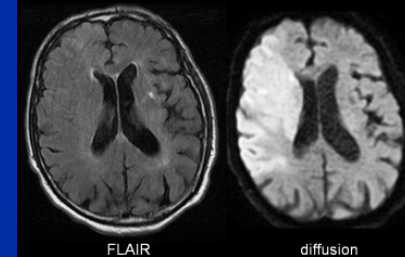


XI EDIZIONE

Giornate Mediche di Santa Maria Nuova 2019

Firenze 3-4 Ottobre 2019



La RM Encefalo in acuto: Guida per l'estensione delle Indicazioni alla Trombolisi nello Stroke

Angela Konze

SOC Radiologia Ospedale S. Maria Nuova, Firenze Direttore Dr. R. Carpi
Dipartimento Dpl, Azienda USL Toscana Centro, Direttore Dr. S. Santini

ICTUS CEREBRALE



- **9000 casi/anno in Toscana**
- **Costi diretti di circa 280 milioni di Euro/anno in Toscana, 3,5 mrd/anno in Italia, 45 mrd/anno in Europa**
- **In Italia vive quasi 1 milione di Pazienti con esiti di ictus, di cui il 35% con disabilità grave**

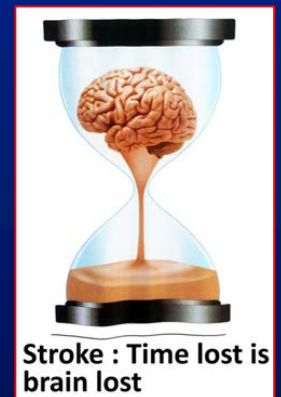
ICTUS ISCHEMICO

Patologia Tempo dipendente

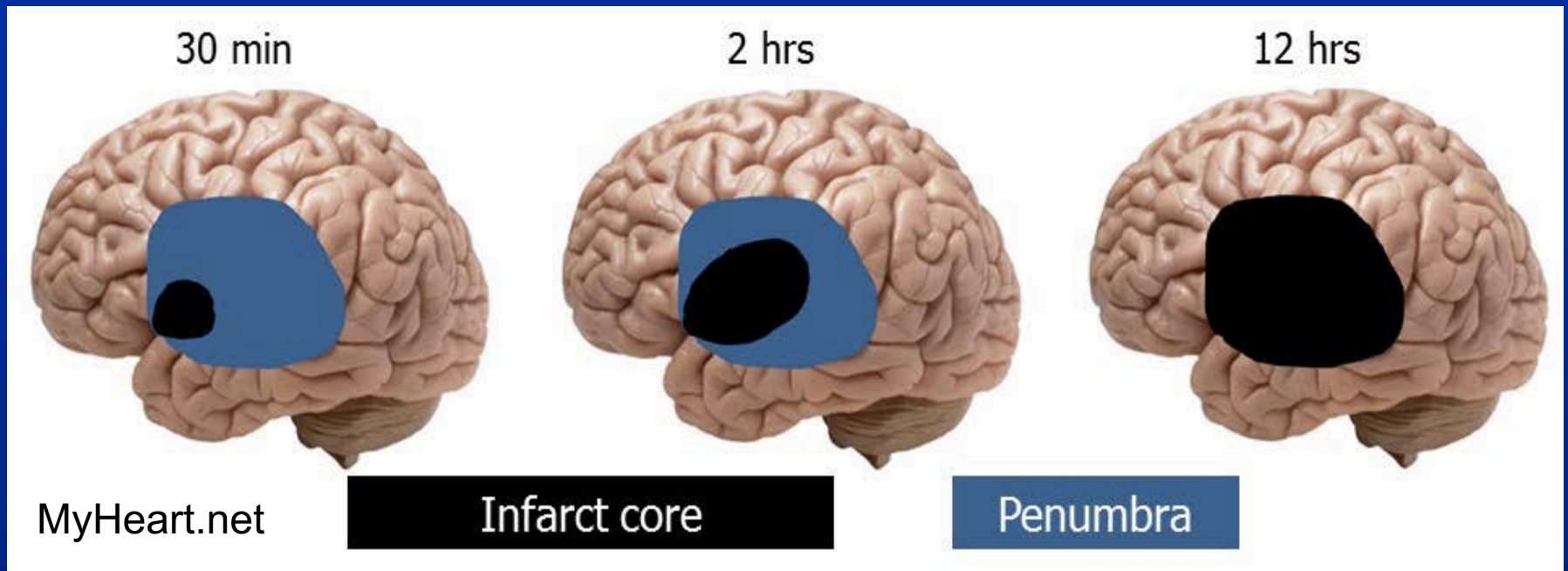


Finestra Terapeutica
STRETTA

Trombolisi con rtPA
entro 4,5 ore
dall'insorgenza dei
sintomi



TIME IS BRAIN



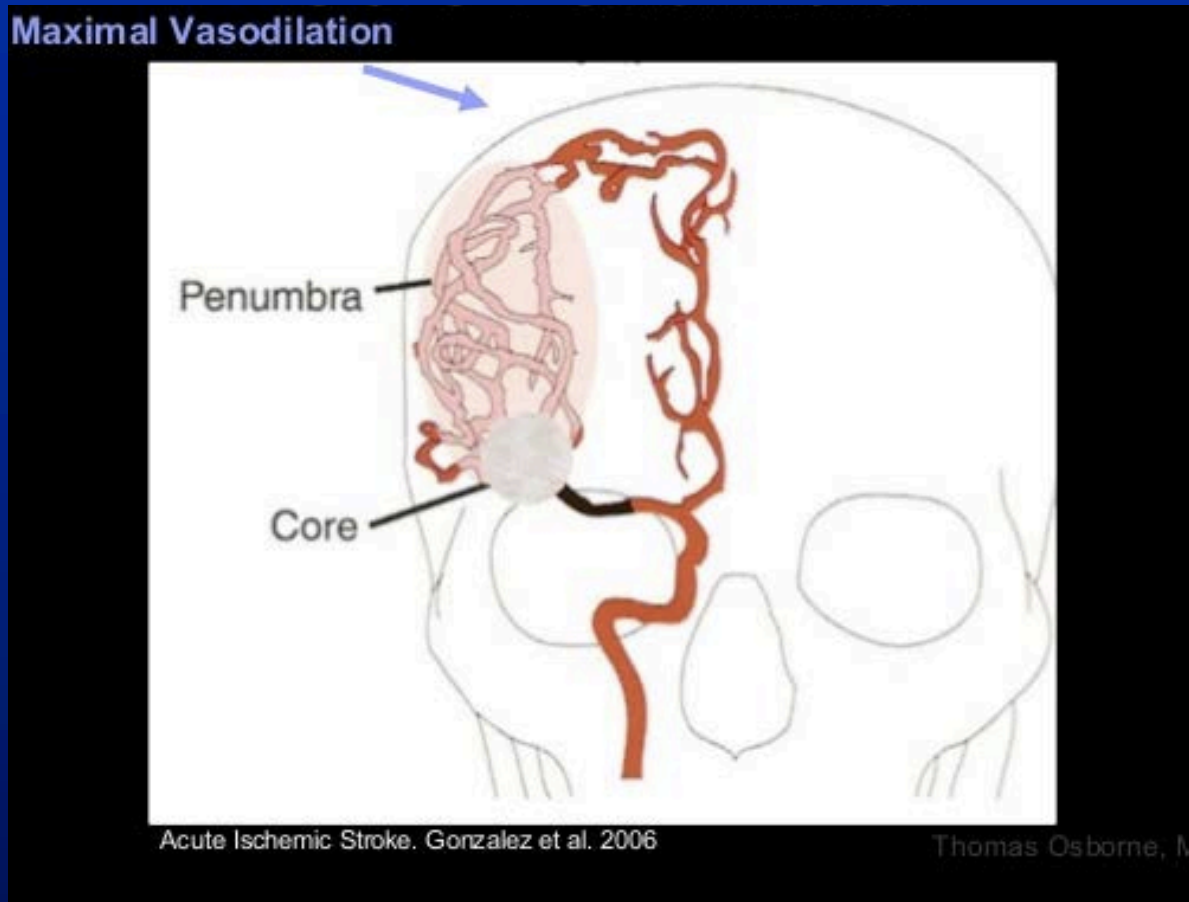
Estimated Pace of Neural Circuitry Loss in Typical Large Vessel, Supratentorial Acute Ischemic Stroke

	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

J. L. Saver, „Time is brain-quantified.,” Stroke, pp. 263-266, 2006.



Riperfondere la penombra prima che diventi core!



ICTUS ACUTO: FASE DI OSPEDALIZZAZIONE

Raccomandazione 9.1

Forte a favore

Grado A

Il trattamento con r-tPA e.v. (0,9 mg/kg, dose massima 90 mg, il 10% della dose in bolo, il rimanente in infusione di 60 minuti) **è raccomandato entro 4.5 ore dall'esordio di un ictus ischemico senza limiti superiori di età e di gravità.**
È comunque indicato che il trattamento sia effettuato il più precocemente possibile.

Raccomandazione 9.2

Forte a favore

Grado B

Il trattamento con r-tPA e.v. entro 4.5 ore dall'esordio dei sintomi è raccomandato in pazienti con deficit lieve o in rapido miglioramento ma ancora rilevabile al momento di iniziare il trattamento.

Raccomandazione 9.12

Forte a favore

Grado B

Le tecniche di trombectomia meccanica sono raccomandate entro 6 ore dall'esordio dei sintomi in pazienti con occlusione di carotide interna intra-cranica, arteria cerebrale media tratti M1-M2, arteria cerebrale anteriore tratto A1, che non rispondono o che non possono essere sottoposti alla trombolisi e.v.

Ictus a insorgenza non nota?

In circa il 14-27% dei casi di ictus l'orario dell'insorgenza dei sintomi non è noto, frequentemente perché i sintomi vengono riscontrati al risveglio

Questi Pazienti generalmente vengono esclusi dal trattamento trombolitico ev con Alteplase

Circa il 30% dei Pazienti potrebbe trarre beneficio dal trattamento trombolitico

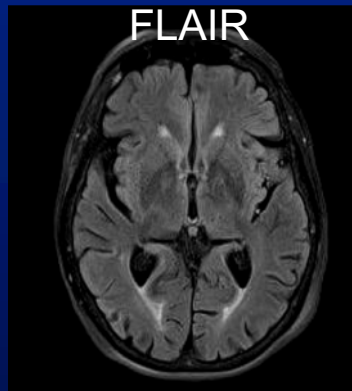
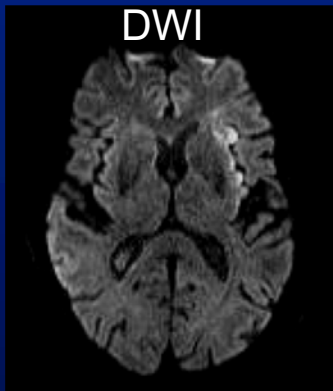


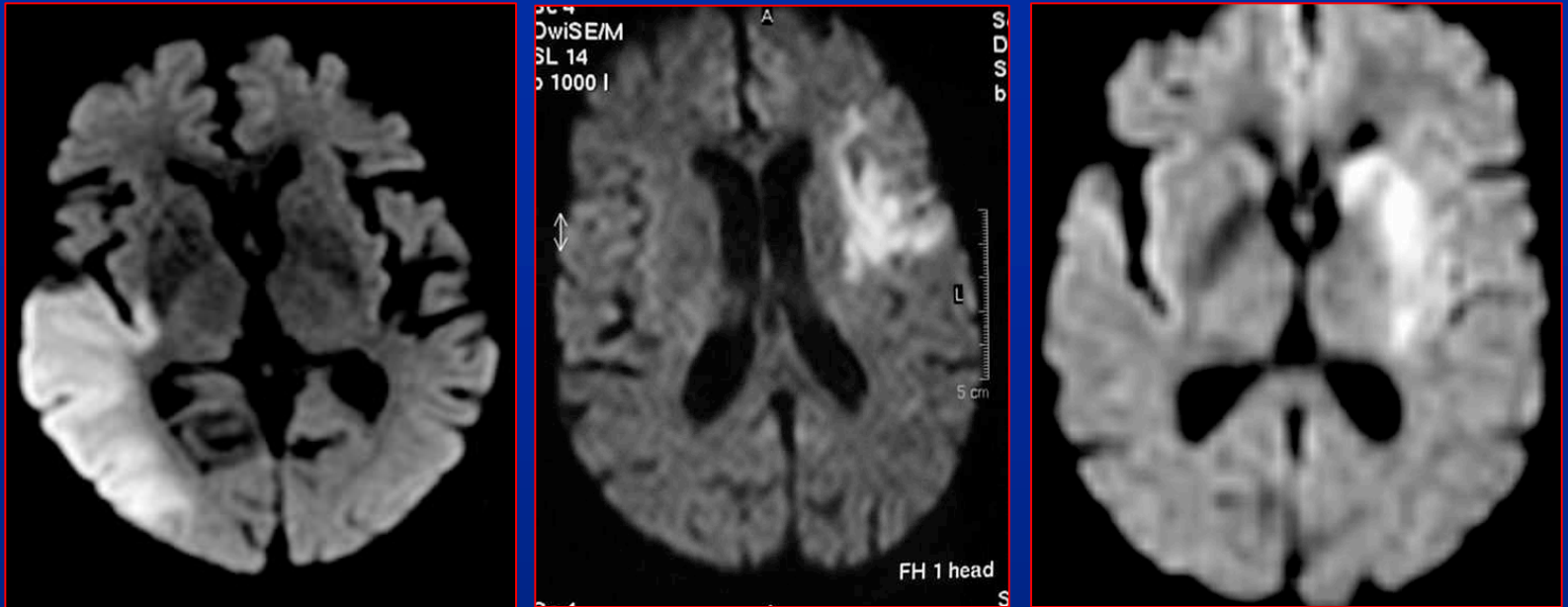
Quale Approccio Diagnostico nell'Ictus non databile?



MISMATCH DWI-FLAIR in RMN

Si basa sul concetto che l'area ischemica risulta apprezzabile dopo pochi minuti dall'esordio con lo studio di diffusione, mentre per essere percepibile come alterazione di segnale in FLAIR ci vogliono alcune ore (3-5)

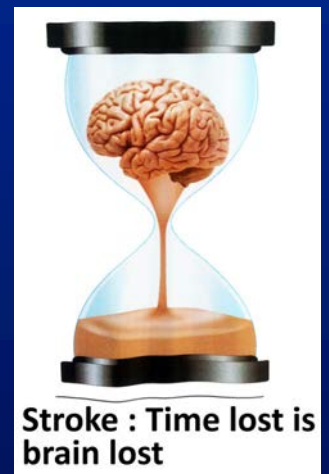
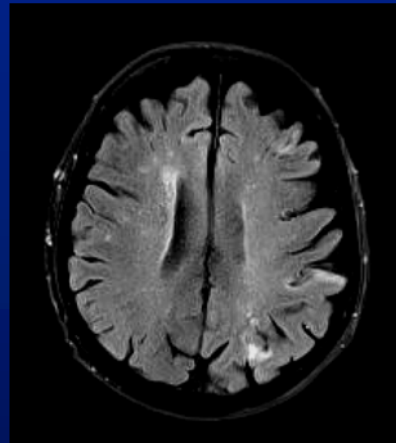
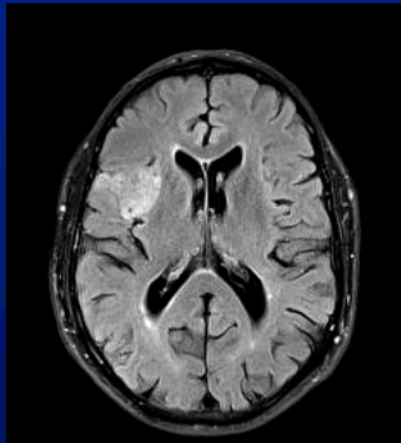




**DWI positiva entro pochi minuti
dall'insulto ischemico**

Segni elementari dell'ictus ischemico all'esame RM convenzionale

- **Dopo 3-5 h iperintensità in FLAIR**
- **Dopo almeno 8 h iperintensità in T2**
- **Dopo 16 h ipointensità in T1**



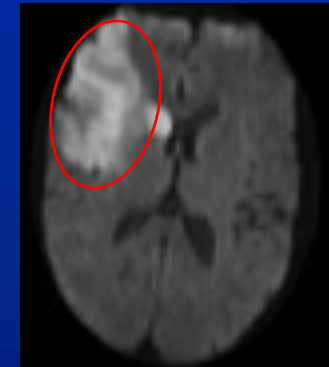
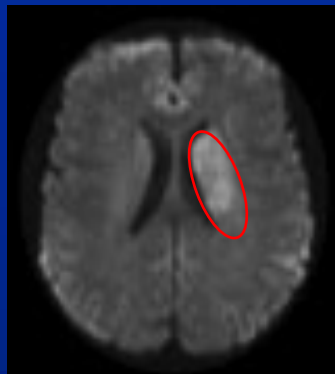
2009

Ann Neurol

Negative Fluid-Attenuated Inversion Recovery Imaging Identifies Acute Ischemic Stroke at 3 Hours or Less

Götz Thomalla, MD,¹ Philipp Rossbach, MSt,¹ Michael Rosenkranz, MD,¹ Susanne Siemonsen, MD,²
Anna Krüzelmann, MD,¹ Jens Fiehler, MD,² and Christian Gerloff, MD¹

DWI



FLAIR



90 min

125 min

282 min

ORIGINAL ARTICLE

MRI-Guided Thrombolysis for Stroke with Unknown Time of Onset

G. Thomalla, C.Z. Simonsen, F. Boutitie, G. Andersen, Y. Berthezene, B. Cheng, B. Cheripelli, T.-H. Cho, F. Fazekas, J. Fiehler, I. Ford, I. Galinovic, S. Gellissen, A. Golsari, J. Gregori, M. Günther, J. Guibernau, K.G. Häusler, M. Hennerici, A. Kemmling, J. Marstrand, B. Modrau, L. Neeb, N. Perez de la Ossa, J. Puig, P. Ringleb, P. Roy, E. Scheel, W. Schonewille, J. Serena, S. Sunaert, K. Villringer, A. Wouters, V. Thijs, M. Ebinger, M. Endres, J.B. Fiebach, R. Lemmens, K.W. Muir, N. Nighoghossian, S. Pedraza, and C. Gerloff for the WAKE-UP Investigators*

BACKGROUND

Under current guidelines, intravenous thrombolysis is used to treat acute stroke only if it can be ascertained that the time since the onset of symptoms was less than 4.5 hours. We sought to determine whether patients with stroke with an unknown time of onset and features suggesting recent cerebral infarction on magnetic resonance imaging (MRI) would benefit from thrombolysis with the use of intravenous alteplase.

METHODS

In a multicenter trial, we randomly assigned patients who had an unknown time of onset of stroke to receive either intravenous alteplase or placebo. Patients had to have had an ischemic lesion that was visible on MRI diffusion-weighted imaging and parenchymal hyperintensity on fluid-attenuated inversion recovery imaging, which indicated that the stroke had occurred approximately within the last 4.5 hours. We excluded patients for whom thrombectomy was planned. The primary outcome was a favorable outcome, as defined by a score of 0 or 1 on the modified Rankin scale of neurologic disability (which ranges from 0 [no symptoms] to 6 [death]). A secondary outcome was the likelihood that alteplase would result in higher scores on the modified Rankin scale than would placebo (shift toward higher scores).

RESULTS

The trial was stopped early owing to cessation of funding after the enrollment of 503 of an anticipated 800 patients. Of these patients, 254 were randomly assigned to receive alteplase and 249 to receive placebo. A favorable outcome at 90 days was reported in 131 of 246 patients (53.3%) in the alteplase group and in 102 of 244 patients (41.8%) in the placebo group (adjusted odds ratio, 1.61; 95% confidence interval [CI], 1.00 to 2.36; $P=0.02$). The median score on the modified Rankin scale at 90 days was 1 in the alteplase group and 2 in the placebo group.

CONCLUSIONS

In patients with acute stroke with an unknown time of onset, intravenous alteplase guided by a mismatch between diffusion-weighted imaging and FLAIR in the region of ischemia resulted in a significantly better functional outcome and numerically more intracranial hemorrhages than placebo at 90 days. (Funded by the European Union Seventh Framework Program; WAKE-UP ClinicalTrials.gov number, NCT01525290; and EudraCT number, 2011-005906-32.)

2018

Raccomandazione 9.3

Debole a favore

Grado D

Il trattamento con r-tPA e.v. è indicato in pazienti con ora di insorgenza dell'ictus non nota o ictus presente al risveglio, qualora le neuroimmagini avanzate (RM DW e PW o pTC) definiscano una zona di mismatch tessutale e/o **consentano di datare l'evento almeno entro le 3 ore (confronto MR DW con MR FLAIR).**

Pistoia, 4 Maggio 2019

Relazione Danilo Toni

Linee guida ISO-SPREAD Possibile nuova raccomandazione

Raccomandazione 9.3

Debole a favore

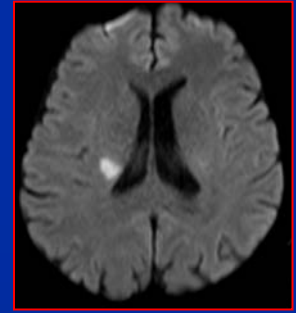
~~Il trattamento con r-tPA e.v. è raccomandato in pazienti con ictus ad ora di insorgenza non nota o al risveglio, qualora le neuroimmagini avanzate (RM DW e PW o pTC) definiscano una zona di mismatch tessutale e/o consentano di datare l'evento almeno entro le 3 ore (confronto RM DW con RM FLAIR)~~

Raccomandazione

Forte a favore

Il trattamento con r-tPA e.v. è raccomandato in pazienti con ictus al risveglio, qualora il confronto fra RM DW e FLAIR consenta di datare l'esordio dell'evento entro le 4.5 ore

Protocollo RM



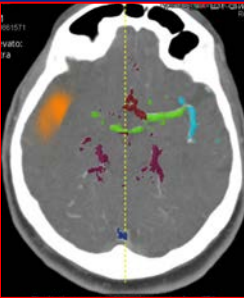
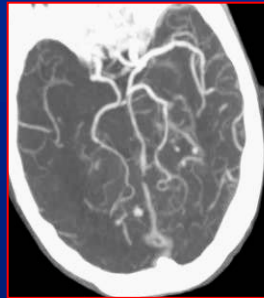
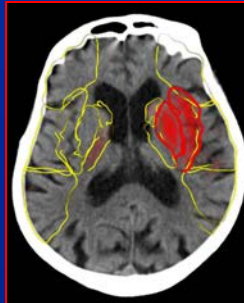
- ✓ **FLAIR**
- ✓ **DWI**
- ✓ **Sequenza sensibile per il sangue**
- ✓ **Angio-RM vasi intracranici TOF**

Durata inferiore a 10 minuti!



Percorso Imaging Ictus non databile

TC



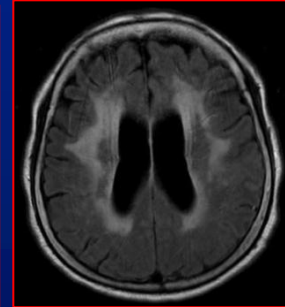
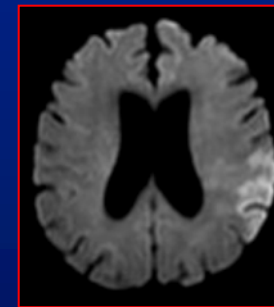
LVO

Eventuale invio alla
Neuroradiologia
interventistica

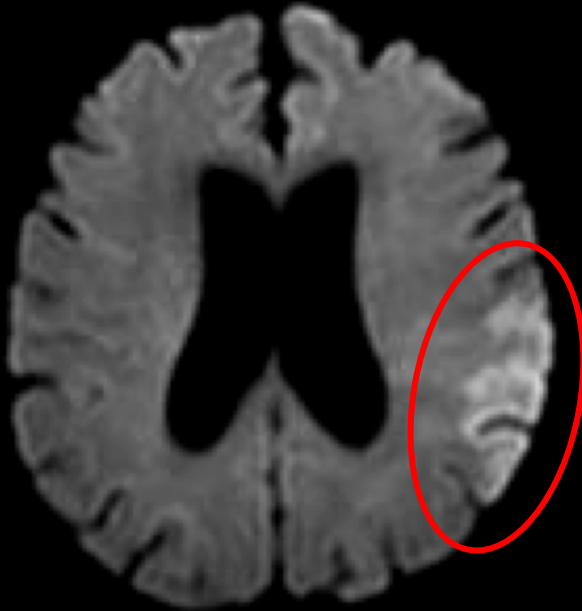
No LVO



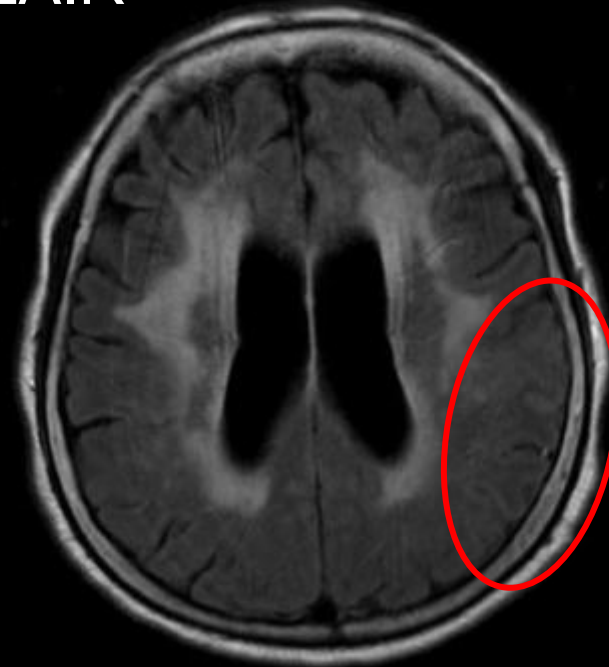
RM



DWI



FLAIR

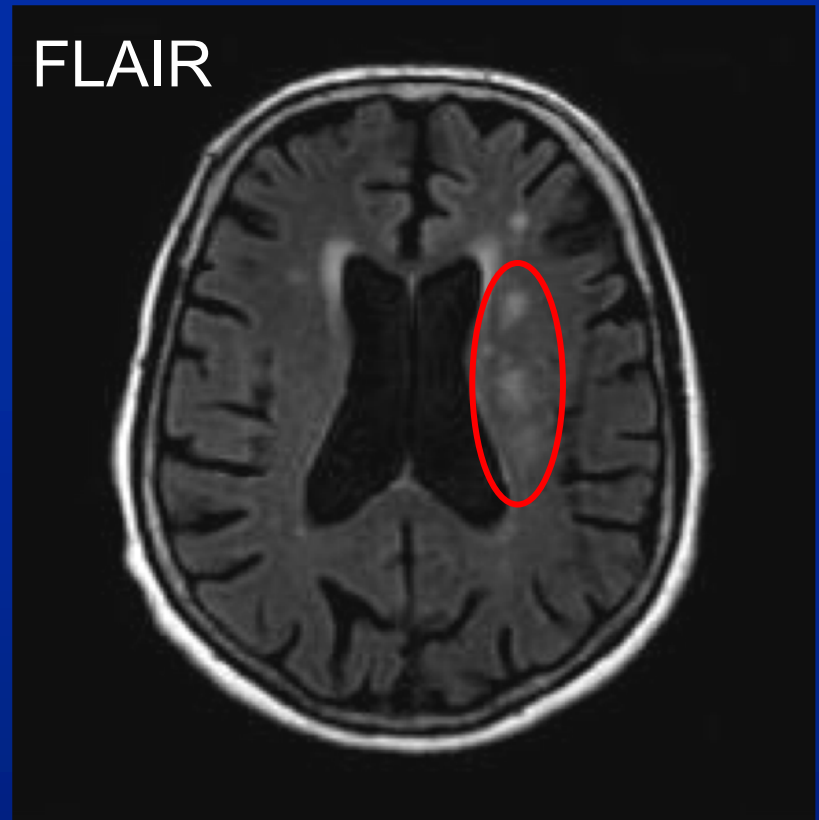
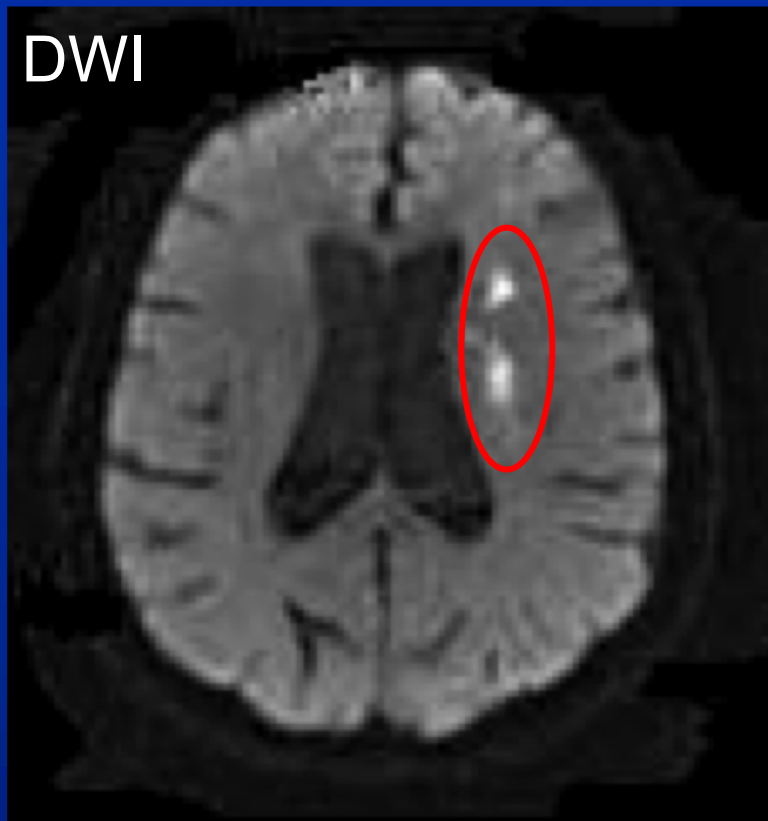


(With Courtesy by Prof. G. Thomalla)

The diffusion restriction (left) is not already visible in the FLAIR image (right), making the patient „FLAIR negative“

Inclusion into the WAKE-UP study





(With Courtesy by Prof. G. Thomalla)

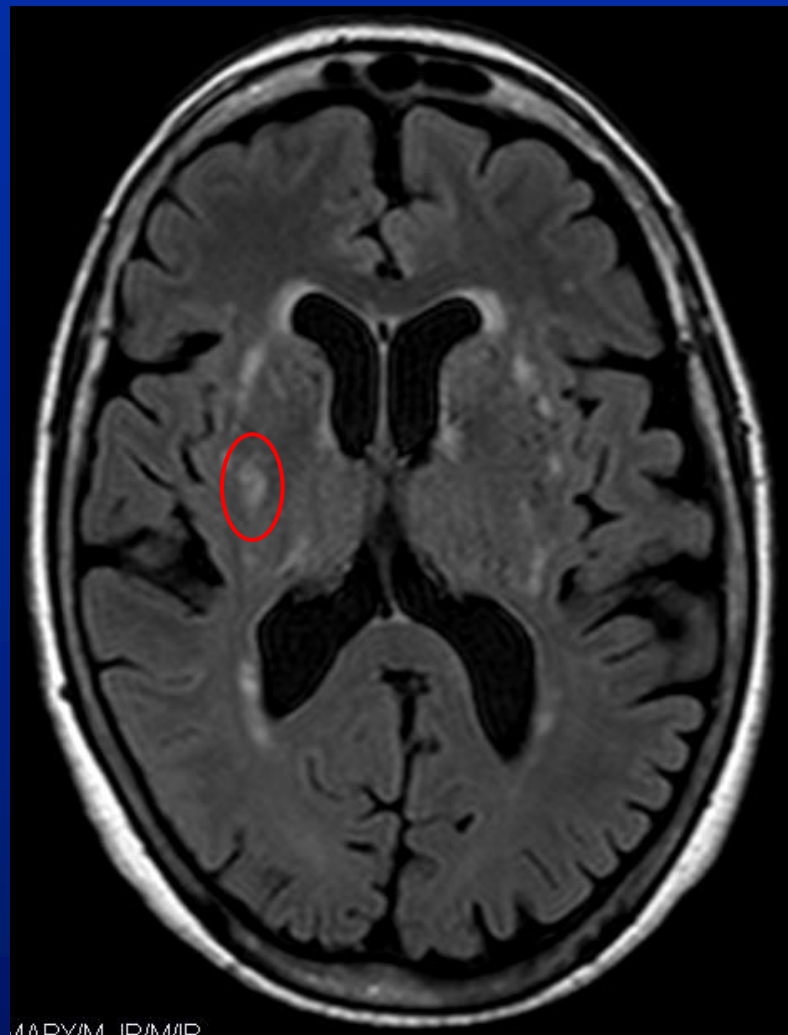
The diffusion restriction (left) is already visible in the FLAIR image (right), making the patient „FLAIR positive“

Exclusion from the WAKE-UP study





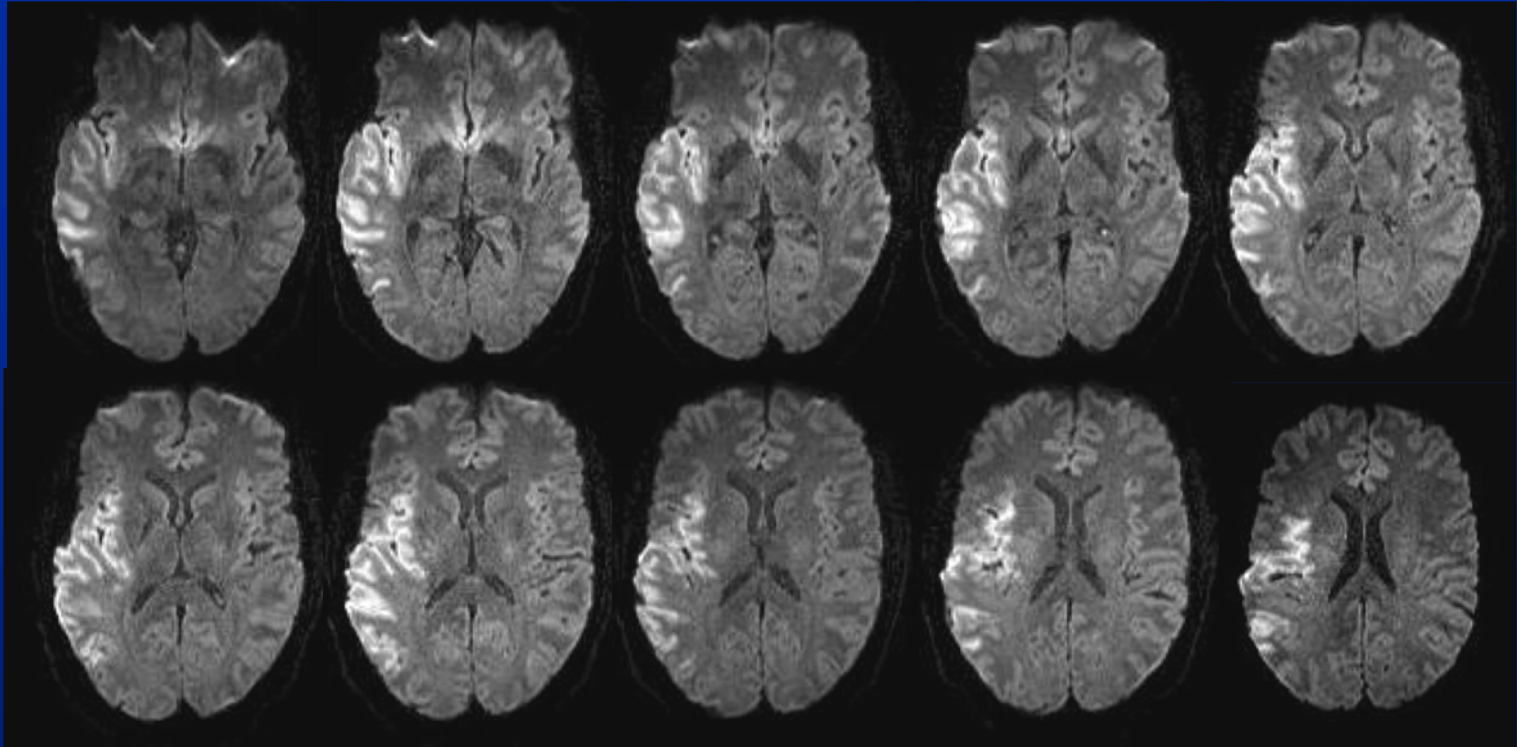
DWI



FLAIR



Estesa lesione ischemica in DWI



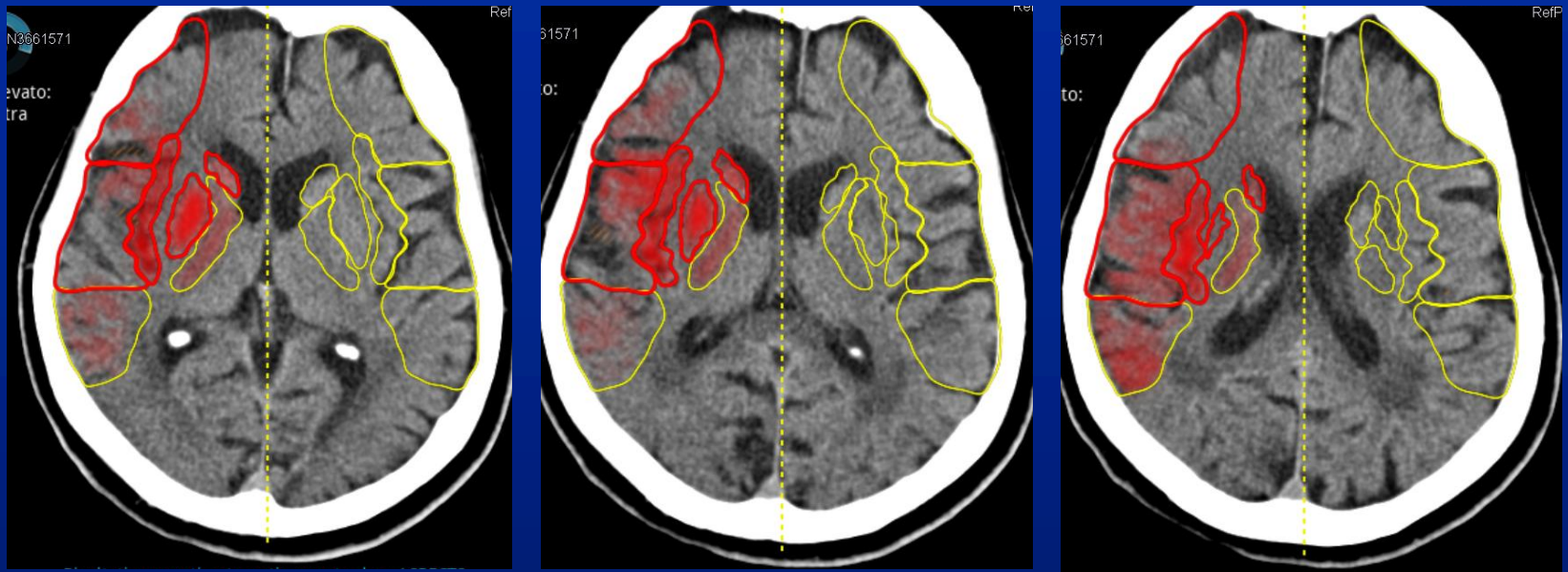
(With Courtesy by Prof. G. Thomalla)

DWI lesion is mainly cortical yet encompassing more than 1/3 of the MCA-territory

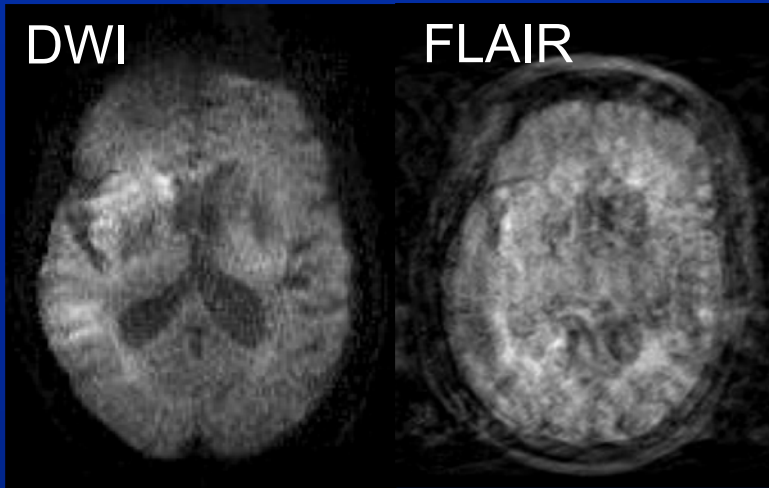
Exclusion from the WAKE-UP study



Estese alterazioni ischemiche acute all'esame TC Cranio diretto (ASPECTS 3 calcolato automaticamente con SW di AI)



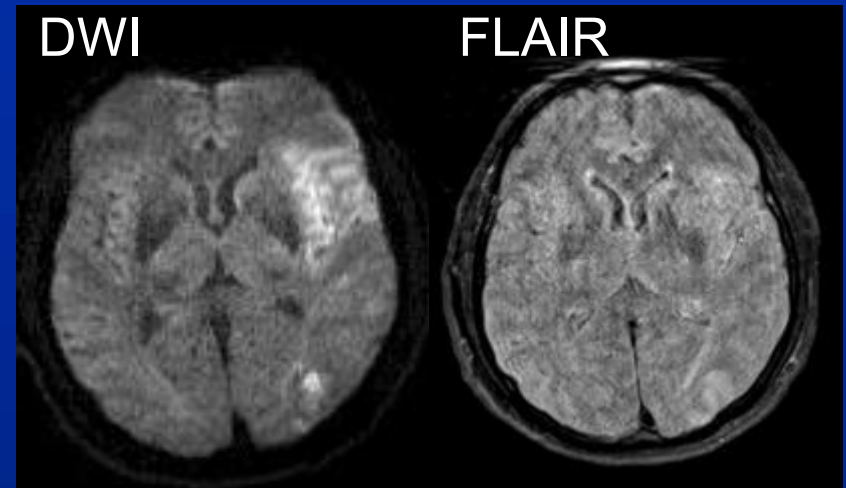
Immagini di scarsa qualità-Artefatti



(With Courtesy by Prof. G. Thomalla)

Bad quality images (both DWI and FLAIR) due to patient movement

Exclusion from the WAKE-UP study

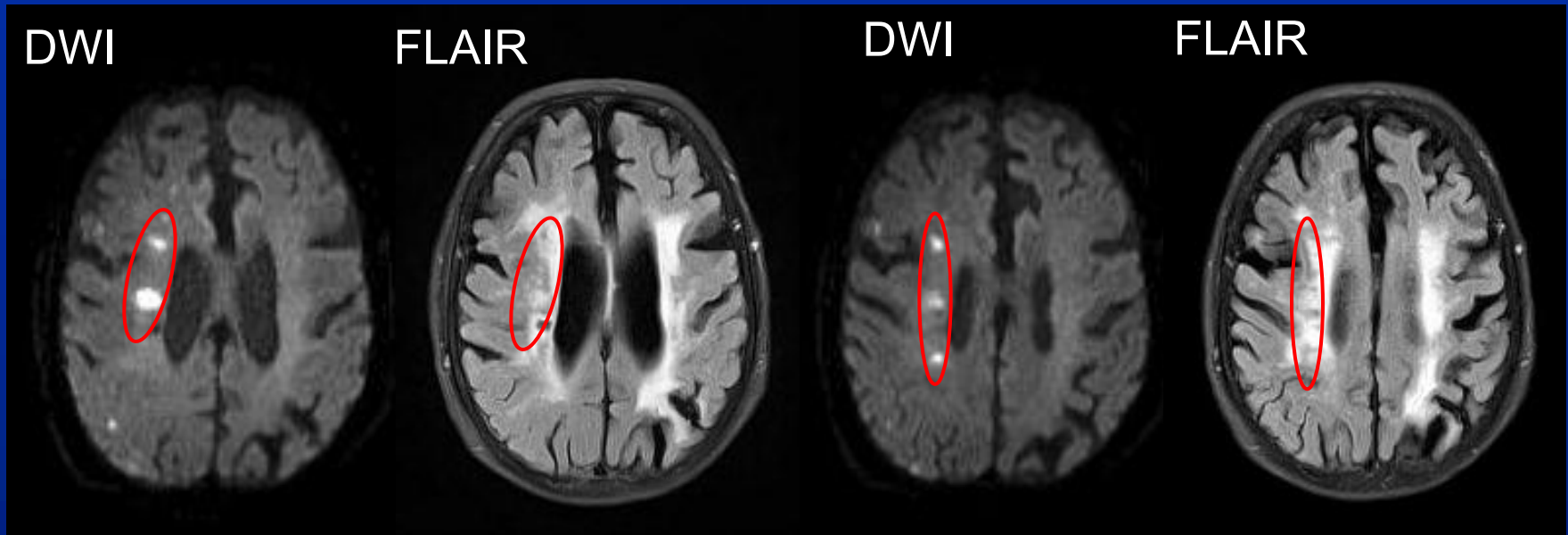


Bad quality images (only FLAIR) due to patient movement

Exclusion from the WAKE-UP study



Leucoaraiosi



(With Courtesy by Prof. G. Thomalla)

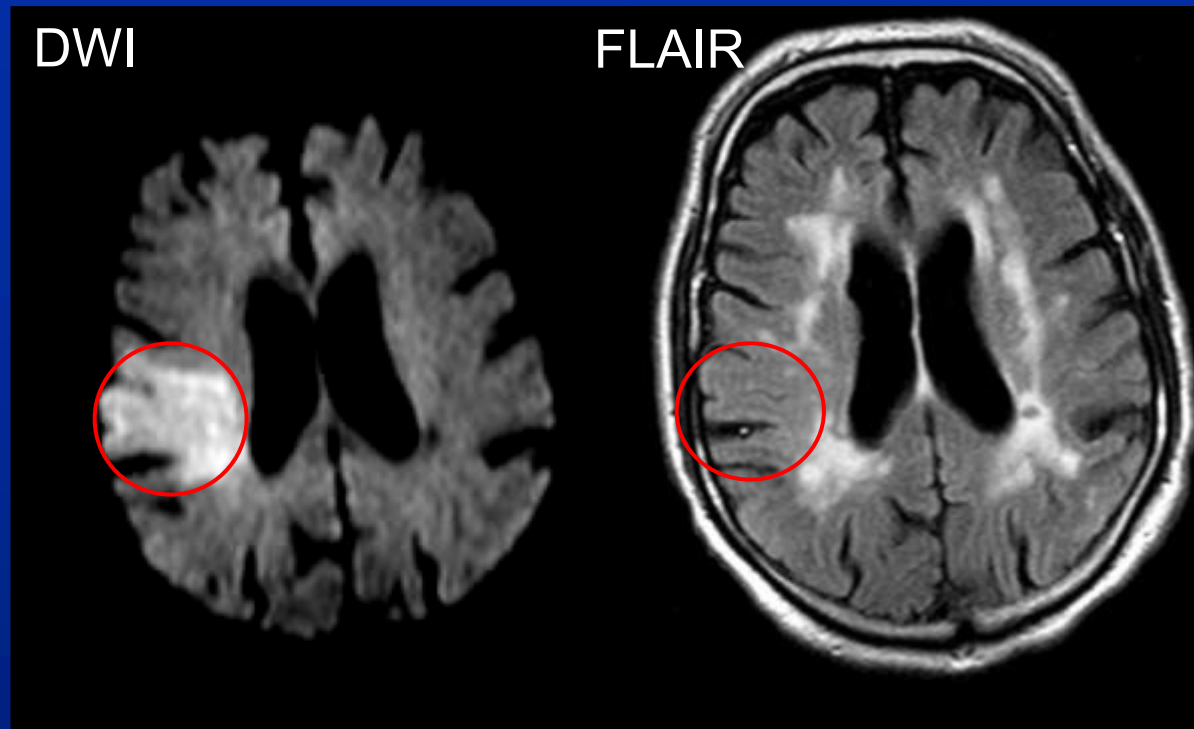
Scattered right, mostly subcortical MCA-territory ischemic stroke

DWI lesions appear in the area of extensive leukoaraiosis and an old lacunar stroke, making visibility difficult to judge in a reliable fashion

Exclusion from the WAKE-UP study



Leucoaraiosi



(With Courtesy by Prof. G. Thomalla)

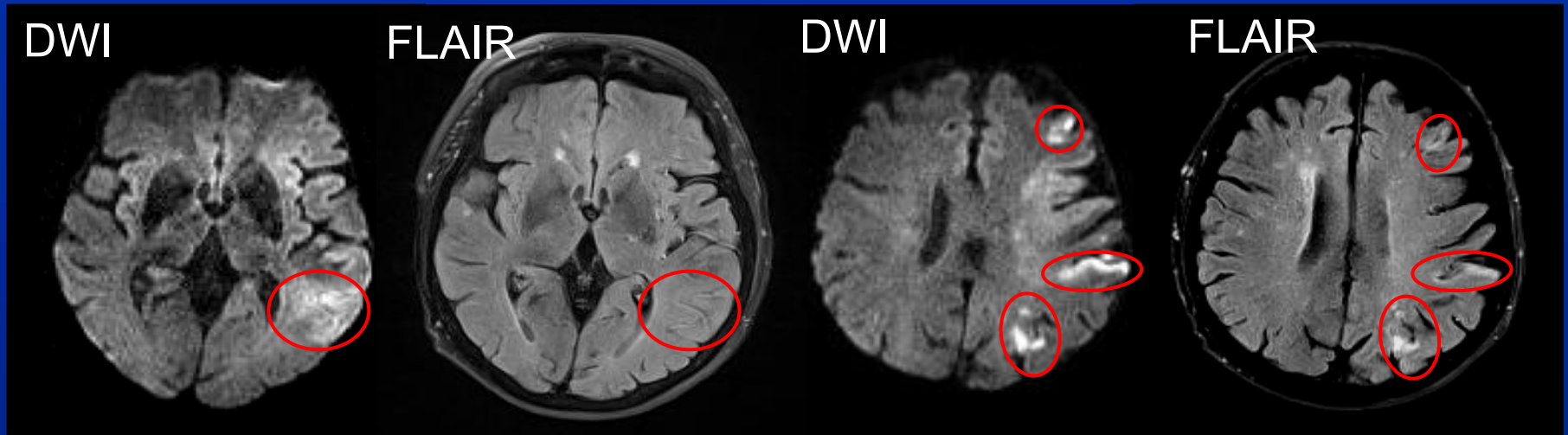
Right-sided MCA-territory ischemic stroke

Although the DWI lesion appears in the area of leukoaraiosis, large portions of the lesion are outside the white matter changes making FLAIR visibility reliable to judge

Inclusion into the WAKE-UP study



FLAIR negativa-FLAIR positiva



(With Courtesy by Prof. G. Thomalla)

Left-sided MCA-territory stroke.

Higher cortical slices showing lesions which are visible in the FLAIR (G. frontalis medius, postcentralis and angularis) whereas lower slices (insula and temporal lobe) are clearly not yet visible in the FLAIR) signaling that this is a time distributed event! If any segment of the acute ischemic lesion is visible in the FLAIR, the patient is considered „FLAIR positive“

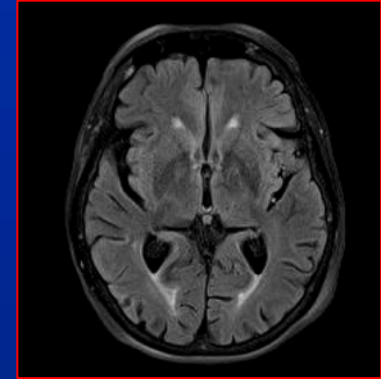
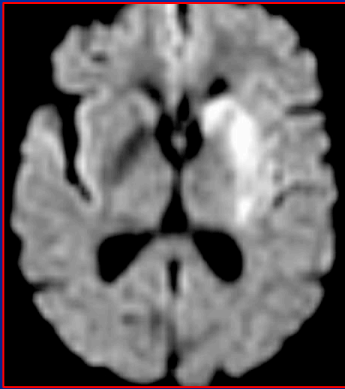
Exclusion from the WAKE-UP study



Imaging: Criteri di Inclusione e Criteri di Esclusione

- Principale criterio di inclusione:
«DWI-FLAIR- Mismatch»= nessuna iperintensità visibile in FLAIR nell'area della lesione visibile in DWI
- Escludere Pazienti con estesa lesione in DWI o estesa lesione alla TC diretta (ASPECTS basso)
- Escludere Pazienti con marcata leucoaraiosi
- Escludere esami di scarsa qualità (artefatti)

Ictus a insorgenza non nota: Il punto di vista del Clinico



Grazie!

