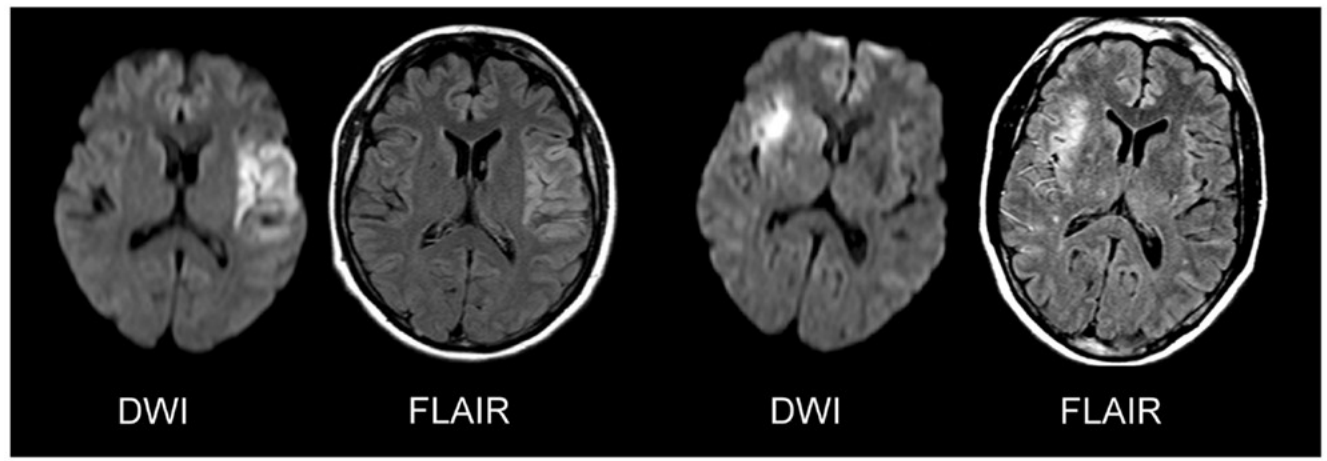
Perfusion CT scan



DWI-FLAIR-mismatch



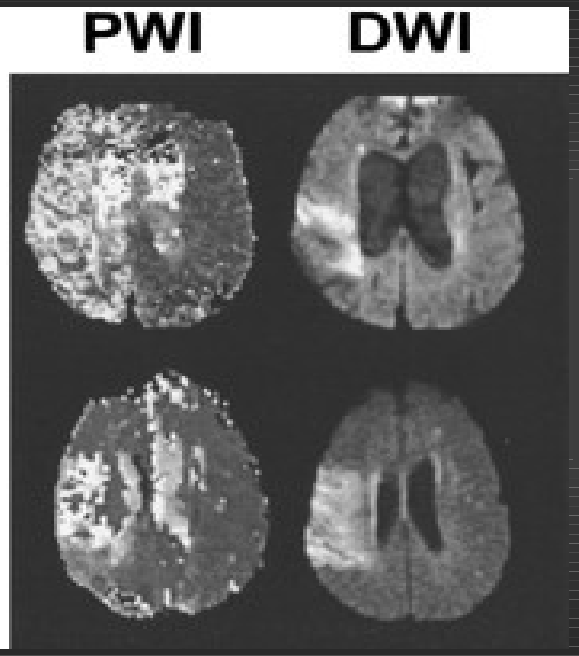
No DWI-FLAIR-mismatch

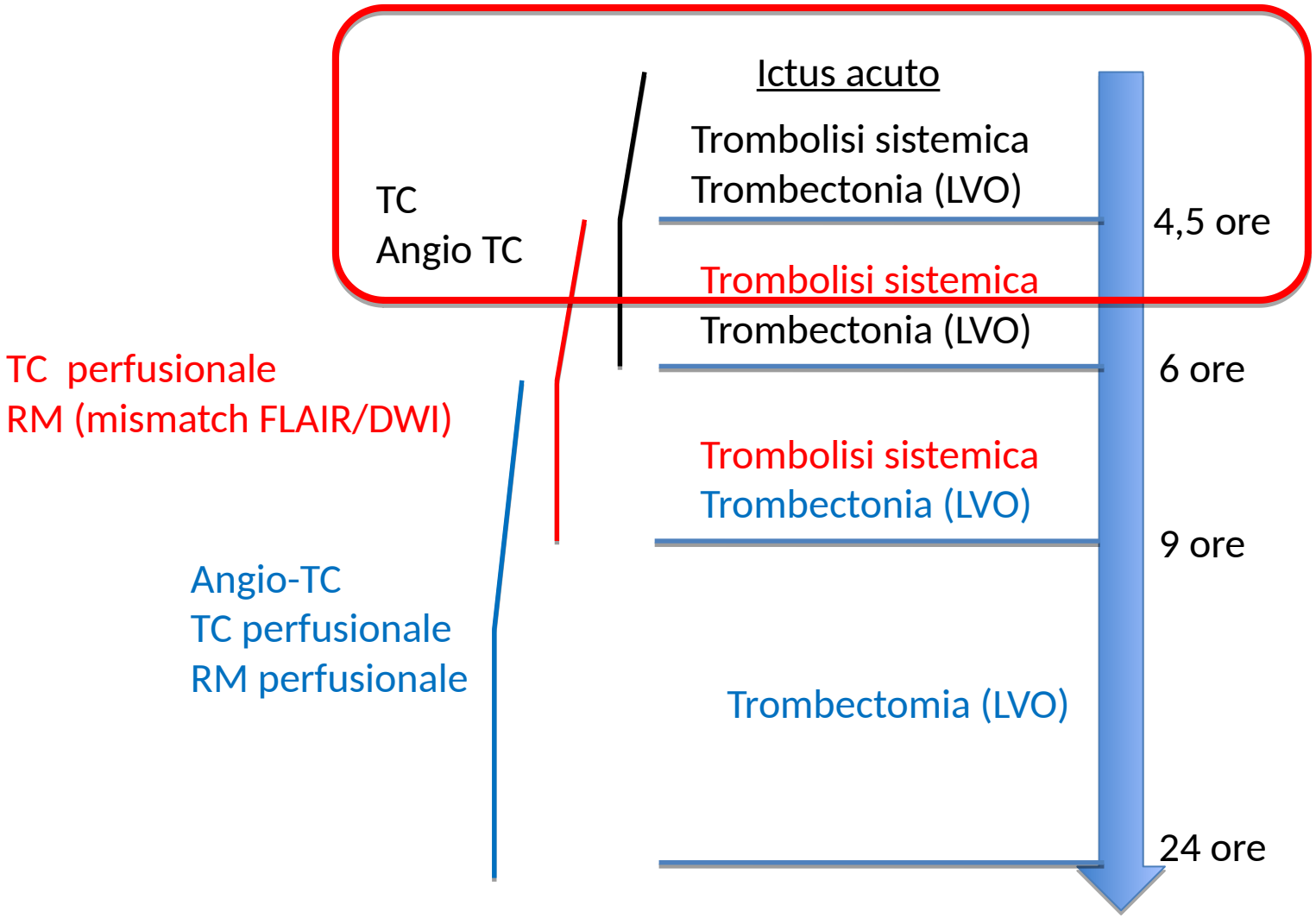


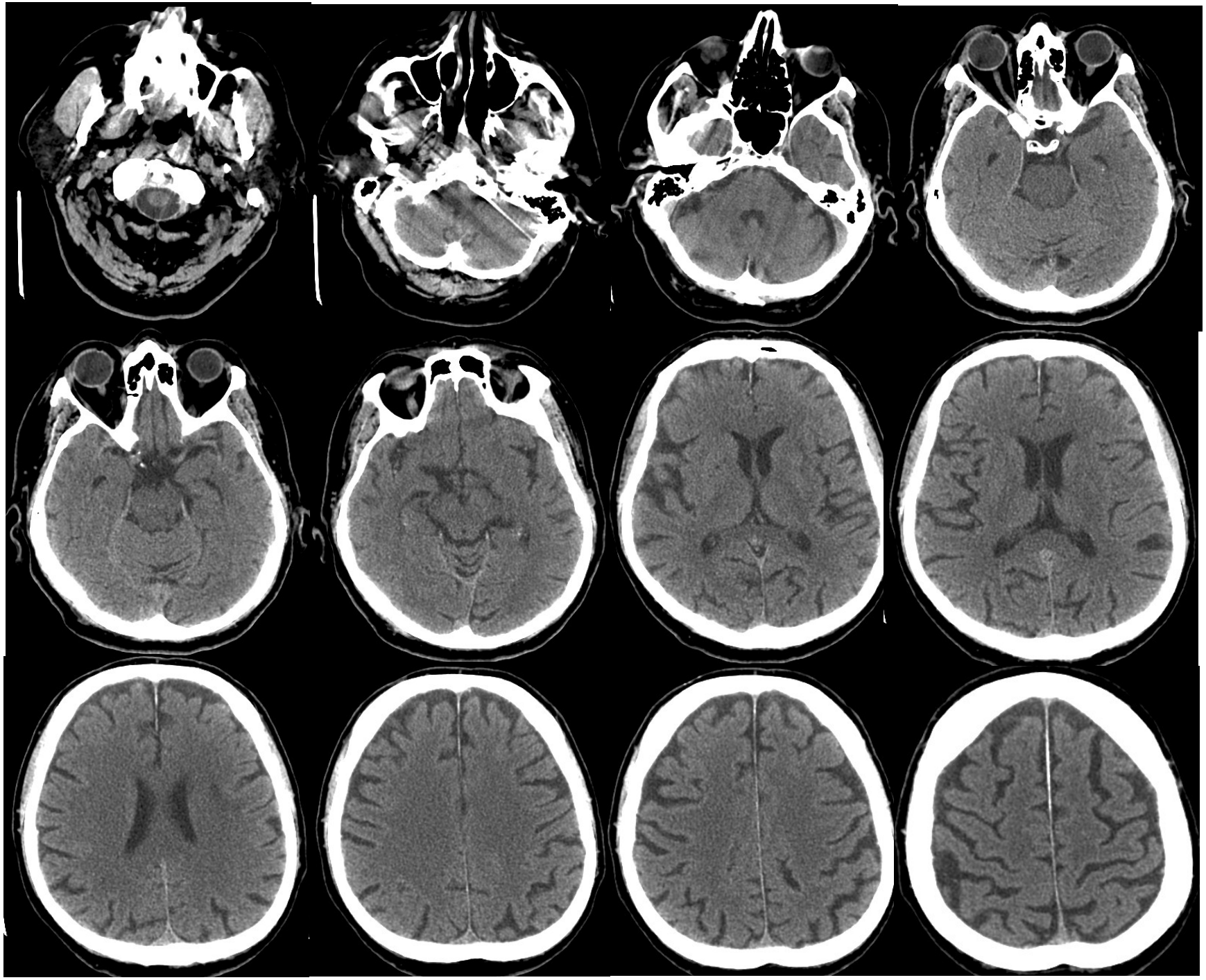
PWI-DWI mismatch

PWI lesion > DWI lesion

PWI lesion = DWI lesion




Ictus acuto
Trombolisi sistemica
Trombectonia (LVO)
4,5 ore
TC
Angio TC
Trombolisi sistemica
Trombectonia (LVO)
6 ore
TC perfusionale
RM (mismatch FLAIR/DWI)
Trombolisi sistemica
Trombectonia (LVO)
9 ore
Angio-TC
TC perfusionale
RM perfusionale
Trombectomia (LVO)
24 ore



Selezione del paziente

- Centro Spoke → centralizzare Centro Hub
- Effetti collaterali
- Costi
- Sovraccarico del sistema

Nella prima ora dall'evento

- Diagnosi
  - Clinica
  - Neuroimmagini

Neurological examination
and clinical syndromes

- Stroke ~ sudden onset of a focal neurological deficit in a recognizable intracranial vascular distribution resulting in a common clinical syndrome due to vascular occlusion or hemorrhage

Segni neurologici focali

- Sintomi motori:

  - debolezza di una metà del corpo in toto o in una sua parte (es. monoparesi)

  - difficoltà nella coordinazione dei movimenti di una metà del corpo in toto o in una sua parte

- Disturbi del linguaggio:

  - difficoltà nella comprensione e nell'espressione del linguaggio (afasia)

  - difficoltà nella lettura (alessia) e nella scrittura (agrafia)

  - difficoltà nel calcolo (acalculia)

  - difficoltà nell'articolazione del linguaggio (disartria)*

- Sintomi sensitivi:

  - negativi (ipoestesia) o positivi (parestesie e disestesie) in una metà del corpo in toto o in una sua parte

- Sintomi visivi:

  - perdita della visione completa o parziale in un occhio

  - perdita della visione in un quarto o in una metà del campo visivo (quadrantopsia o emianopasia)

  - cecità in entrambi gli occhi

  - diplopia*

- Sintomi vestibolari:

  - vertigini*

- Disturbi cognitivi o comportamentali:

  - difficoltà nel vestirsi, nel lavarsi (aprassia); disfunzioni percettive visuo-spaziali (es. emidisattenzione)

*isolati non possono essere considerati segni neurologici focali

1. **Hemorrhage:** Exclude acute intracranial hemorrhage, including parenchymal hemorrhage and subarachnoid hemorrhage, as this is a critical triage branch point and exclusion for revascularization therapy.

2. **Ischemia:** When acute ischemic stroke signs are identified, both the extent of baseline ischemic damage and the underlying cause should be determined during the initial triage phase if possible.

3. **Mimics:** Stroke mimics, including seizures, tumor, infection, migraine, and other acute neurologic conditions should be detected by imaging, or at least suggested in the differential diagnosis.

Cincinnati Pre-hospital Stroke Scale

1. FACIAL DROOP: *Have patient show teeth or smile.*

Normal: both sides of the face move equally

Abnormal: one side of face does not move as well as the other side

2. ARM DRIFT: *Patient closes eyes & holds both arms out for 10 sec.*

Normal: both arms move the same or both arms do not move at all

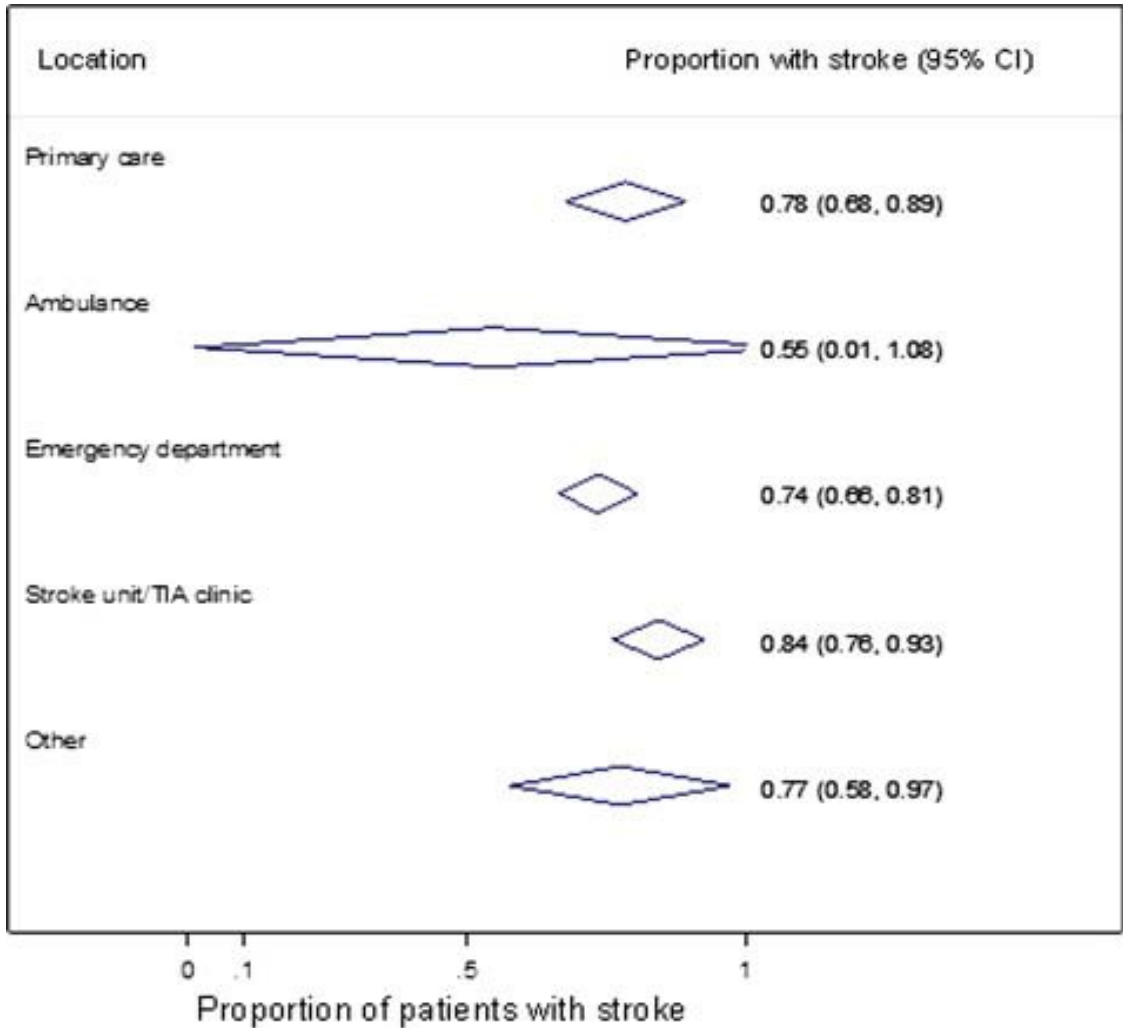
Abnormal: one arm does not move or drifts down compared to the other

3. ABNORMAL SPEECH: *Have the patient say "you can't teach an old dog new tricks."*

Normal: patient uses correct words with no slurring **Abnormal**: patient slurs words, uses the wrong words, or is unable to speak

INTERPRETATION: If any 1 of these 3 signs is abnormal, the probability of a stroke is 72%.

Stroke mimics account for 20-25% of suspected stroke depending on the context



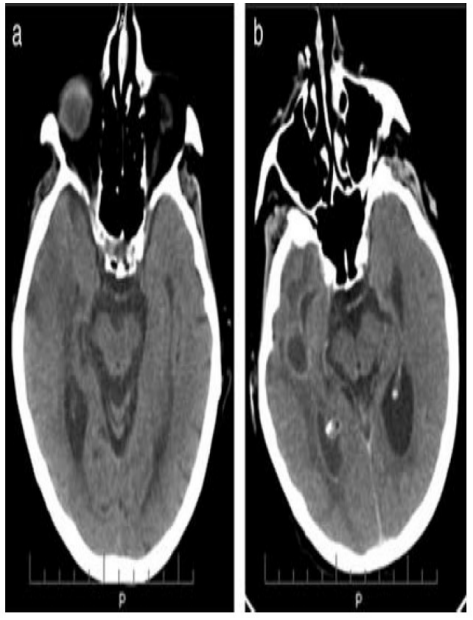
Imaging leads to more accurate diagnosis

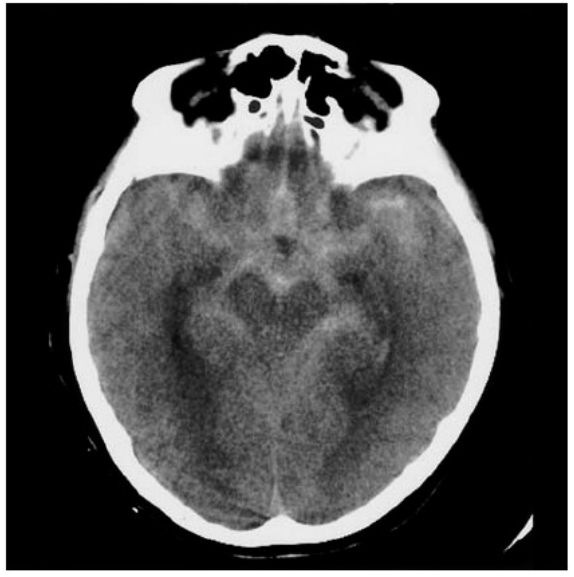
misdiagnosis

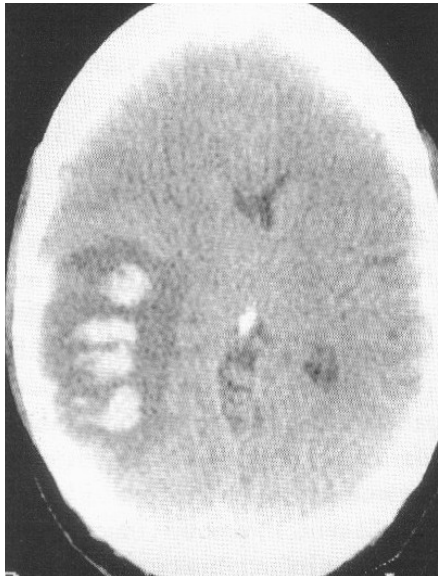
- History, physical and lab work alone: 20%

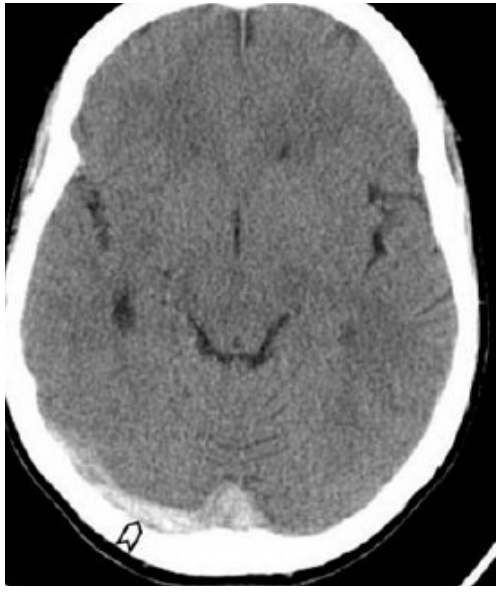
Huff JS Emerg Med Clin N Am 2002;
Ay Neurology 1999

CT scan to exclude for other causes









Imaging leads to more accurate diagnosis

misdiagnosis

- History, physical and lab work alone: 20%
- Non contrast brain CT 5-10%

Huff JS Emerg Med Clin N Am 2002;
Ay Neurology 1999

Imaging leads to more accurate diagnosis

misdiagnosis

- History, physical and lab work alone: 20%
- Non contrast brain CT 5-10%
- Cerebral DWI MRI/perfusion CT 2-5%

Huff JS Emerg Med Clin N Am 2002;
Ay Neurology 1999

- **CT: contraindications**
  - There is **no absolute contraindication if benefits weigh risks**.
  - X-ray related: in pregnant patients and children
  - Contrast related:
    - Hypersensitivity to iodinated contrast medium.
    - History of seafood allergy is NOT a contraindication to iodinated contrast medium administration. Although, if other allergic disorders coexist, this will increase the chance of having contrast hypersensitivity.
    - Asthma, allergic disorders increase risk of hypersensitivity.
    - Renal failure, diabetes, current use of metformin contribute to increased risk of contrast-related renal failure.

- **MRI contraindications**:

1. Implanted cardiac pacemaker or defibrillator
2. Cochlear Implants
3. Ocular foreign body (for example, metal shavings)
4. Embedded shrapnel fragments
5. Central nervous system aneurysm clips
6. Implanted neural stimulator
7. Any implanted device that is incompatible with MRI
8. Unsatisfactory performance status as judged by the physician such that the participant could not tolerate an MRI scan
9. Participants requiring monitored sedation for MRI studies
10. Participants with a condition precluding entry into the scanner (for example, morbid obesity, claustrophobia)

Magnetic resonance imaging and computed tomography in emergency assessment of patients with suspected acute stroke: a prospective comparison

Julio A Chalela, Chelsea S Kidwell, Lauren M Nentwich, Marie Luby, John A Butman, Andrew M Demchuk, Michael D Hill, Nicholas Patronas, Lawrence Latour, Steven Warach

	n	Acute stroke		Acute ischaemic stroke	
		CT	MRI	CT	MRI
Sensitivity					
All	356	26% (20–32)	83% (78–88)	16% (12–23)	83% (77–88)
>12 h	135	22% (14–33)	91% (82–96)	16% (9–27)	92% (83–97)
3–12 h	131	29% (19–41)	81% (70–89)	20% (12–33)	81% (69–90)
<3 h	90	27% (17–40)	76% (64–86)	12% (5–24)	73% (59–84)
Specificity					
All	356	98% (93–99)	97% (92–99)	98% (94–99)	96% (92–99)
>12 h	135	98% (89–100)	96% (86–99)	98% (90–100)	97% (88–99)
3–12 h	131	97% (87–99)	98% (90–100)	96% (87–99)	99% (91–100)
<3 h	90	100% (85–100)	96% (79–100)	100% (89–100)	92% (78–98)

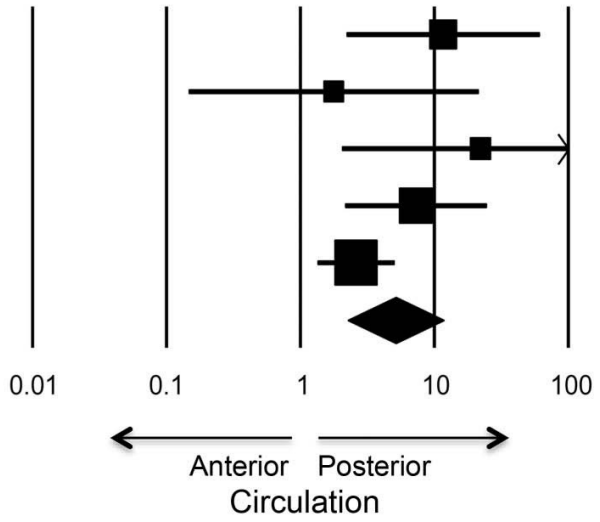
Data in parentheses are 95% CI.

Table 4: Sensitivity and specificity of blinded imaging diagnosis by time from onset to scan

Lancet 2007; 369: 293–98

Diagnosis of DWI-negative acute ischemic stroke

Study	n	OR	95% CI	*p*
Ref #24 (2000A)	130	11.6	2.2, 61.2	0.004
Ref #26 (2000B)	59	1.8	0.1, 21.4	0.652
Ref #e2 (2001)	79	22.1	2.0, 239.2	0.011
Ref #11 (2007)	190	7.3	2.2, 25.0	0.001
Ref #7 (2015)	565	2.6	1.3, 5.0	0.004
Total	**1,023**	**5.1**	**2.3, 11.6**	**<0.001**



Edlow et al, Neurology 2017

Imaging leads to more accurate diagnosis

misdiagnosis

- History, physical and lab work alone: 20%
- Non contrast brain CT 5-10%
- Cerebral DWI MRI/perfusion CT 2-5%
- Other exams 0

Huff JS Emerg Med Clin N Am 2002;
Ay Neurology 1999

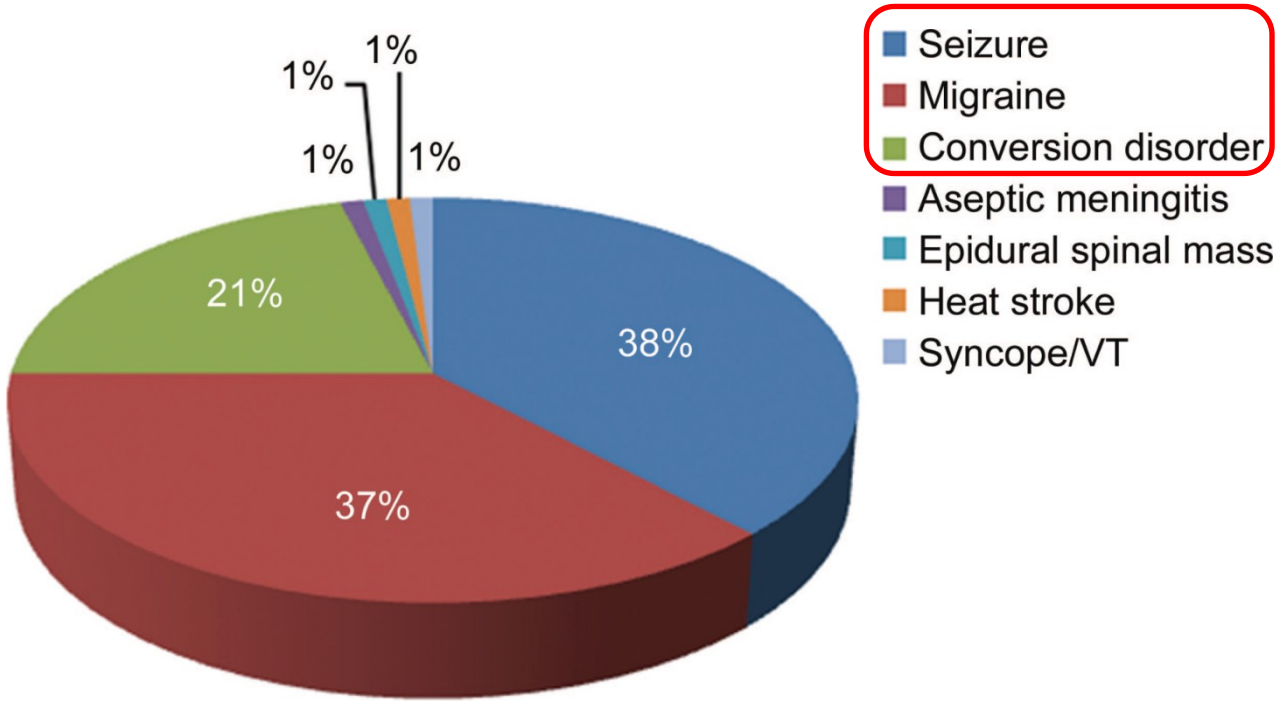
Common stroke mimics

- **CENTRAL NERVOUS SYSTEM CONDITIONS:**
  - Post-ictal state with focal neurological signs (Todd's paresis)
  - Nonconvulsive status epilepticus
  - Hemiplegic migraine
  - Subdural hematoma
  - Brain abscess
  - Infective encephalitis
  - Intracranial tumour (primary / metastatic)
  - Multiple sclerosis

- **METABOLIC / SYSTEMIC CONDITIONS:**
  - Hypoglycemia / hyperglycemia
  - Posterior reversible encephalopathy (PRES)

- **PSYCHIATRIC CONDITIONS:**
  - Conversion disorder
  - Factitious disorder

The most common stroke mimics: acute phase



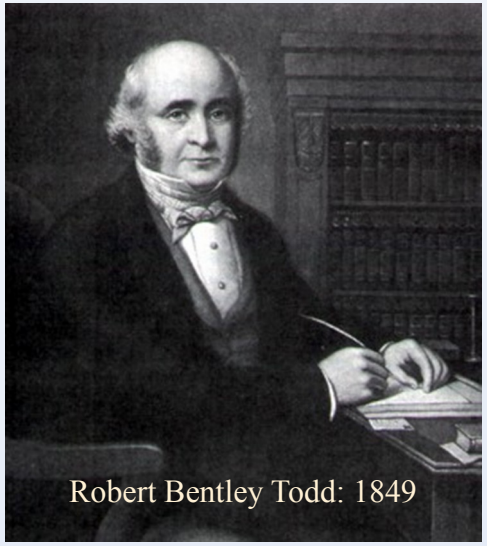
Neurology® 2010;74:1340 –1345

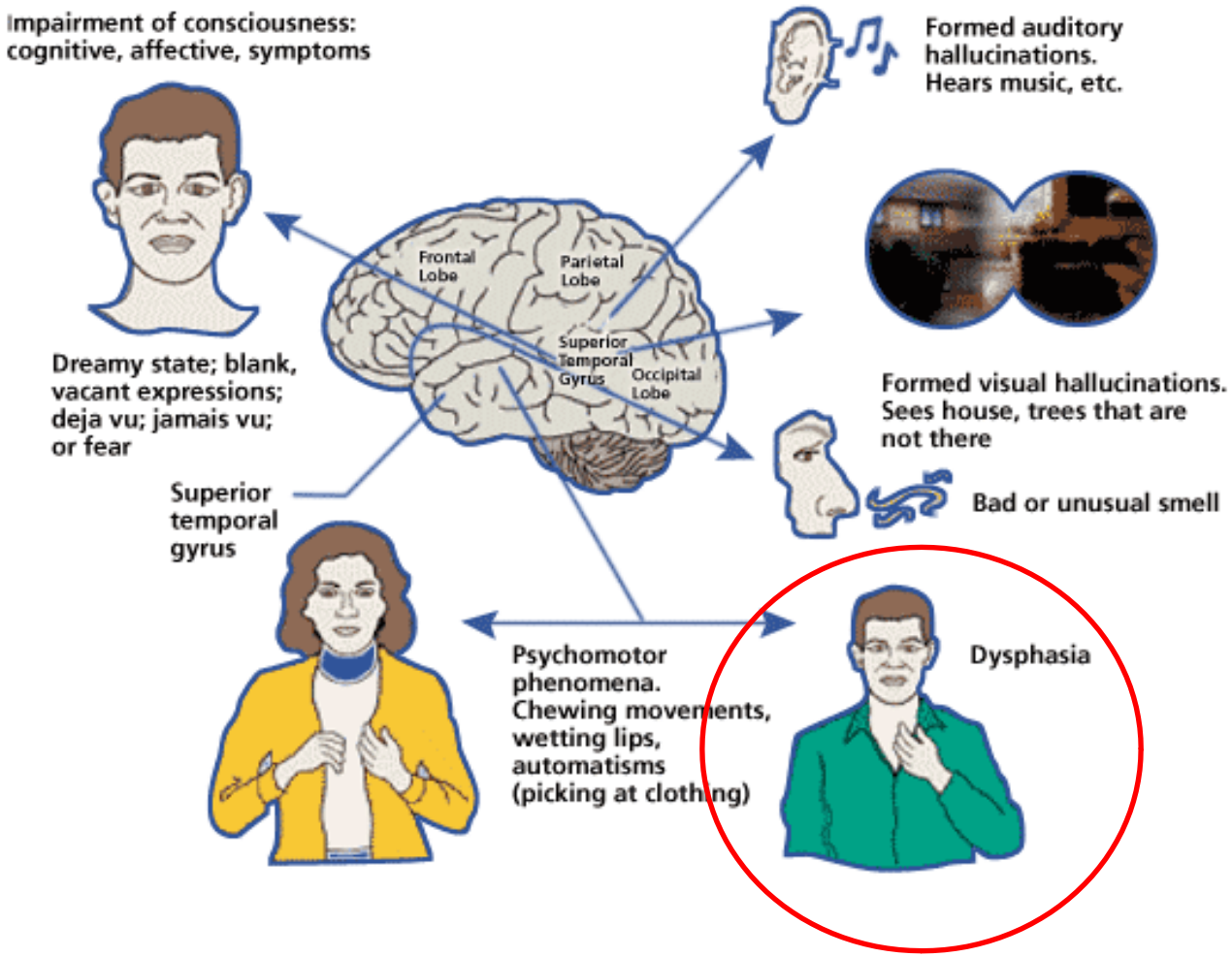
Todd's Paresis

- ≅ 15% of seizures.
- Most common after GTC especially after clonic activity.
- Usually causes a hemiparesis.
- Can cause aphasia, sensory loss or visual field defect (uncommonly)
- Usually lasts minutes but can last hours or even days
- Confusional state
- Patients could not remember the event

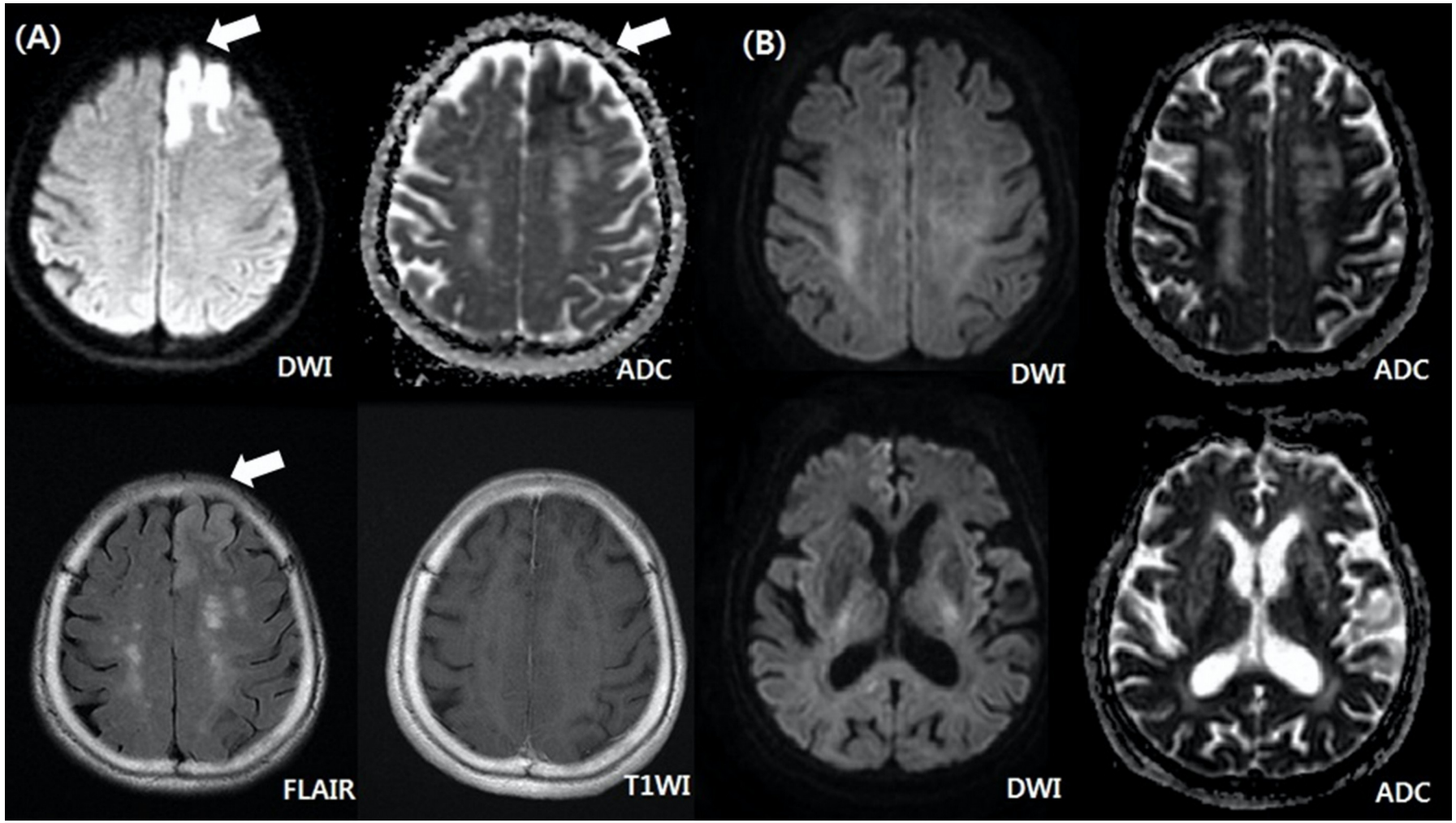
BUT

- 2% of patients have a seizure at stroke onset.


Robert Bentley Todd: 1849

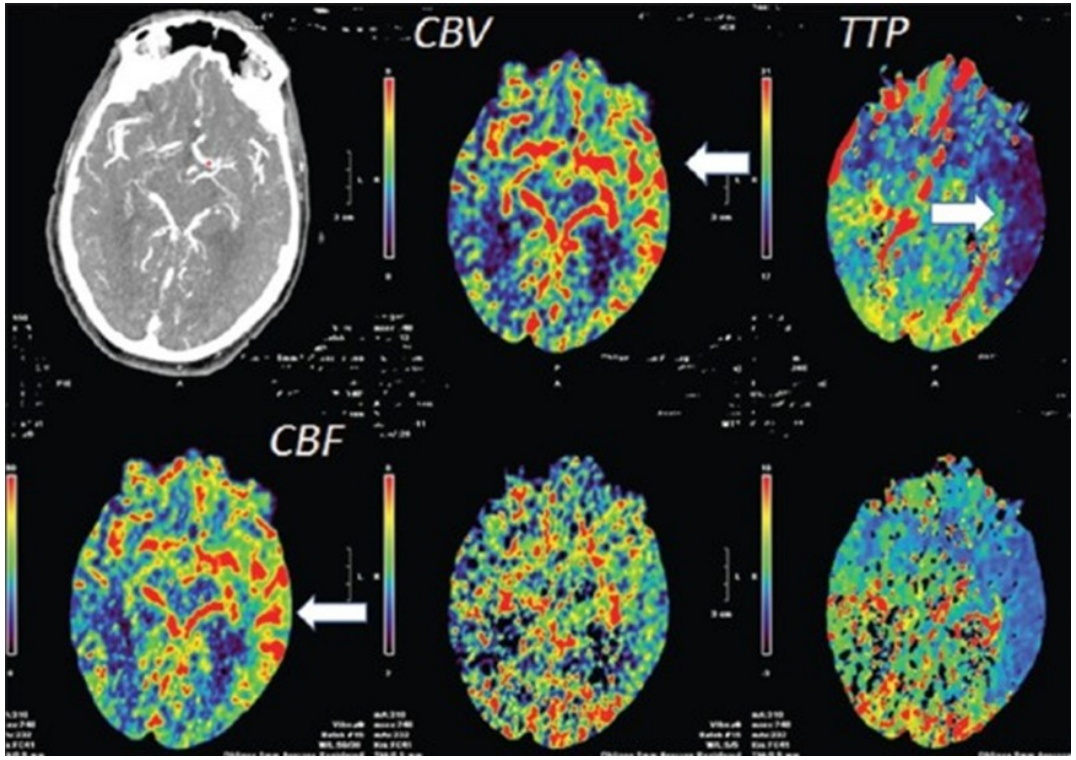

Impairment of consciousness: cognitive, affective, symptoms
Formed auditory hallucinations. Hears music, etc.
Frontal Lobe
Parietal Lobe
Superior Temporal Gyrus
Occipital Lobe
Dreamy state; blank, vacant expressions; deja vu; jamais vu; or fear
Formed visual hallucinations. Sees house, trees that are not there
Bad or unusual smell
Superior temporal gyrus
Psychomotor phenomena. Chewing movements, wetting lips, automatisms (picking at clothing)
Dysphasia

Characteristics of seizure-induced signal changes on MRI in patients with first seizures



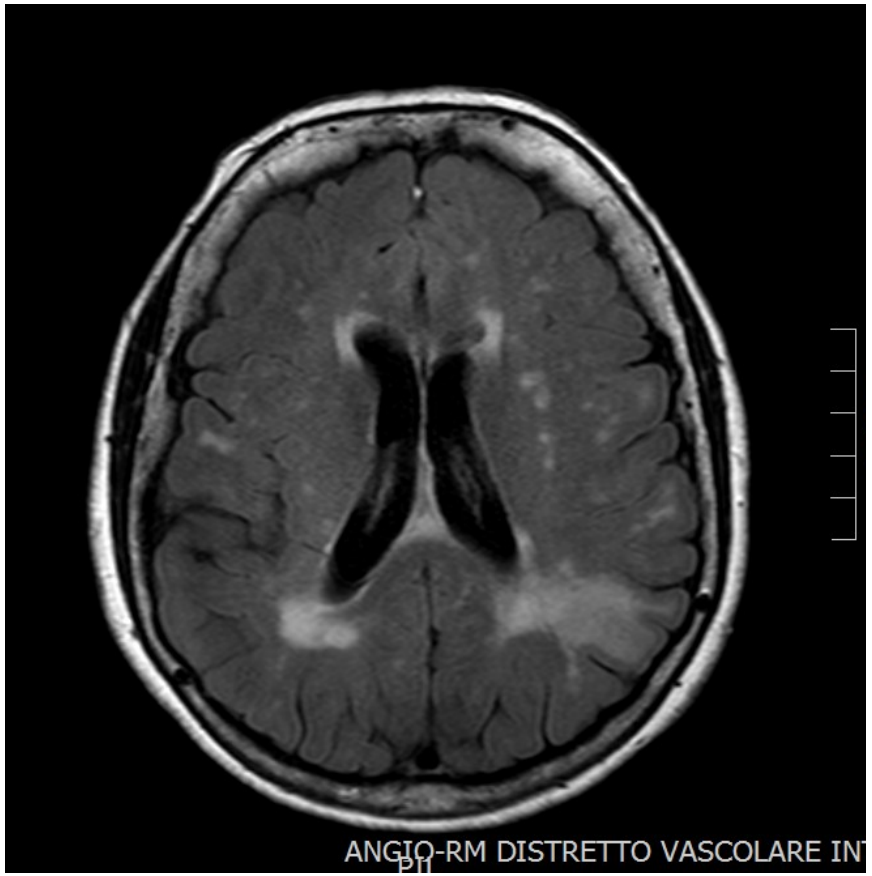
Si Eun Kim et al, Seizure 2017

Seizure Mimicking Stroke: CT Perfusion



	TTP	CBF		CBV
Infarct		↑	↓	↓
Penumbra		↑	↓	↑
Epilepsy		↓	↑	↑

Hedna et al, J Clin Imaging Sci 2012:2:32

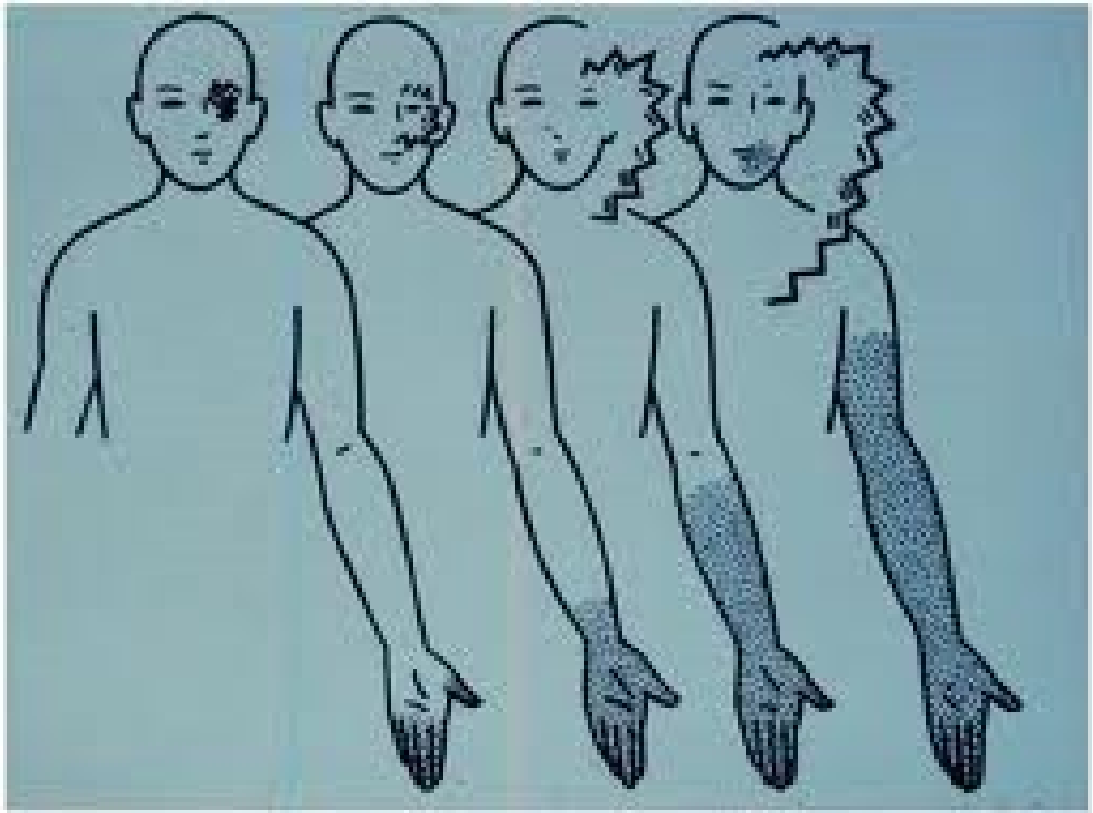


Attenzione anche a:

- Verificare la presenza di vecchie cicatrici
- presenza di morsus
- incontinenza sfinterica
- amnesia dell’accaduto
- rapida ripresa dei sintomi
- presenza di stato confusionale

Migraine aura

- Gradual onset
- Positive symptoms
- Symptoms spread from several seconds to minutes
- Gradual resolution over 20-60 minutes
- Headache
- Recurrent stereotyped attacks
- Typically young



Functional disorders

- Conversion reaction
- Factitious or feigned stroke

They frequently manifest as:

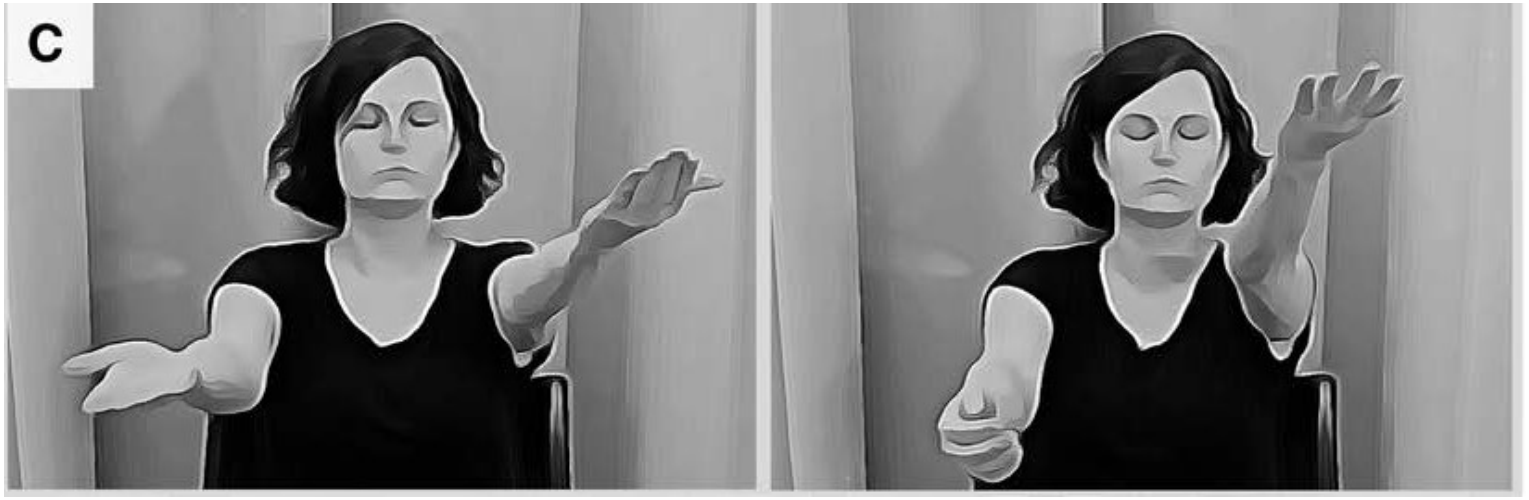
- Acute weakness
- Acute sensory disturbances
- Acute visual disturbances

Babinski sign

«The presence of the toe phenomenon excludes hysteria»

Joseph Félix Francois Babinski (1898)

Drift without pronation



mimic

stroke

Unilateral lip pulling with ipsilateral platysma contraction in functional facial dystonia.

Popkirov et al, Stroke 2020

Distinguishing features of stroke and mimics

Stroke

- An exact onset can be established
- Definitive history of focal neurological deficit
- Any abnormal vascular findings*
- NIHSS>10
- Vascular risk factors
- Urinary retention

Mimics

- Signs not corresponding to vascular territory
- Non lateralizing symptoms
- Signs inconsistent with symptoms
- No facial deficit
- History of cognitive impairment
- Confusion at onset
- Pace of symptoms (march)
- Previous similar episodes

*Systolic blood pressure >150 mm Hg, atrial fibrillation, valvular heart disease, or absent peripheral pulses; †respiratory, abdominal, or other abnormal signs; ‡NIHSS=0 was entered as the reference group (therefore it does not have a coefficient).

Suggerimenti generali finali per riconoscere uno stroke mimic

- Evitare errore di fissazione
- Utilizzare tutte le risorse disponibli
- Attenta anamnesi personale e farmacologica
- Attento esame obiettivo neurologico
- Attento esame obiettivo generale
- Attenta verifica delle neuroimmagini disponibli (es. se solo TC cercare i segni indiretti di una eventuale ischemia o vecchie cicatrici)
- Se rimane il dubbio ed il deficit è invalidante → trattare il paziente con rt-PA

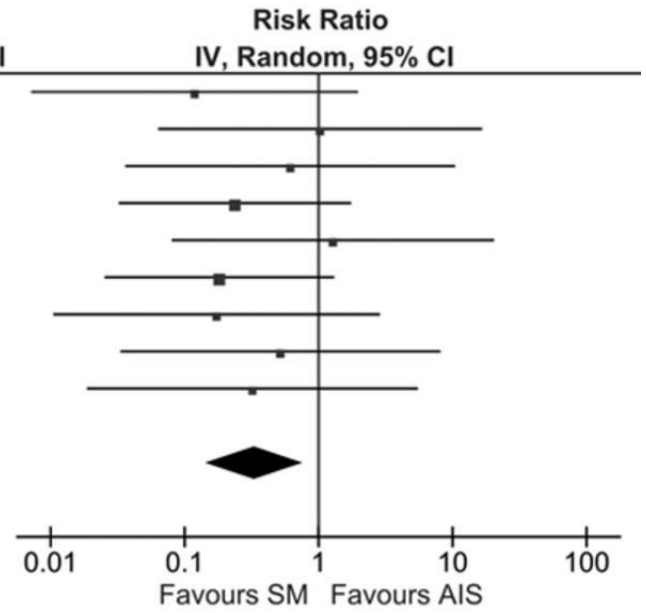
Safety of Intravenous Thrombolysis in Stroke Mimics

A

Study or Subgroup	Stroke Mimics Events	Total	Acute ischemic Stroke Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Houston	0	69	24	406	9.0%	0.12 [0.01, 1.93]
Madrid	0	15	18	606	9.2%	1.03 [0.06, 16.28]
Mannheim	0	42	11	606	8.9%	0.61 [0.04, 10.24]
Memphis	1	75	29	516	17.9%	0.24 [0.03, 1.72]
Michigan	0	6	8	151	9.3%	1.28 [0.08, 19.97]
Multicenter	1	100	275	4995	18.4%	0.18 [0.03, 1.28]
Phoenix	0	56	24	483	9.0%	0.17 [0.01, 2.81]
Pittsburgh	0	9	21	222	9.4%	0.52 [0.03, 7.96]
St. Louis	0	20	7	100	8.8%	0.32 [0.02, 5.40]
Total (95% CI)		**392**		**8085**	**100.0%**	**0.33 [0.14, 0.77]**
Total events	2		**417**			

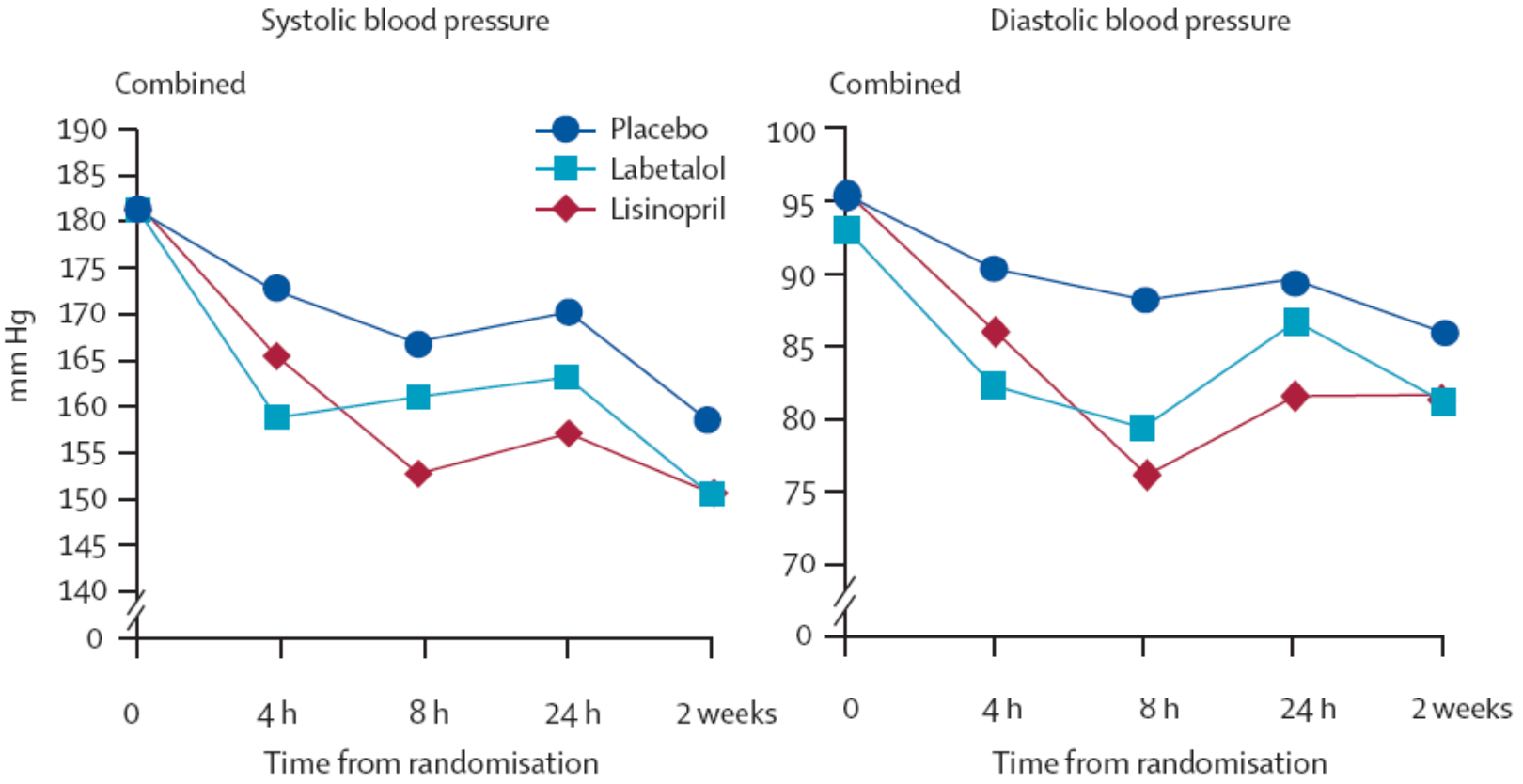
Heterogeneity: Tau² = 0.00; Chi² = 3.06, df = 8 (P = 0.93); I² = 0%

Test for overall effect: Z = 2.58 (P = 0.010)



Tsivgoulis et al, Stroke 2015

The hypertensive response: self-limiting nature



Potter JF, Lancet Neurology 2009

Current Guidelines: when antihypertensive treatment is indicated

	Systolic BP	Diastolic BP
SPREAD	≥220	≥120
European Stroke Organization	≥220	≥120
American Heart Association	≥220	≥120
Stroke Foundation New Zeland	≥220	≥120
Hong Kong Consensus Statement	≥220	≥120
National Stroke Foundation	≥220	≥120
American Accademy of Neurology	≥220	≥140

Current Guidelines: when antihypertensive treatment is indicated

Patients candidates for iv rt-PA	Systolic BP	Diastolic BP
SPREAD	≥185	≥110
European Stroke Organization	≥185	≥110
American Heart Association	≥185	≥110
Stroke Foundation New Zeland	≥185	≥110
Hong Kong Consensus Statement	≥185	≥110
National Stroke Foundation	≥185	≥110
American Accademy of Neurology	≥185	≥110

Current Guidelines: when antihypertensive treatment is indicated

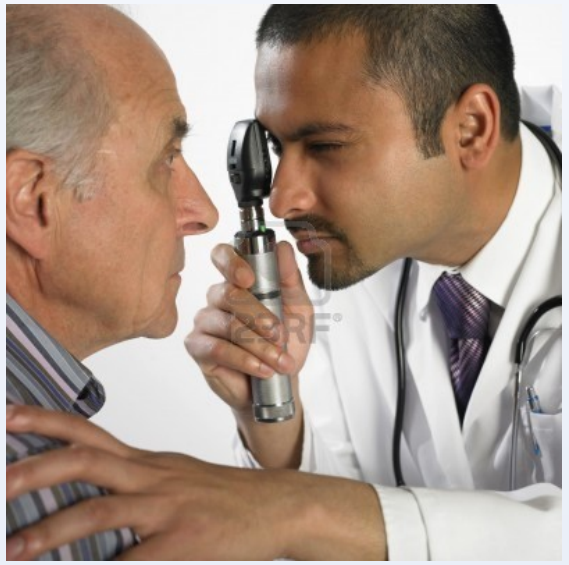
Indications to actively lower blood pressure

- ✓ hypertensive encephalopathy
- ✓ aortic dissection
- ✓ heart failure
- ✓ acute myocardial infarction
- ✓ acute renal failure
- ✓ preeclampsia and eclampsia

"*The world is full of obvious things which nobody by any chance ever observes*"

The Hound of the Baskervilles

Sir Arthur Conan Doyle (Author of the adventures of Sherlock Holmes)



….anything can be underestimated!