# IRM dans la SEP: Faut-il injecter?

Thomas Tourdias [1, 2]
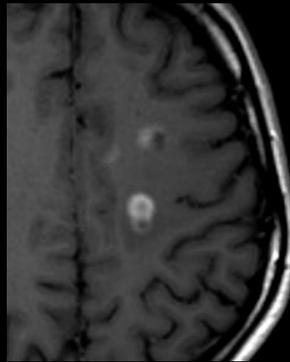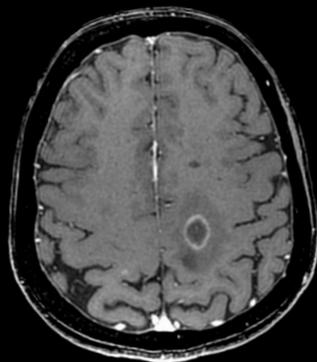
(1) Service de NeuroImagerie Diagnostique et Thérapeutique, CHU Bordeaux, Université de Bordeaux
(2) Neurocentre Magendie, INSERM U 1215, Université de Bordeaux

# Gadolinium et inflammation

Barrière intacte

Jonction serrée

Pied astrocytaire
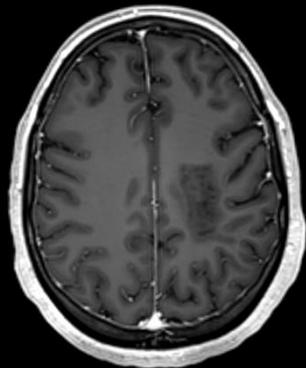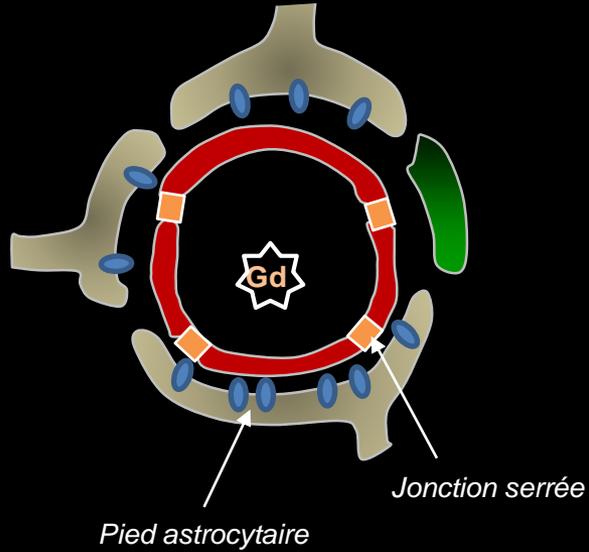
Gadolinium et inflammation

Barrière intacte
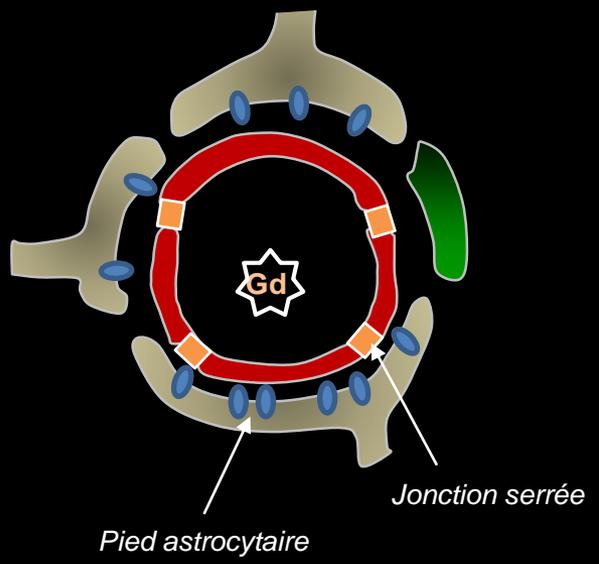
Barrière "altérée", inflammation

Jonction serrée

Pied astrocytaire
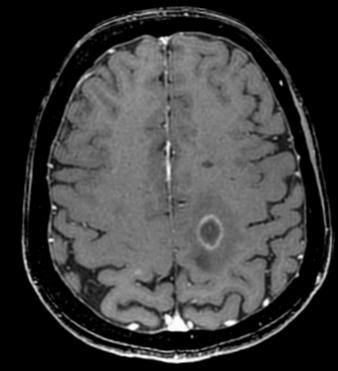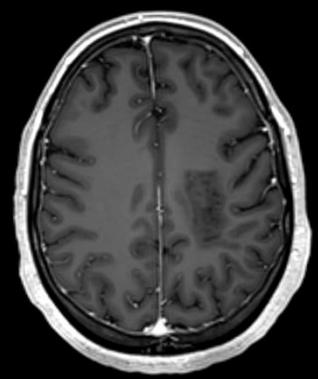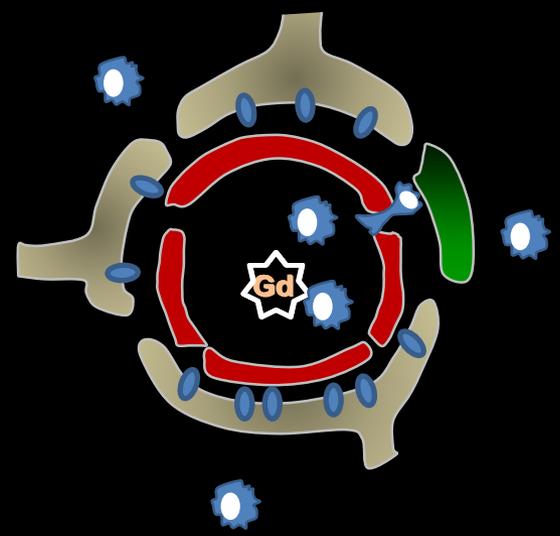
Gadolinium = marqueur de la composante inflammatoire

Les séquences injectées sont recommandées
CIS ou suivi de SEP

REVIEW

OFSEP, a nationwide cohort of people with multiple sclerosis: Consensus minimal MRI protocol

F. Cotton [a,*,b], S. Kremer [c], S. Hannoun [b], S. Vukusic [d], V. Dousset [e,f,g], for the Imaging Working Group of the ''Observatoire français de la sclérose en plaques'' (OFSEP)

Cotton *et al.* J neuroradiol 2015;42:133-40

- 3D T1 sans injection
- Diffusion
- 3D T2

Injection

- 3D FLAIR
- 3D T1 post injection

EVIDENCE-BASED GUIDELINES

MAGNIMS consensus guidelines on the use of MRI in multiple sclerosis—establishing disease prognosis and monitoring patients

Mike P. Wattjes, Àlex Rovira, David Miller, Tarek A. Yousry, Maria P. Sormani, Nicola de Stefano, Mar Tintoré, Cristina Auger, Carmen Tur, Massimo Filippi, Maria A. Rocca, Franz Fazekas, Ludwig Kappos, Chris Polman, Frederik Barkhof and Xavier Montalban on behalf of the MAGNIMS study group

Wattjes *et al.* Nature Reviews Neurology 2015;11:597-606

Anatomic 3D inversion recovery–prepared T1 gradient echo (eg, 1.0- to 1.5-mm thickness)
Gadolinium single dose, 0.1 mmol/kg given for 30 seconds[a]
3D sagittal T2WI FLAIR[b] (eg, 1.0- to 1.5-mm thickness)
3D T2WI [b] (eg, 1.0- to 1.5-mm thickness)
2D axial DWI (≤5-mm sections, no gap)
3D FLASH (non-IR prep) postgadolinium[b] (eg, 1.0- to 1.5-mm thickness)
3D series would be typically reconstructed to 3-mm thickness for display and subsequent comparison for lesion counts

Traboulsee *et al.* AJNR 2015;Nov 2 [Epub ahead of print]

Faut-il injecter?

Un nouveau risque potentiel?

Une information importante: produit théranostique

# Un risque potentiel?

Accumulation intracérébrale de gadolinium

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Drug Safety Communications

FDA evaluating the risk of brain deposits with repeated use of gadolinium-based contrast agents for magnetic resonance imaging (MRI)

ORIGINAL RESEARCH ■ **NEURORADIOLOGY**

High Signal Intensity in the Dentate Nucleus and Globus Pallidus on Unenhanced T1-weighted MR Images: Relationship with Increasing Cumulative Dose of a Gadolinium-based Contrast Material[1]
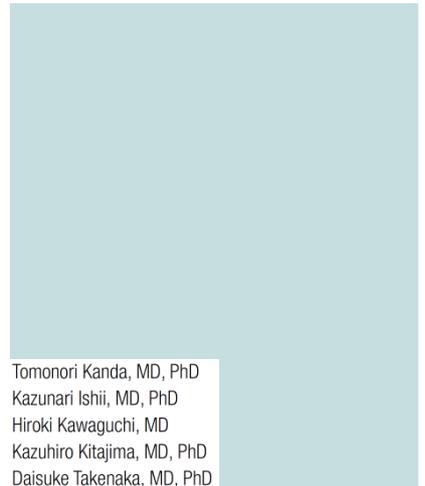
Tomonori Kanda, MD, PhD
Kazunari Ishii, MD, PhD
Hiroki Kawaguchi, MD
Kazuhiro Kitajima, MD, PhD
Daisuke Takenaka, MD, PhD

radiology.rsna.org ■ **Radiology:** Volume 270: Number 3—March 2014

Radiology

Un risque potentiel?

Accumulation intracérébrale de gadolinium

n=381

Kanda *et al*. Radiology 2014; 270:834-41

Errante *et al*. Invest Radiol 2014; 49:685-90
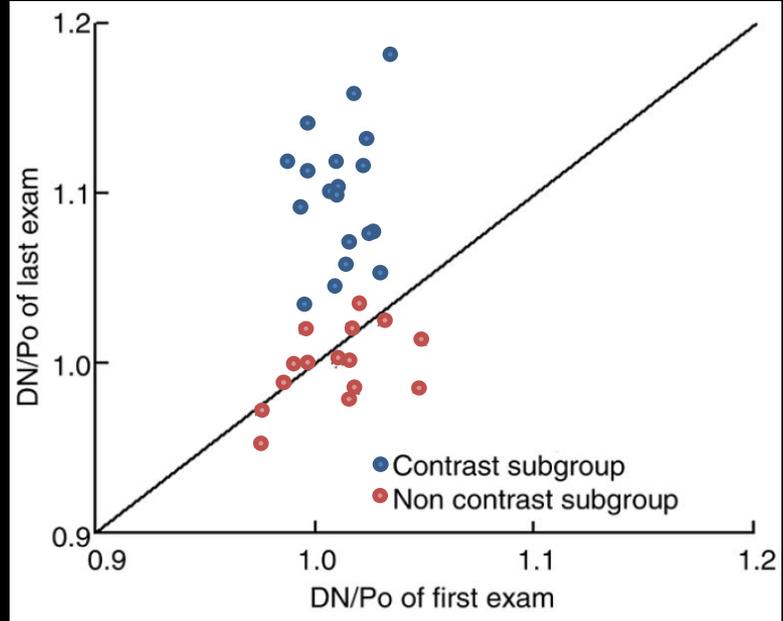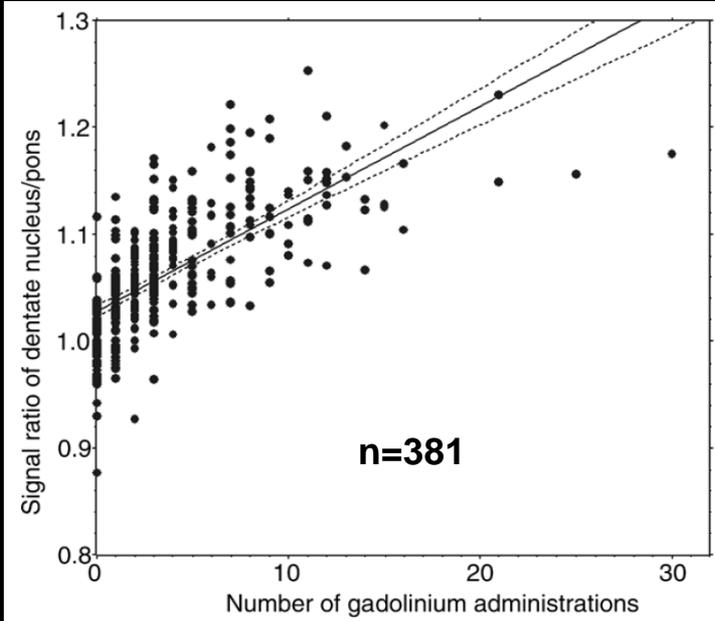
Un risque potentiel?

Accumulation intracérébrale de gadolinium

Linéaires
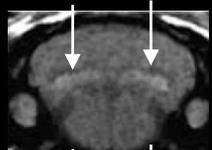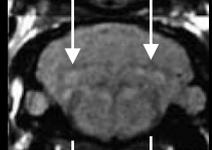
Macrocycliques

Kanda *et al.* Radiology 2015; 275:803-809
Radbruch *et al.* Radiology 2015; 783-91

Un risque potentiel?

Accumulation intracérébrale de gadolinium

Robert *et al.* Invest Radiol 2015; 50:473-80
Robert *et al.* Invest Radiol 2015; 51:73-82

Un risque potentiel?

Accumulation intracérébrale de gadolinium

Gd intracérébral

McDonald *et al*. Radiology 2015; 275:772-82
Kanda *et al*. Radiology 2015; 276:228-32

Un risque potentiel?

Accumulation intracérébrale de gadolinium

Gd intracérébral

McDonald *et al.* Radiology 2015; 275:772-82
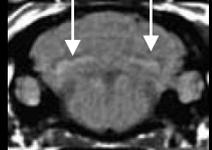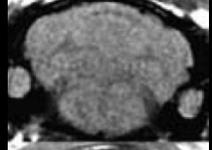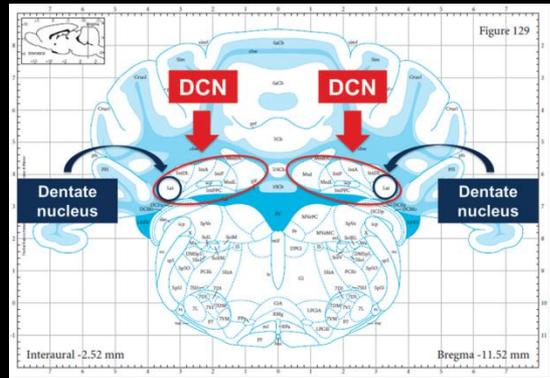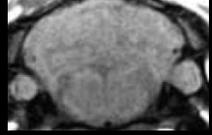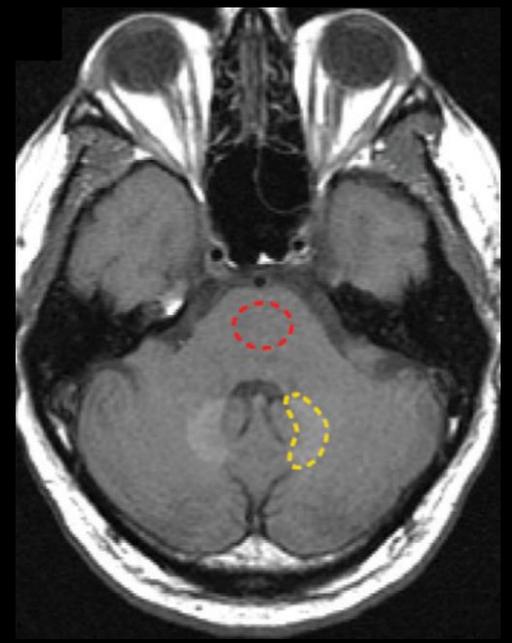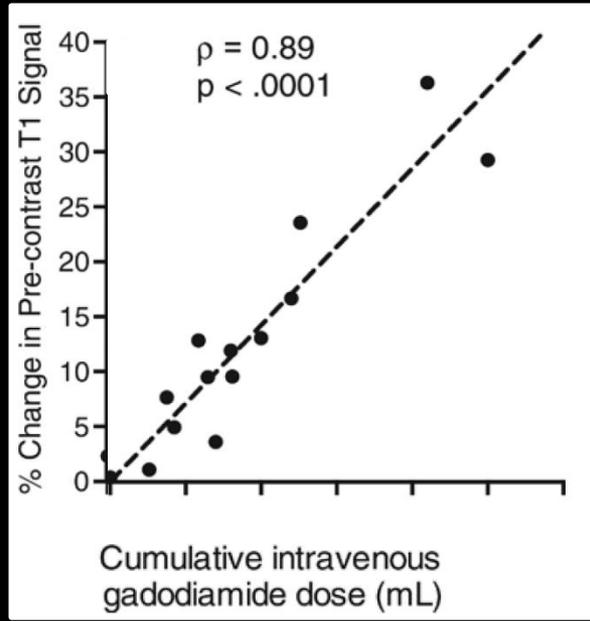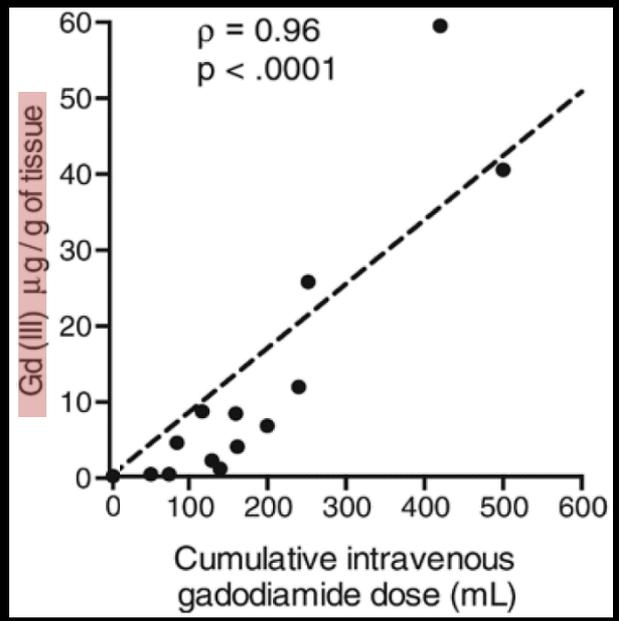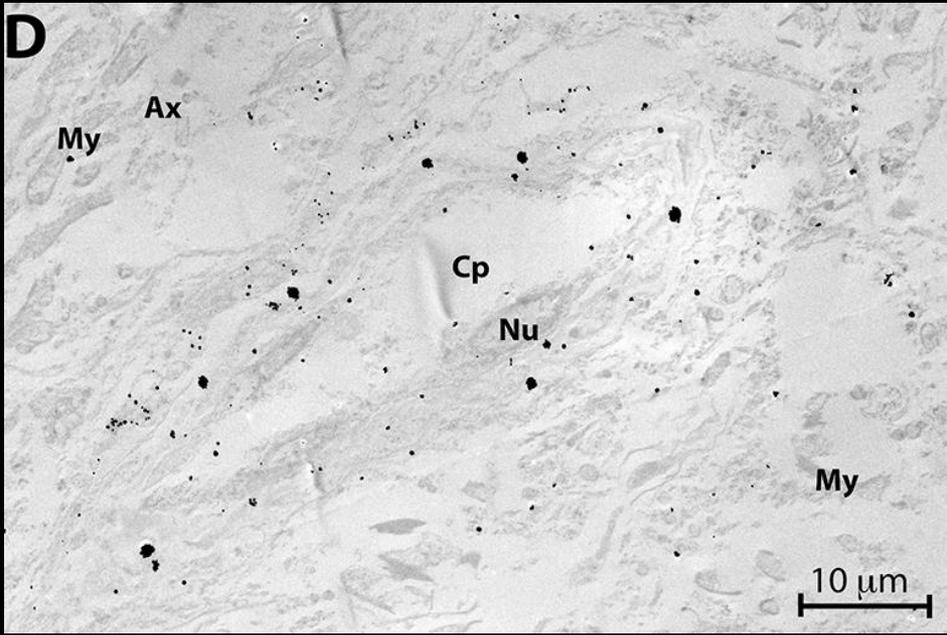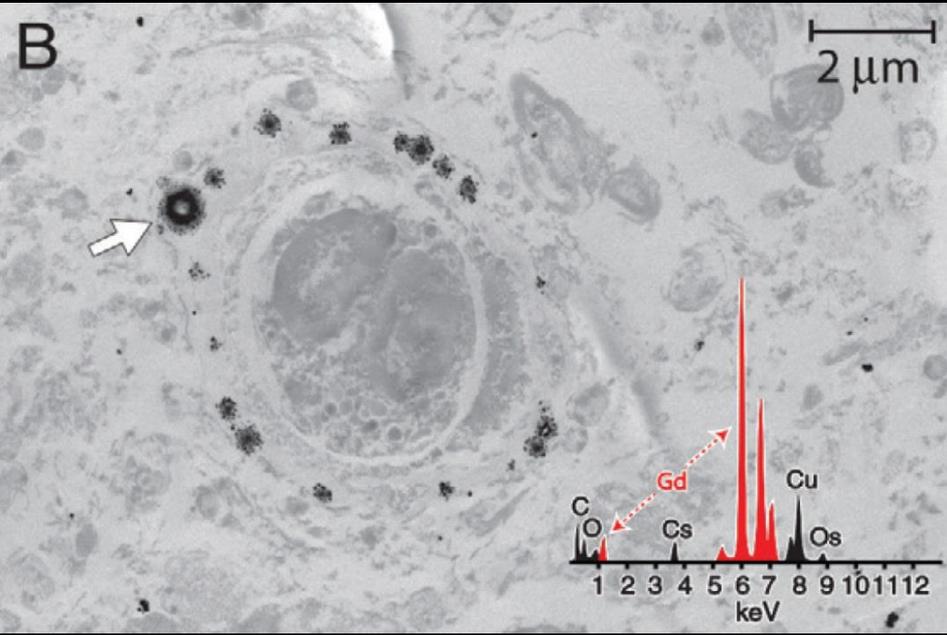
Un risque potentiel?

Accumulation intracérébrale de gadolinium

- ***<u>Fonction rénale normale</u>*** (≠ fibrose systémique néphrogénique).

- ***<u>Pas de wash-out</u>*** (effet cumulatif).
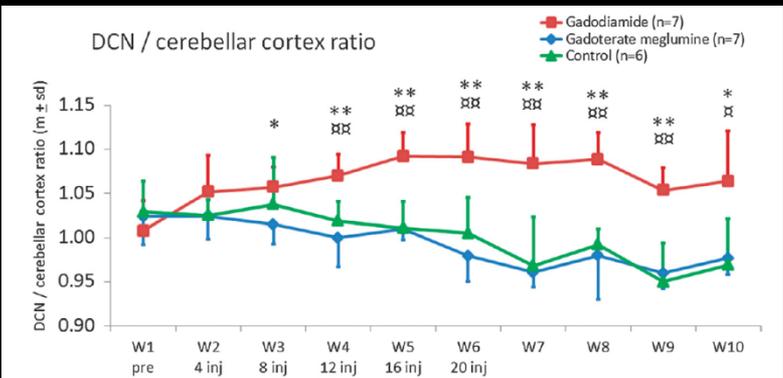
McDonald *et al.* Radiology 2015; 275:772-82
Robert *et al.* Invest Radiol 2015; 50:473-80

- ***<u>En dehors de pathologie cérébrale</u>*** (BHE intacte).

Kanda *et al.* Radiology 2015; 276:228-32
McDonald *et al.* Radiology 2015; 275:772-82

Un risque potentiel?
Accumulation intracérébrale de gadolinium

- ***Passage de Gd libre non chélaté??***
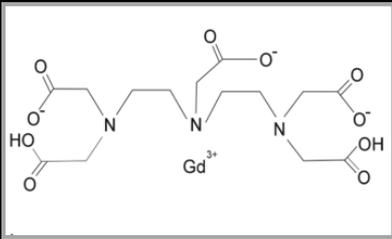
Kanda *et al.* Radiology 2015; 275:803-809
Radbruch *et al.* Radiology 2015; 783-91

- ***Toxicité??***

- ***Pas de démonstration histologique d'altération tissulaire.***
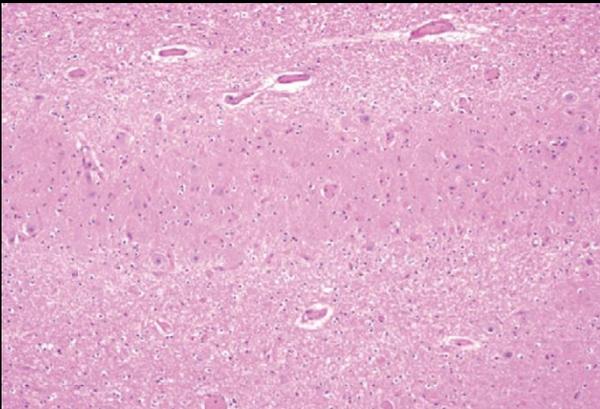
McDonald *et al.* Radiology 2015; 275:772-82

- ***Pas d'élément sur le retentissement clinique.***

Un risque potentiel?

Accumulation intracérébrale de gadolinium

Multiple Sclerosis: Hyperintense Dentate Nucleus on Unenhanced T1-weighted MR Images Is Associated with the Secondary Progressive Subtype[1]

Radiology

Luca Roccatagliata, MD, PhD
Luisa Vuolo, MD
Laura Bonzano, PhD
Anna Pichiecchio, MD
Giovanni Luigi Mancardi, MD

Radiology: Volume 251: Number 2—May 2009

Absinta *et al.* AJNR 2011; 32:E120-1
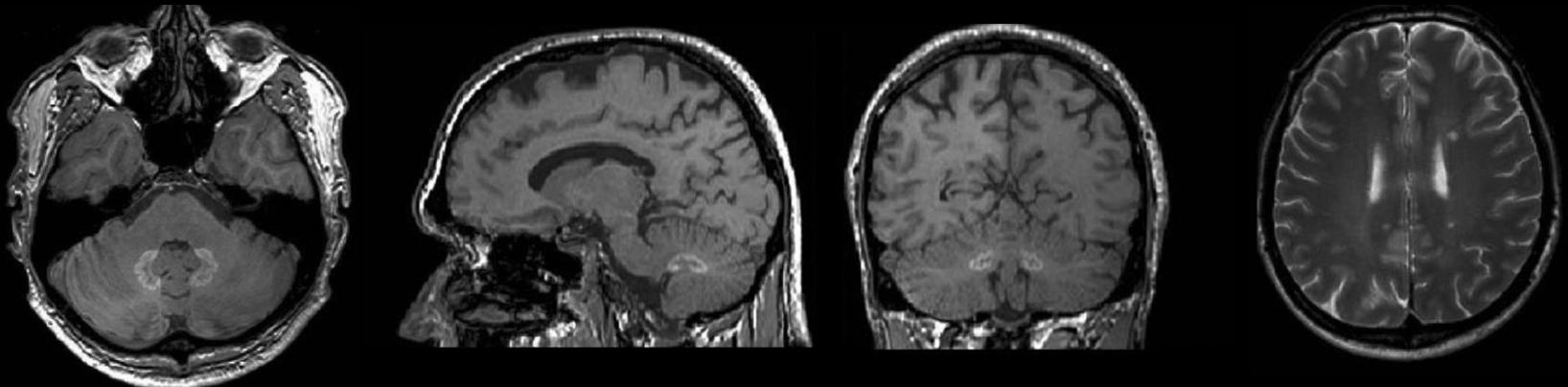
Faut-il injecter?

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Une information importante: produit théranostique

Residual or Retained Gadolinium: Practical Implications for Radiologists and Our Patients[1]

Emanuel Kanal, MD
Michael F. Tweedle, PhD

Une forte actualité thérapeutique

INJECTION

- Glatiramere acetate (Copaxone®) – 1996
- Interferon β-1a (Avonex®) – 1996
- Interferon β-1a (Rebif®) – 1998
- Interferon β-1b (Betaseron®) – 1993
- Interferon β-1b (Extavia®) – 2009
- Interferon β-1a pegylé (Plegridy®) – 2014

ORAL

- Dimethyl fumarate (Tecfidera®) – 2013
- Finfolimod (Gilenya®) – 2010
- Teriflunomide (Aubagio®) – 2012

PERFUSION

- Alemtuzumab (Lemtrada®) – 2014
- Mitoxantrone (Novantrone®) – 2000
- Natalizumab (Tysabri®) - 2006

TRENDS in Pharmacological Sciences
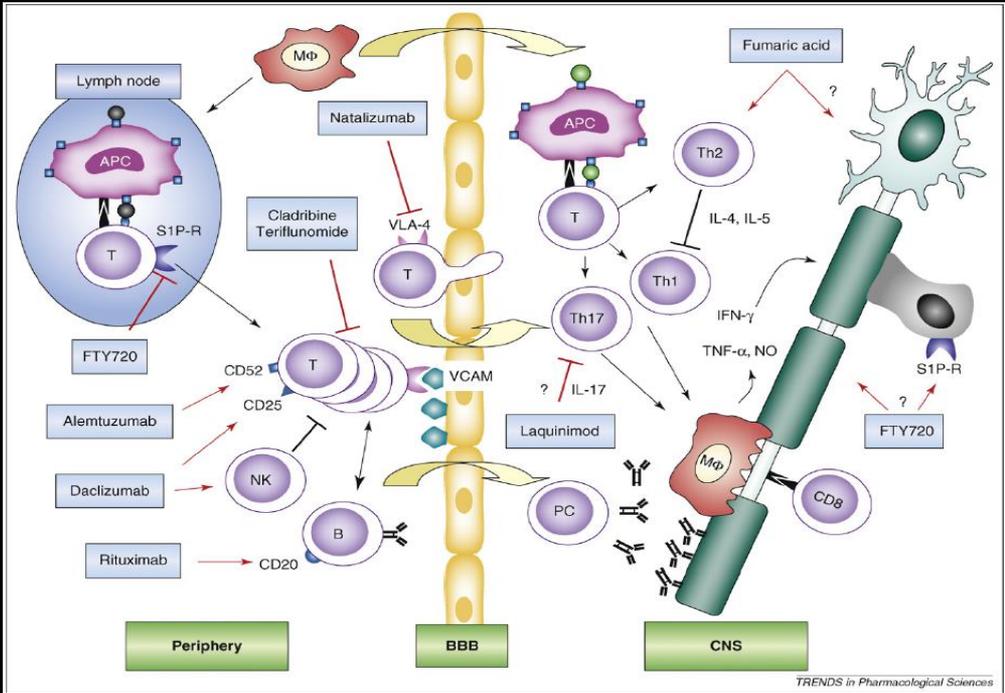
Théranostique **= diagnostique + thérapeutique**
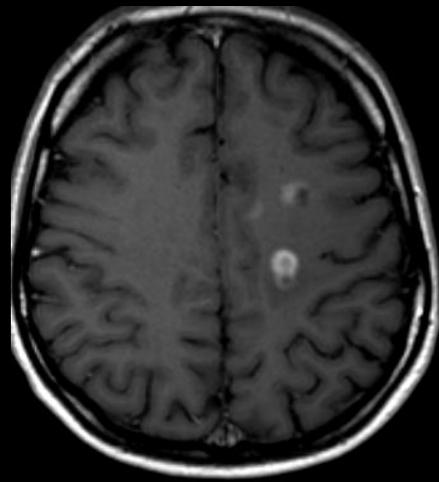
Guide le choix
thérapeutique
Efficacité - Tolérance

# Imagerie et thérapeutique
Diagnostic et traitement précoce

Diagnostic Criteria for Multiple Sclerosis: 2010 Revisions to the McDonald Criteria

Rovira *et al.* Arch Neurol 2009;66:587-92
Polman *et al.* Ann Neurol 2011;69:292-302

DISSEMINATION dans le *TEMPS*
- Lésions Gd- et Gd+ simultanées
- ≥1 nouvelle lésion T2 *au suivi*

Ziemssen *et al.* J Neurol 2015;Dec24
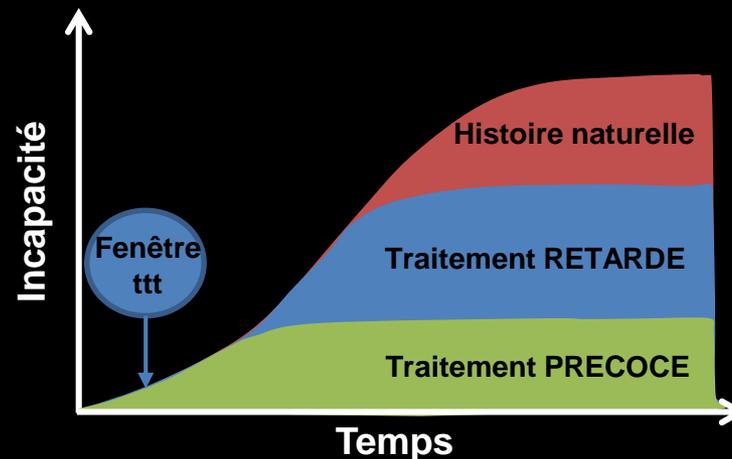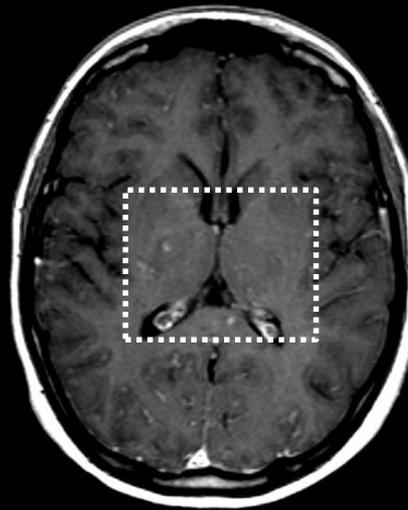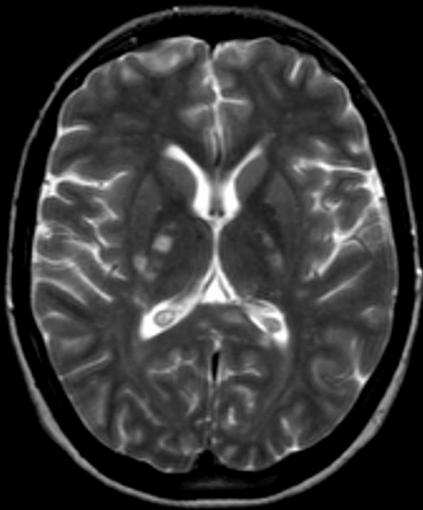
Imagerie et thérapeutique

Adaptation thérapeutique

VIEWS & REVIEWS

Defining the clinical course of multiple sclerosis

The 2013 revisions

Lublin *et al.* Neurology 2014; 83:278-86

**Phénotype SEP
Version 1996**

RRMS

**Phénotype SEP
Révision 2013**

RRMS → **Active ***

→ **Non active**

***: clinique et/ou nouvelle lésion T2, gadolinium**

- *NEDA: "No evidence of disease activity"*
  - *Pas de poussée,* pas de progression de l'EDSS
  - *Pas de nouvelle lésion T2 ou de lésion active aprés gadolinium*

Incapacité

Histoire naturelle

Fenêtre ttt

Fenêtre ttt

Fenêtre ttt

Traitement RETARDE

Traitement PRECOCE

Temps

Ziemssen *et al.* J Neurol 2015;Dec24
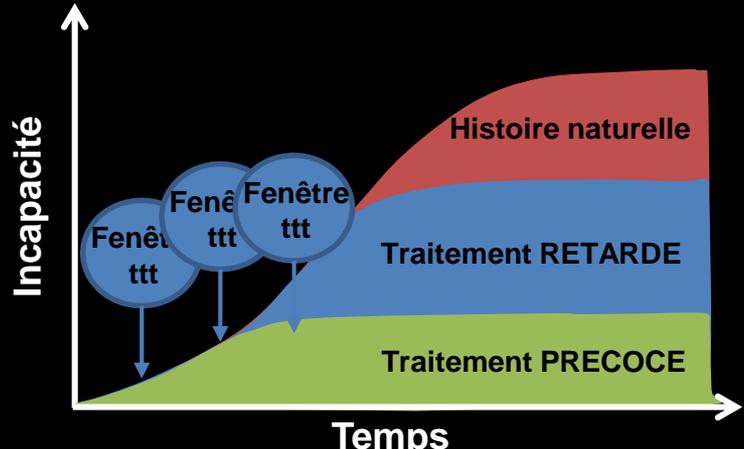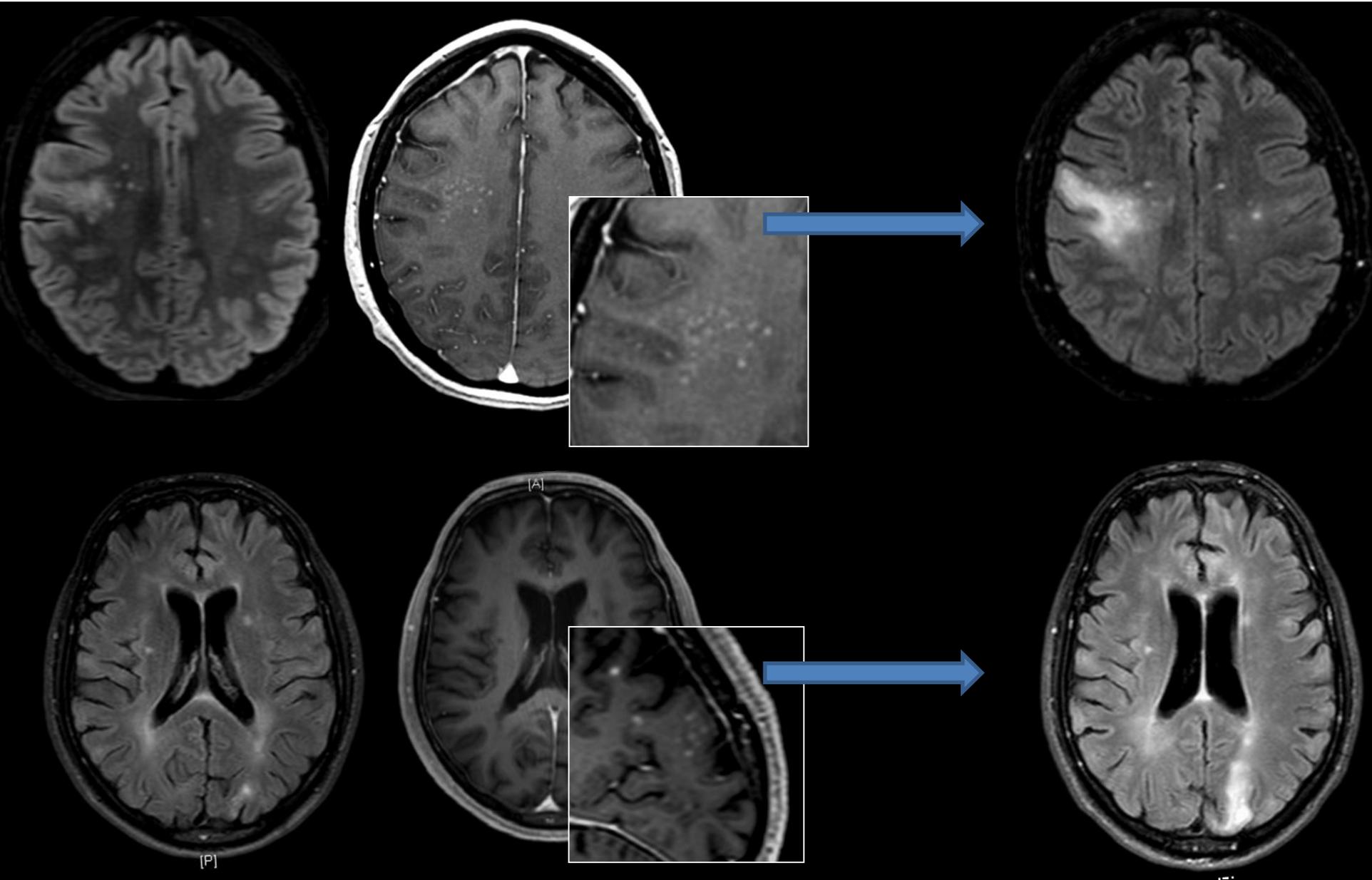
Imagerie et thérapeutique
Essais cliniques

Phase	Objective
I	Define safety, toxicity profile and maximal tolerated dose of agent
II	Determine efficacy of the agent
III	Compare new agent to standard therapy or placebo
IV	Define long-term and rare effects, effects in different patient populations

- *Modulateurs sélectifs des récepteurs de la sphingosine-1-phosphate: ozanimod*

	Placebo (n=88)	Ozanimod 0·5 mg (n=87)	Ozanimod 1 mg (n=83)
MRI outcomes			
Mean (SD) cumulative number of gadolinium-enhancing lesions, weeks 12–24 (primary endpoint)	11·1 (29·9)	1·5 (3·7)	1·5 (3·4)
Odds ratio (95% CI) *vs* placebo	··	0·16 (0·08–0·30); p<0·0001	0·11 (0·06–0·21); p<0·0001
Mean (SD) number of gadolinium-enhancing lesions, week 24 (secondary endpoint)	3·2 (9·8)	0·3 (0·9)	0·2 (0·6)
Odds ratio (95% CI) *vs* placebo	··	0·16 (0·07–0·34); p<0·0001	0·06 (0·02–0·15); p<0·0001
Mean (SD) cumulative number of new or enlarging T2 lesions, weeks 12–24 (secondary endpoint)	9·0 (20·9)	1·4 (3·2)	0·8 (1·9)
Odds ratio (95% CI) *vs* placebo	··	0·17 (0·10–0·30); p<0·0001	0·08 (0·04–0·14); p<0·0001
Clinical outcome			
Mean (95% CI) annualised relapse rate (secondary endpoint)*	0·5 (0·2–1·2)	0·35 (0·2–0·8)	0·24 (0·1–0·6)
Odds ratio (95% CI) *vs* placebo	··	0·69 (0·36–1·34); p=0·2714	0·47 (0·22–1·01); p=0·0531

Cohen *et al.* Lancet Neurology 2016; 15:373-81

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Residual or Retained Gadolinium: Practical Implications for Radiologists and Our Patients[1]

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Radiology: Volume 275: Number 3—June 2015

CrossMark

REVIEW

Advances in and Algorithms for the Treatment of Relapsing-Remitting Multiple Sclerosis

Jens Ingwersen[1] · Orhan Aktas[1] · Hans-Peter Hartung[1]

- ## *Quantification T1/T2/DP*

 **Blystad *et al.* AJNR 2016; 37:94-100**
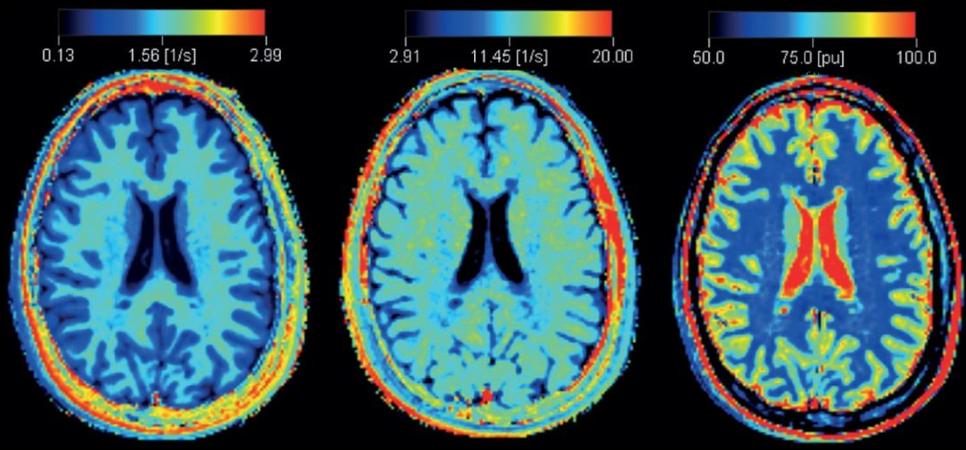
- ## *DBSI diffusion basis spectrum imaging*

  Wang *et al.* Brain 2015; 138:1223-38
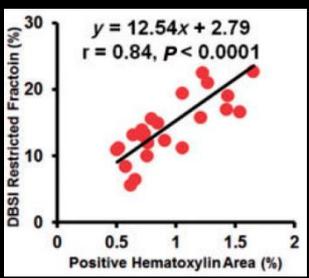
- ## *Phase à très haut champs*

 **Absinta *et al.* Ann Neurol 2013; 74:669-78**
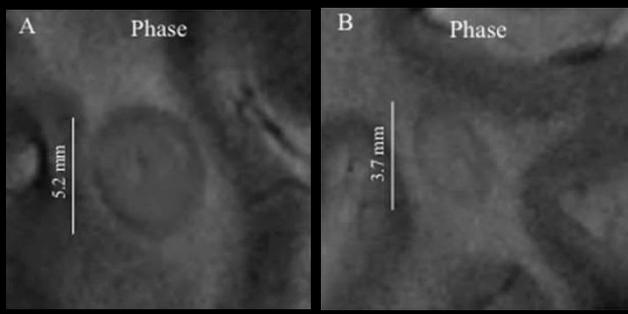
Identification de l'activité sans injection

## Evolution de la charge lésionnelle T2

IRM initiale

IRM de suivi à 3 mois
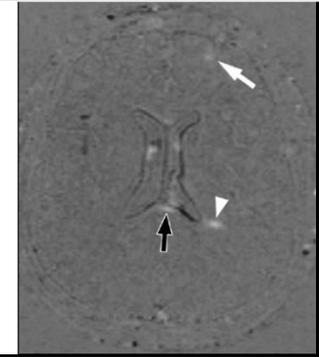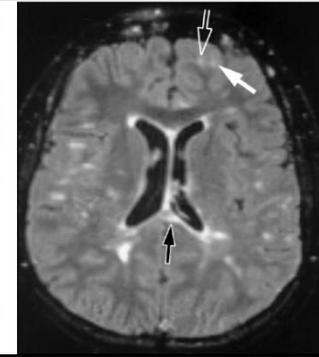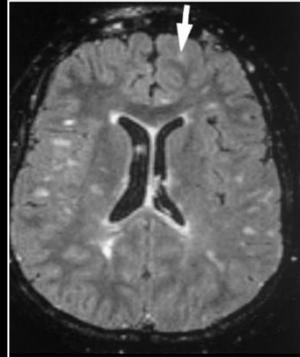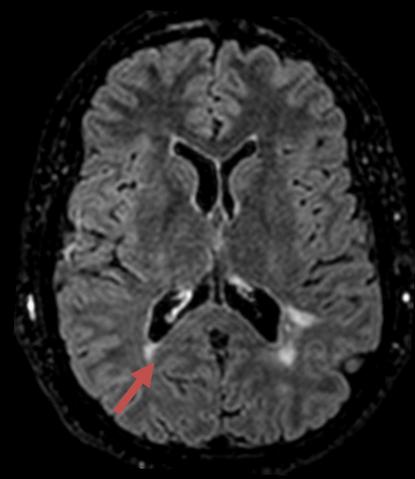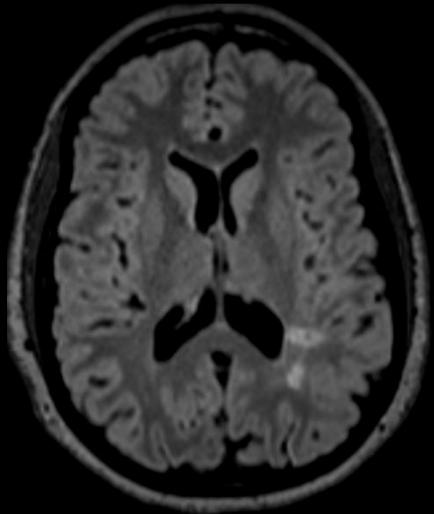
Moraal et al. Radiology 2010; 255:154-63
Battaglini et al. 2014; 39:1543-49
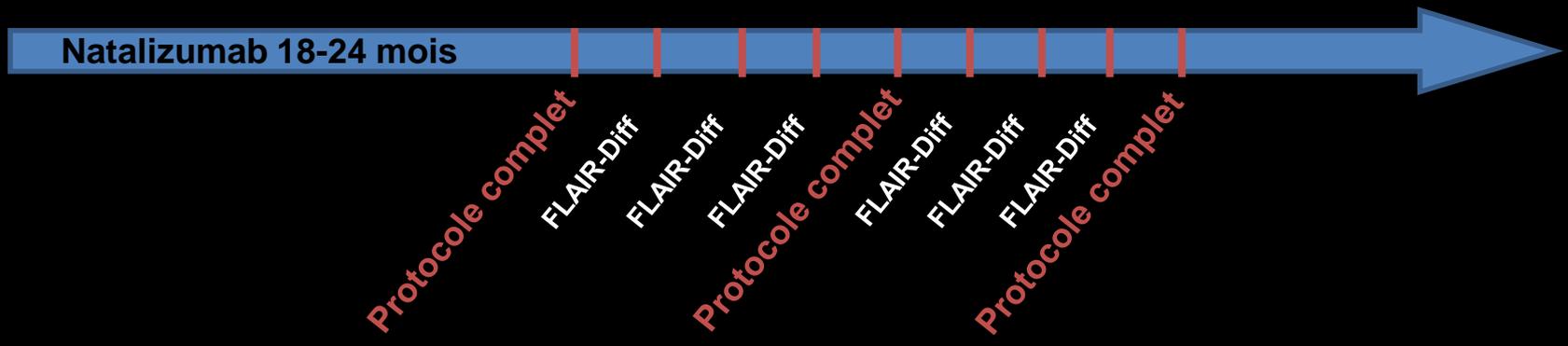
Natalizumab 18-24 mois

Protocole complet
FLAIR-Diff
FLAIR-Diff
FLAIR-Diff
Protocole complet
FLAIR-Diff
FLAIR-Diff
FLAIR-Diff
Protocole complet

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Radiology

Neurotherapeutics (2016) 13:47–57
DOI 10.1007/s13311-015-0412-4

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Jens Ingwersen[1] · Orhan Aktas[1] · Hans-Peter Hartung[1]

MERCI…
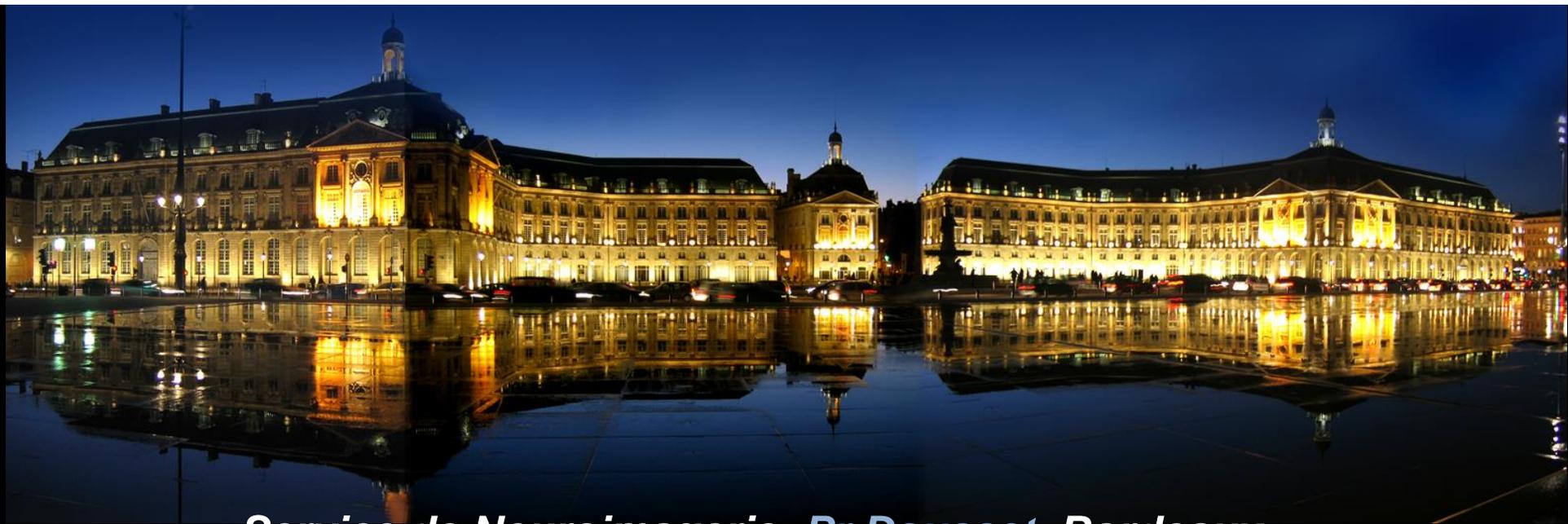
Service de Neuroimagerie: *Pr Dousset, Bordeaux*
X.Barreau; A. Bigourdan; J.Berge; E.De Roquefeuil;
JP. Lafourcade; G.Marnat; S. Molinier; P.Ménégon

Neurocentre Magendie INSERM U862; *Dr Oliet, Bordeaux*