Cours nationaux de radiothérapie SFJRO 11 mars 2017

Evaluation de la réponse thérapeutique après radiothérapie stéréotaxique intracrânienne

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Gustave Roussy

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Evaluation post thérapeutique

Métastases cérébrales

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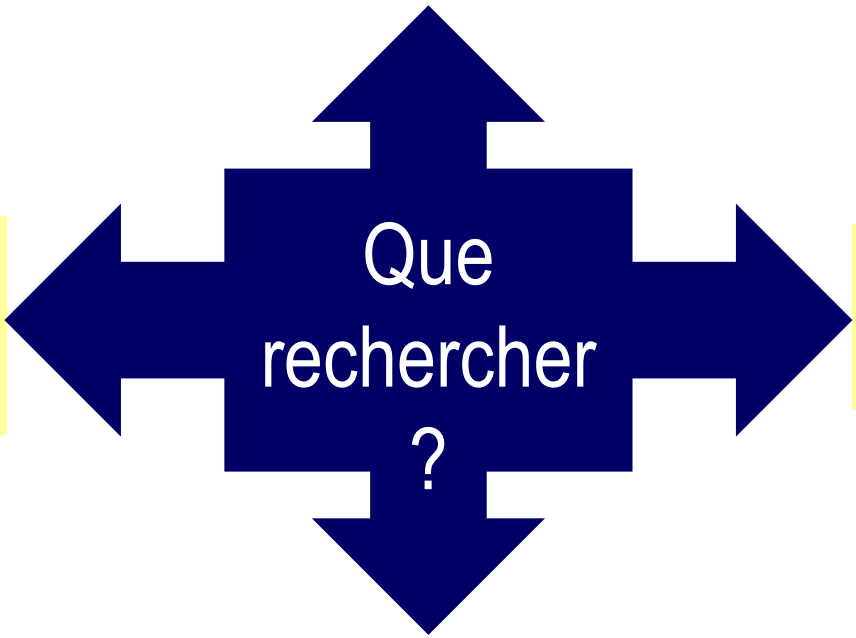
Evaluation post-thérapeutique MC

PROGRESSION

RADIONECROSE



NOUVELLES LESIONS

TRANSFORMATION HEMORRAGIQUE

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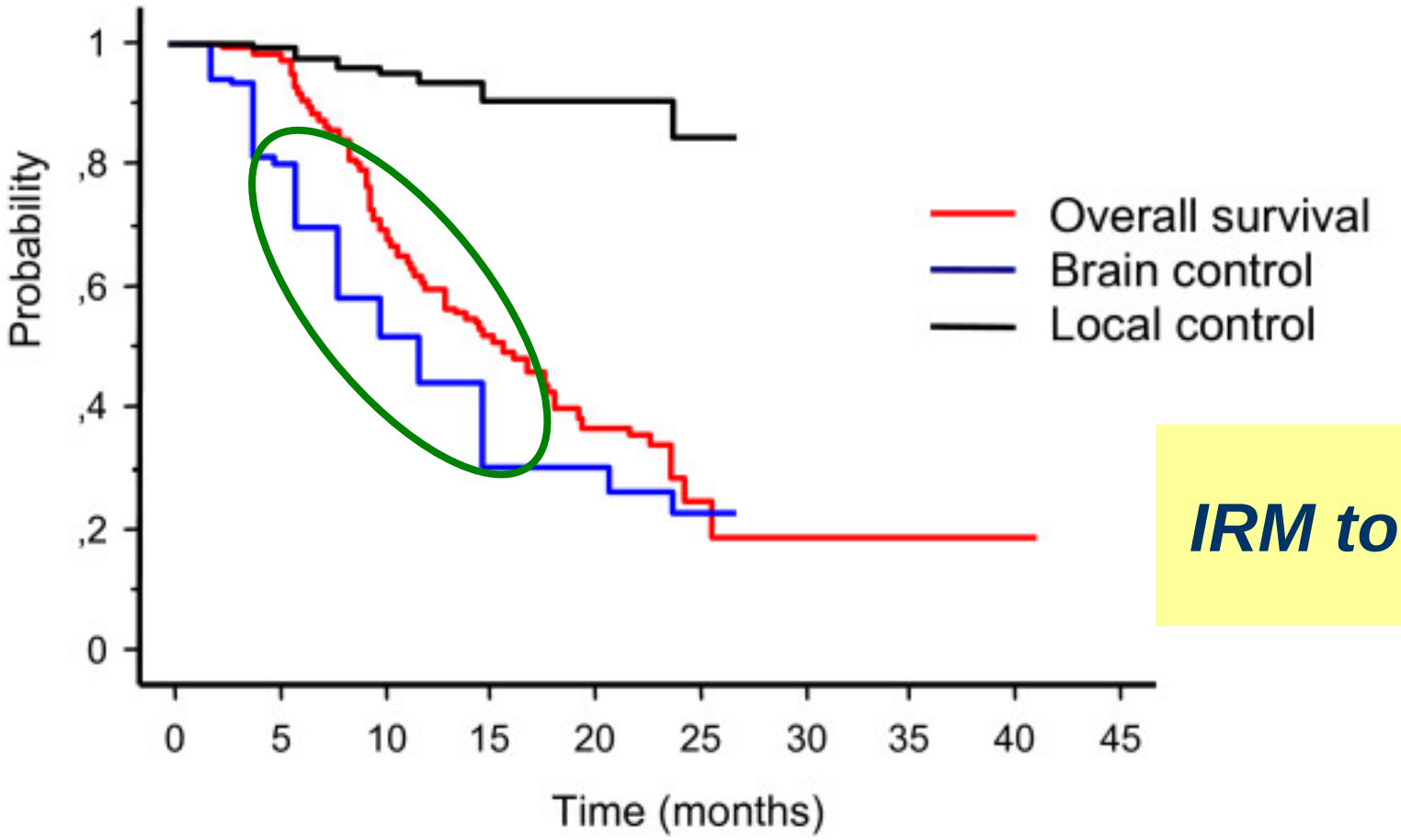
Evaluation post-thérapeutique MC

- 80 à 90 % de contrôle local à 1 an
- 50 % de risque de nouvelles lésions



IRM tous les 3 mois

Minniti *et al. Radiation Oncology* 2011

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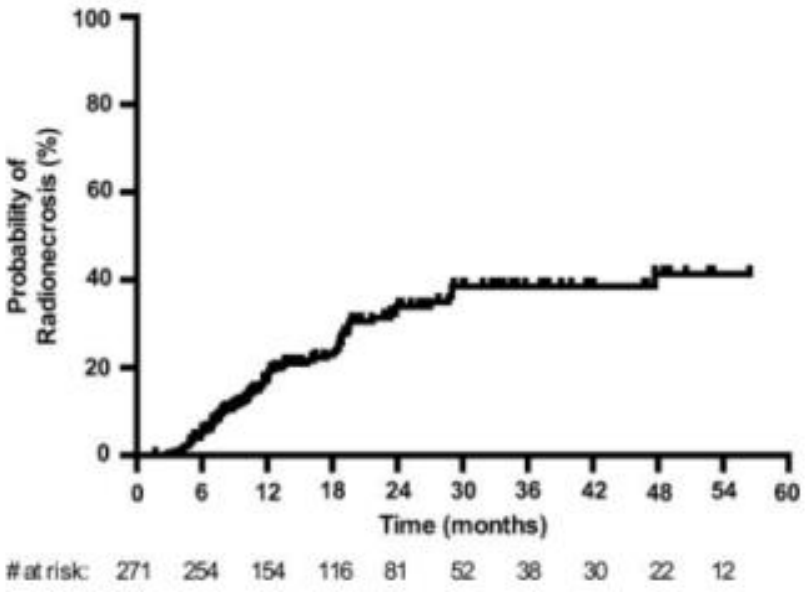
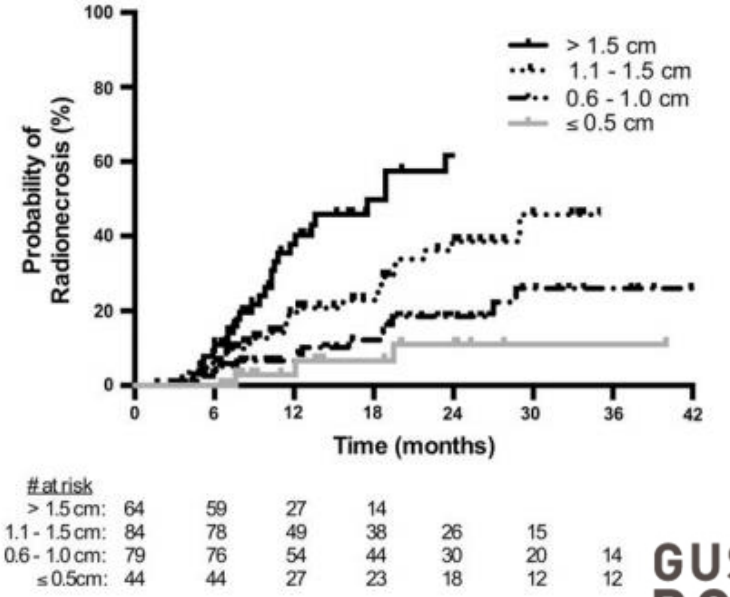
Radionécrose

- Incidence longtemps sous-évaluée, suivi long
- 15-20 % à 1 an, 35-40% à 2 ans, tps médian 11 m
- Quasiment jamais dans les 3 premiers mois
- 15% des patients avec RN vont développer des symptômes invalidants (céphalées, nausées, ataxie, déficits neurologiques focaux)





Kohutek et al., Journal of Neurooncol, 2015

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Evaluation de la réponse thérapeutique

Critères RANO spécifiques pour les métastases cérébrales

Response assessment criteria for brain metastases: proposal from the RANO group

Nancy U Lin, Eudocia Q Lee*, Hidefumi Aoyama, Igor J Barani, Daniel P Barboriak, Brigitta G Baumert, Martin Bendszus, Paul D Brown, D Ross Camidge, Susan M Chang, Janet Dancey, Elisabeth G E de Vries, Laurie E Gaspar, Gordon J Harris, F Stephen Hodi, Steven N Kalkanis, Mark E Linskey, David R Macdonald, Kim Margolin, Minesh P Mehta, David Schiff, Riccardo Soffietti, John H Suh, Martin J van den Bent, Michael A Vogelbaum, Patrick Y Wen, for the Response Assessment in Neuro-Oncology (RANO) group*

Lin et al, Lancet Oncology,16, 2-9, 2015

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Evaluation de la réponse thérapeutique

	Complete response	Partial response	Stable disease	Progressive disease
Target lesions	None	≥30% decrease in sum longest distance relative to baseline	<30% decrease relative to baseline but <20% increase in sum longest distance relative to nadir	≥20% increase in sum longest distance relative to nadir*
Non-target lesions	None	Stable or improved	Stable or improved	Unequivocal progressive disease*
New lesion(s)†	None	None	None	Present*
Corticosteroids	None	Stable or decreased	Stable or decreased	Not applicable‡
Clinical status	Stable or improved	Stable or improved	Stable or improved	Worse*
Requirement for response	All	All	All	Any‡

*Progression occurs when this criterion is met. †A new lesion is one that not present on prior scans and is visible in minimum two projections. If a new le… continued therapy can be considered, and follow-up assessment will clarify if the new lesion is new disease. If repeat scans confirm there is d… of the initial scan showing the new lesion. For immunotherapy-based approaches, new lesions alone to do not define progressio… progression in the absence of persistent clinical deterioration.

Table 2: **Summary of the response criteria for CNS metastases proposed by RANO …**

Comment faire après Stéréo ?

On the …ature review and extensive discussions, we …d the literature insufficiently robust to conclude that any one modality or approach can be recommended across all patients to distinguish between radiation necrosis and true progression. Instead, we recommend clinical judgment and involvement of a multidisciplinary team.

Lin et al, Lancet Oncology,16, 2-9, 2015

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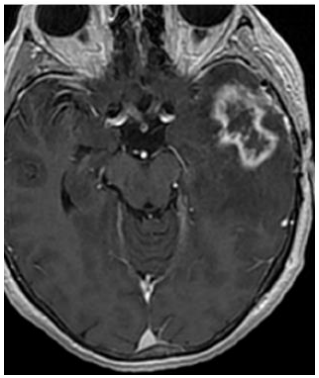
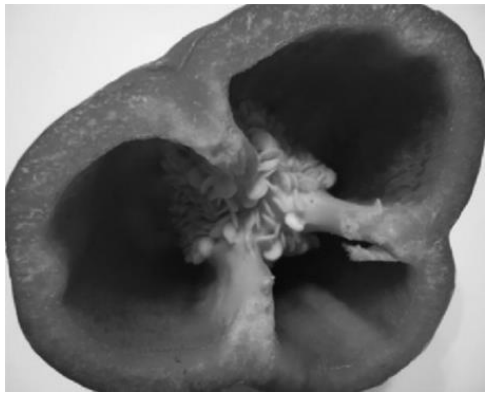
Progression ou radionécrose ?

IRM Morphologique

- Aspect en “poivron coupé”





- Augmentation du volume de plus de 65 %

- Rapport volume T2/T1

- Mismatch T1/T2

IRM Multimodale

- <u>La perfusion :</u> hyperperfusion en cas de progression
rCBV > 1,75-2

- <u>La spectroscopie :</u>
Cho/NAA ou Cho/creatine > 1.8
Cho lésion/Cho controlat > 1.2
Lipide/Cho > 3
→ Récidive tumorale

Menoux et al., Cancer/Radiothérapie, 2016

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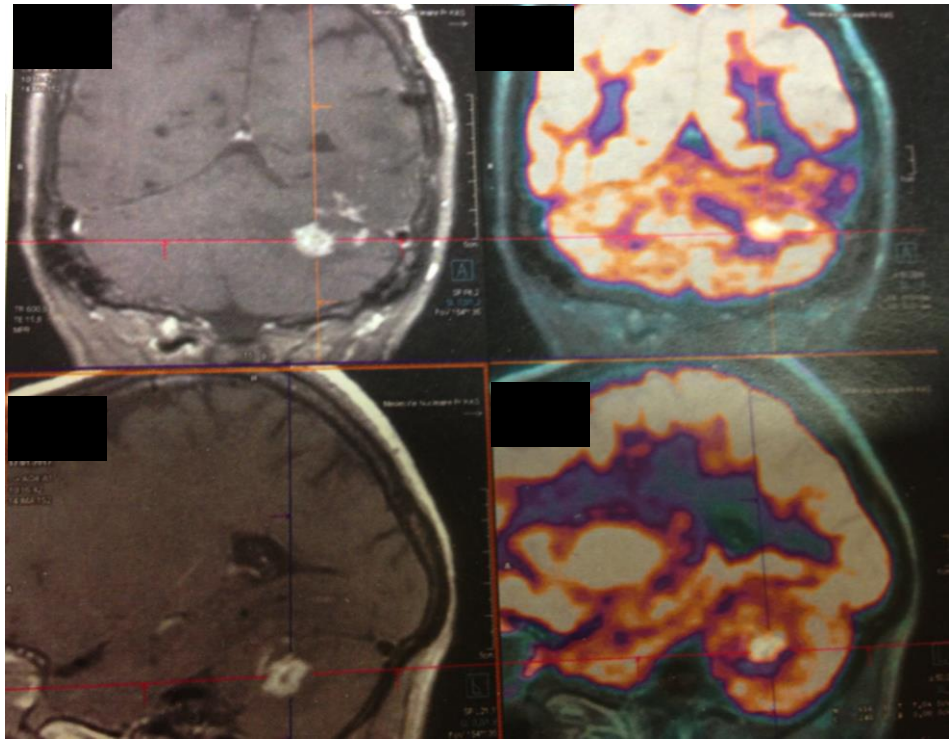
Progression ou radionécrose ?

TEP/TDM ou TEP/IRM

- TEP au ^{18}FDG :
  - Hypercaptation : progression tumorale versus hypofixation : Radionécrose
  - Faux positifs : inflammation
  - Faux négatifs : petite lésion

- Intérêt des nouveaux traceurs ?
  - ^{18}F-DOPA
  - FET
  - FluoroCholine
  - ^{11}C-Méthionine
  - Accès compliqué en pratique courante



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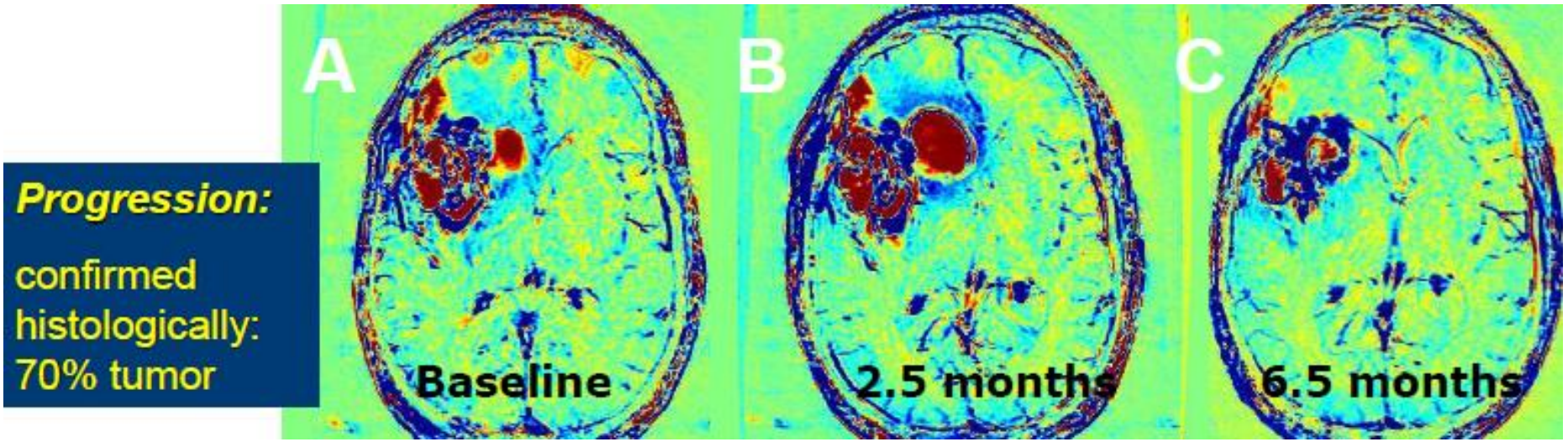
Progression ou radionécrose ?

Delayed contrast extravasation MRI

- Acquisition à 2 min et à 75 minutes après injection
- Analyse de la soustraction des images (cartographie de la lésion)
- Wash out du produit de contraste = progression tumorale



Zach et al., Neuro-oncology, 2015

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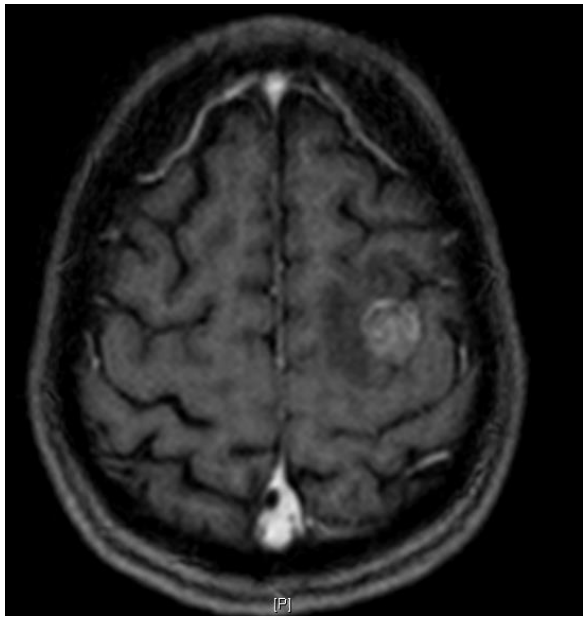
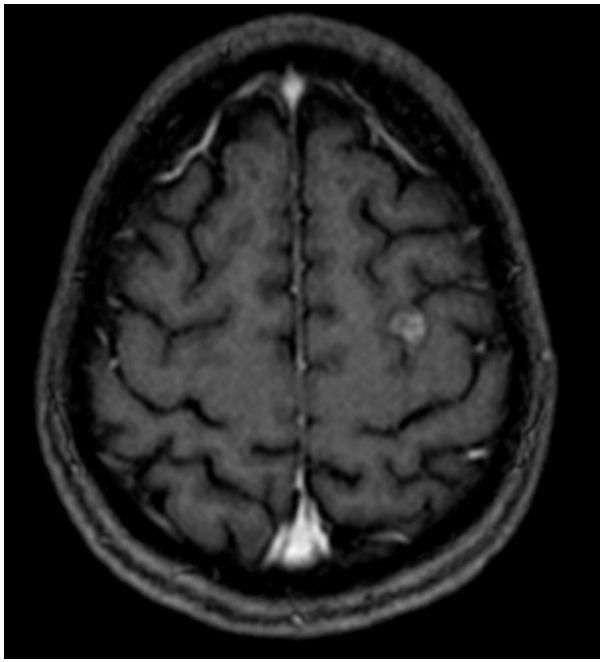
Progression ou radionécrose ?

Sept 2015, 1 x 20 Gy

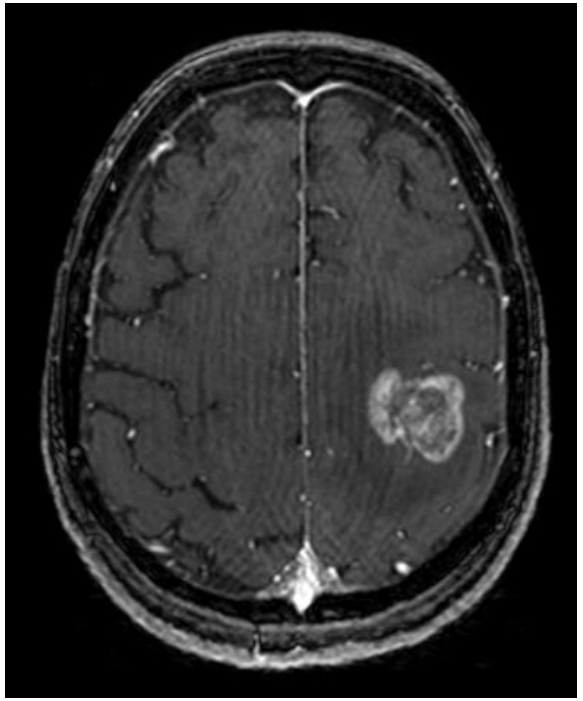


Métastase unique cancer bronchique

Janvier 2016



Octobre 2016



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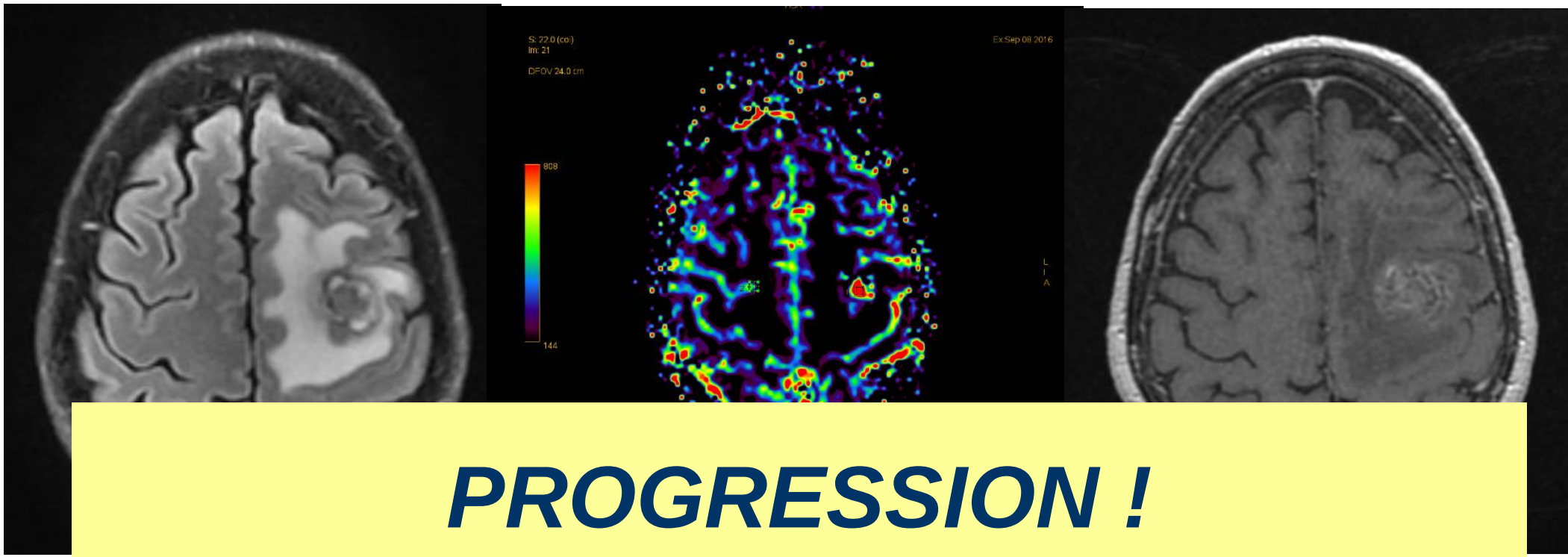
Progression ou radionécrose ?

IRM de perfusion, séquence tardive post gado



PROGRESSION !

- Hyperperfusion
- Wash out au temps tardif

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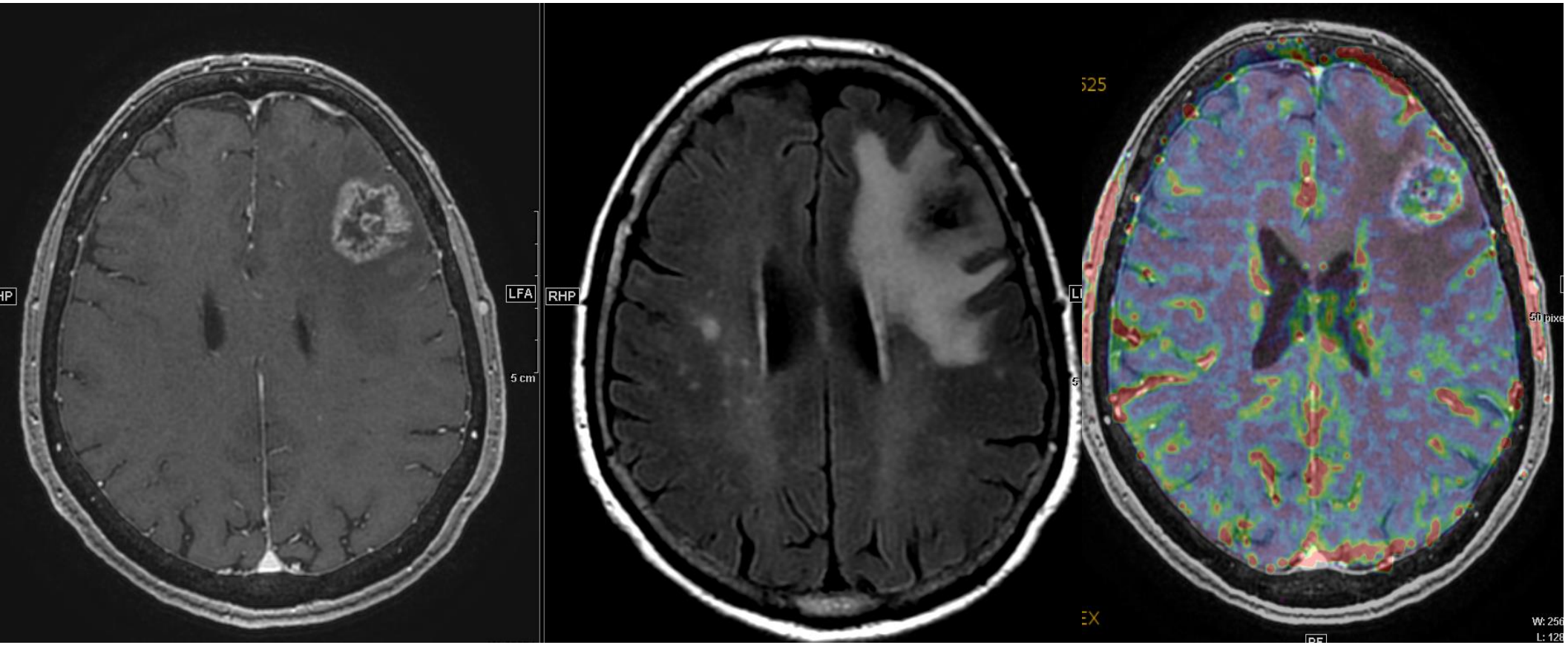
Progression ou radionécrose ?



3D T1GADO FLAIR cartographie cbv/3D T1

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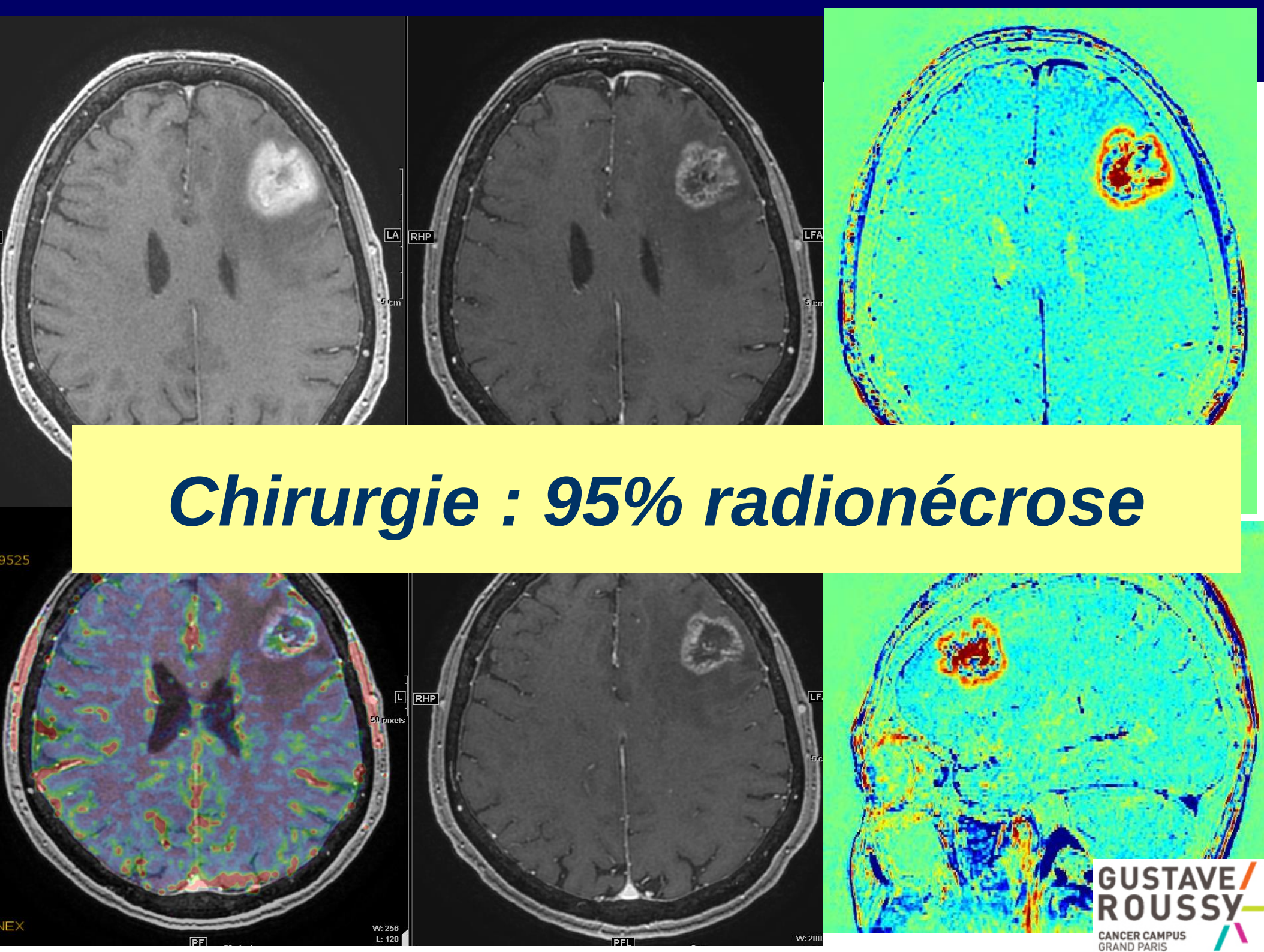

Chirurgie : 95% radionécrose

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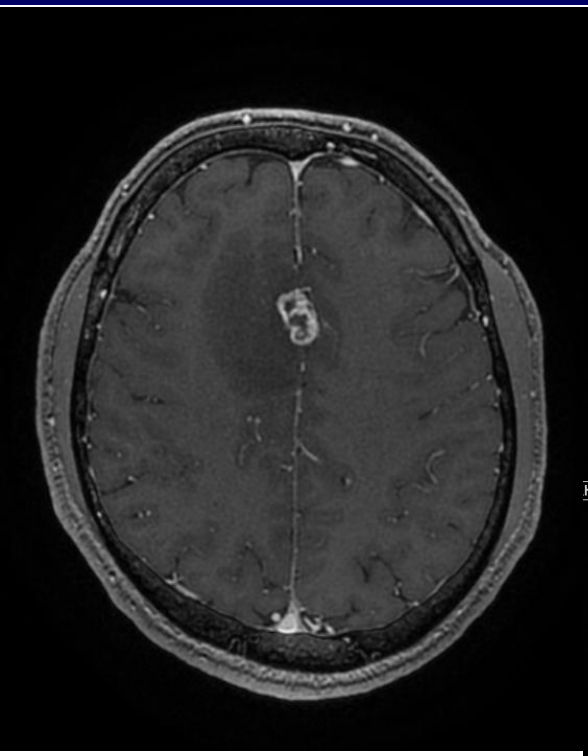
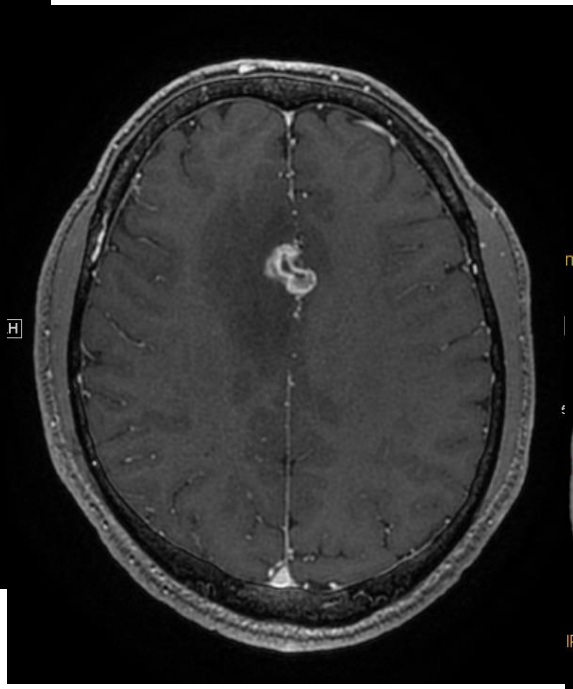
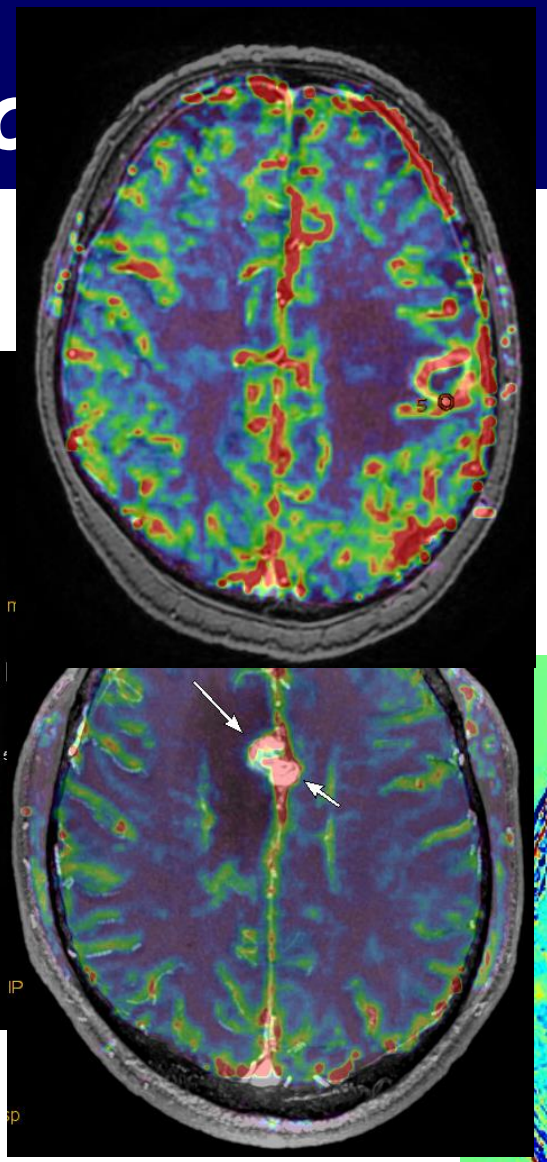
Progression ou rc ?



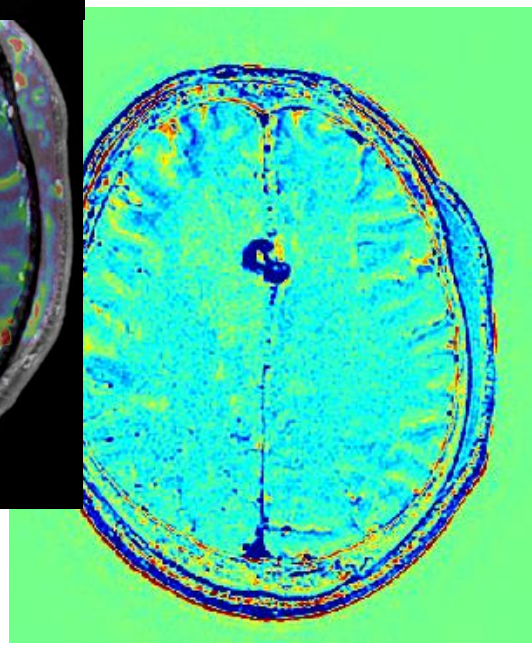
3D T1GADO
Pré RT



3D T1GADO
En PostRT



Perfusion



Soustraction

Lésion tumorale

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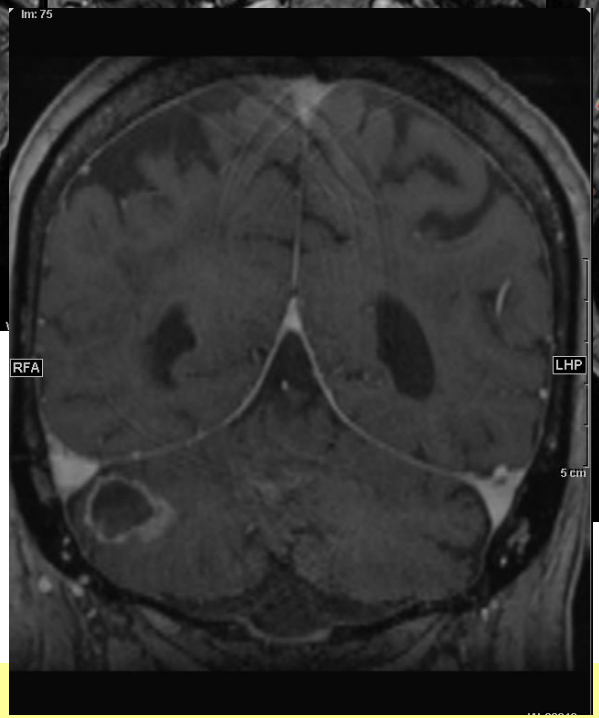
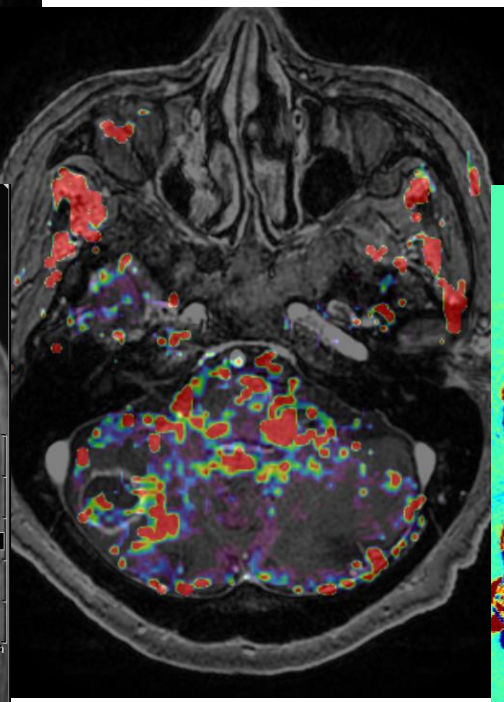
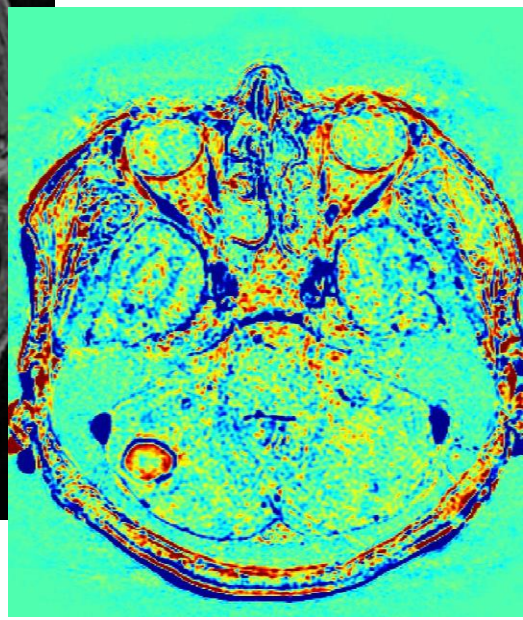
Progression ou radionécrose ?

3D T1GADO
Pré RT





Perfusion



Soustraction

Lésion tumorale

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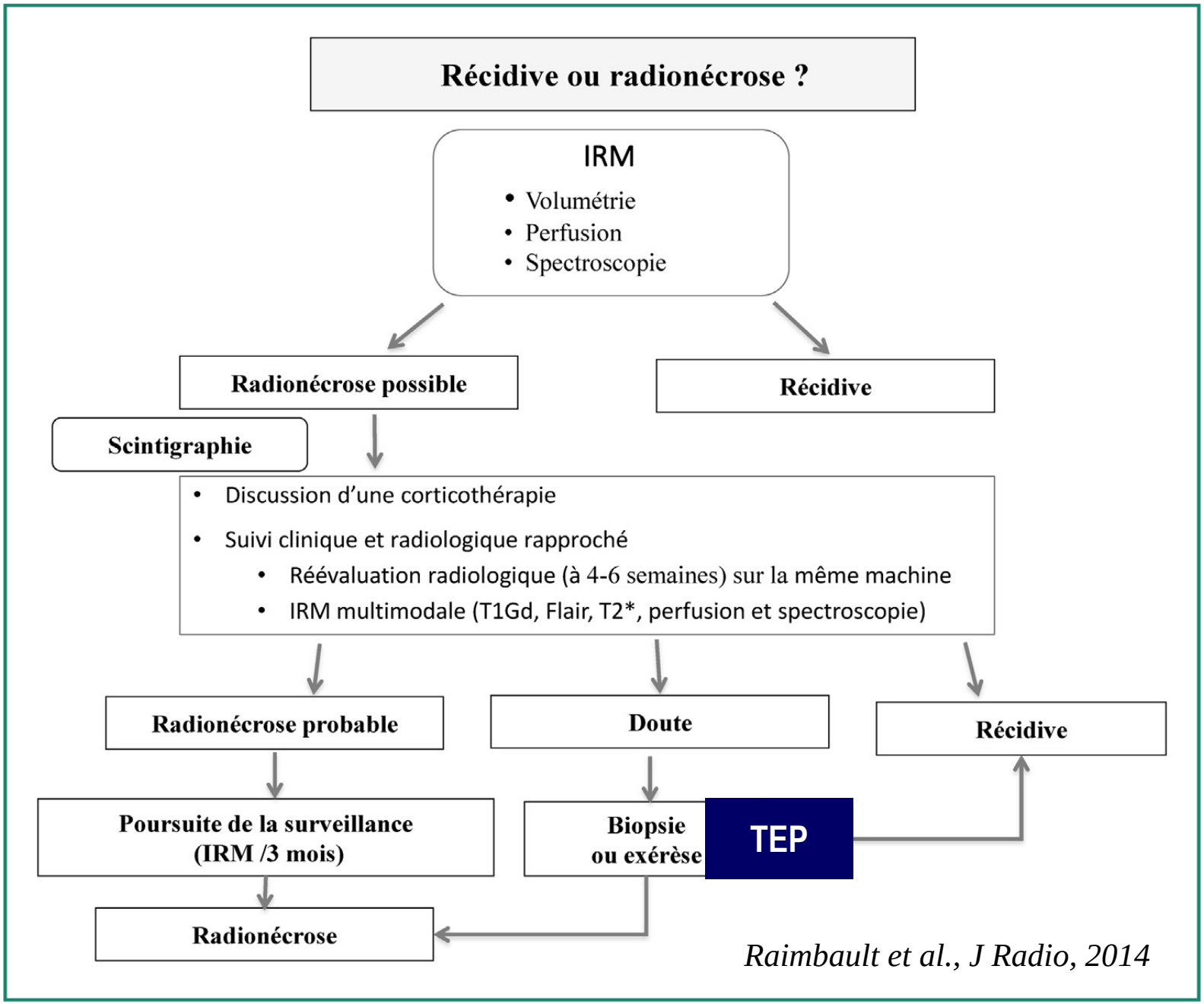
Arbre décisionnel



Raimbault et al., J Radio, 2014

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Traitement de la radionécrose

- **Corticoïdes :**

Traitement symptomatique, dose minimale efficace, altération clinique majeure des patients au long cours

- **Chirurgie d'exérèse :**

Diminution de la prise de corticoïdes, 50 % d'aggravation neurologique (11 pts) (1)

- **Bevacizumab :**

Diminution de la prise de corticoïdes (75 % des pts), 100 % de réponse radiologique, 80 % d'amélioration de l'état général (2) (3)

- **Oxygène hyperbare :**

Cas cliniques rapportés…

(1) McPherson et al, J Neurooncol, 2004
(2) Levin et al., IJROB, 2011
(3) Tye et al., J Neurooncol, 2014

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Postopératoire de MC ?

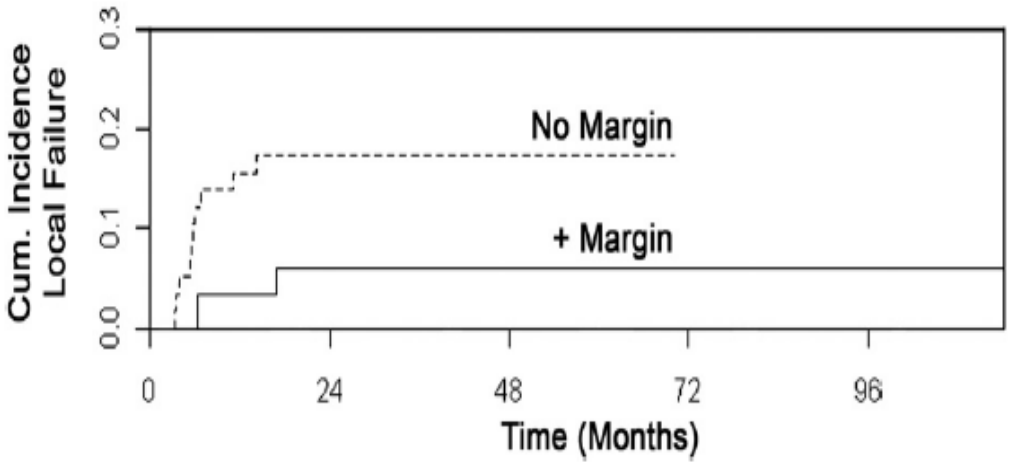
- Risque de radionécrose

Taux de radionécroses dans les études de radiothérapie stéréotaxique postopératoire de métastases cérébrales.
Radiation necrosis rates in the different studies of stereotactic radiotherapy after resection of brain metastasis.

Étude	Nombre de lésions traitées	Schémas d'irradiation	Taux de contrôle local à 1 an (%)	Radionécrose
Ahmed et al., 2014 [11]	65	20 à 30 Gy en 5 fractions	87	1,5 %
Brennan et al., 2014 [6]	40	15 à 22 Gy en 1 séance	78	17,5 %
Minniti et al., 2013 [7]	101	27 Gy en 3 fractions	93	9 % 5 % de symptomatique
Broemme et al., 2013 [8]	44	24 à 40 Gy en 6 à 10 fractions	77	2,3 %
Choi et al., 2012 [9]	120	12 à 30 Gy en 1 à 5 fractions	90,5	3 % sans marge de 2 mm 8 % avec marge de 2 mm
Prabhu et al., 2012 [10]	64	18 à 20,4 Gy en 1 séance	78	8 % de symptomatique

Doré et al, Cancer/Radiothérapie, 2014

- Volume de traitement important
- Marges de CTV +++



Choi et al, IJROBP, 2012

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Post opératoire de MC

Stereo cavité opératoire

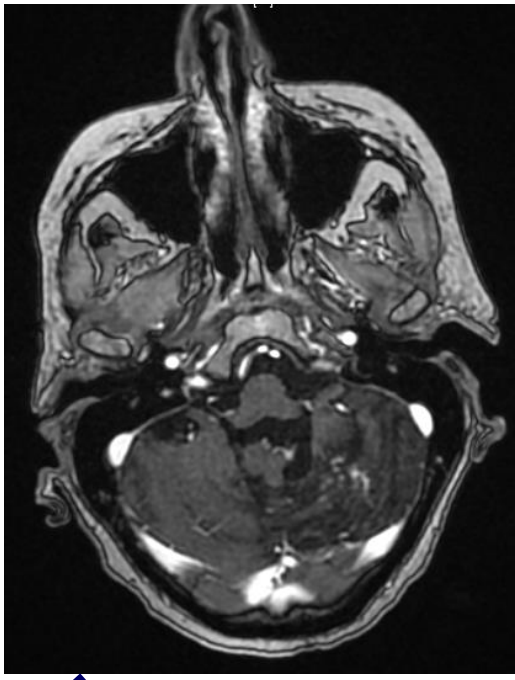
Prises de contraste

Encéphale in toto

Aggravation

Avastin

Régression



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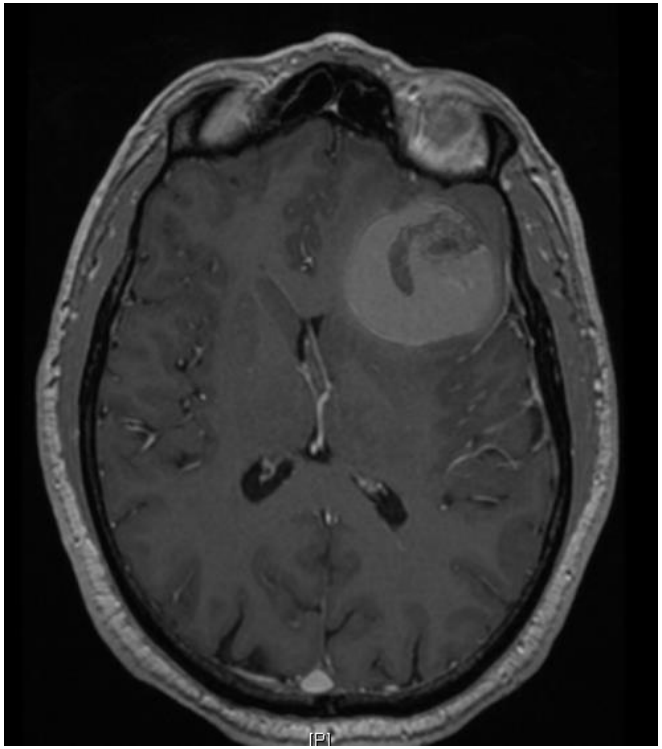
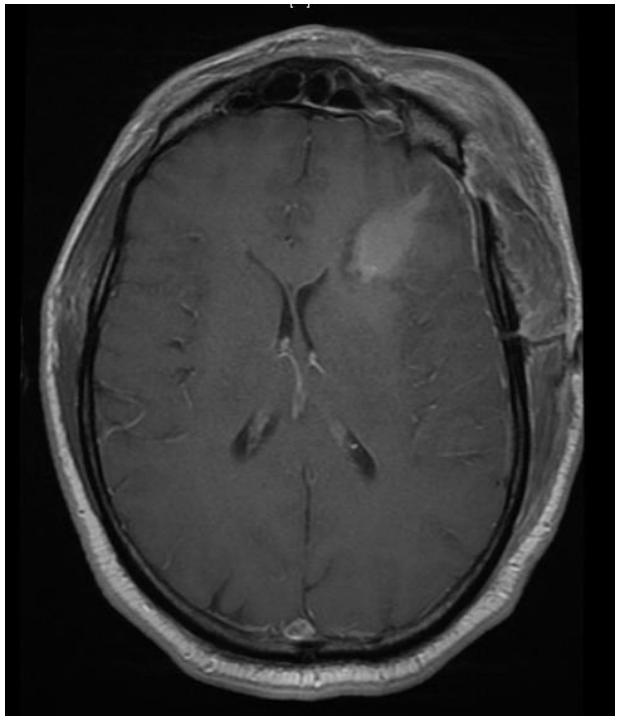
Transformation hémorragique

Melanome 1x20 Gy sous pembro

3 mois plus tard



Chirurgie : tumeur



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Transformation hémorragique

Clinical outcomes of melanoma brain metastases treated with stereotactic radiation and anti-PD-1 therapy FREE

K. A. Ahmed; D. G. Stallworth; Y. Kim; P. A. S. Johnstone; L. B. Harrison; J. J. Caudell; H. H. M. Yu; A. B. Etame; J. S. Weber; G. T. Gibney ✉

Ann Oncol (2016) 27 (3): 434-441. **DOI:** https://doi.org/10.1093/annonc/mdv622
Published: 27 December 2015 **Article history** ▾

4 cas de transformation hémorragiques classés comme progression (SRS + Nivolumab)

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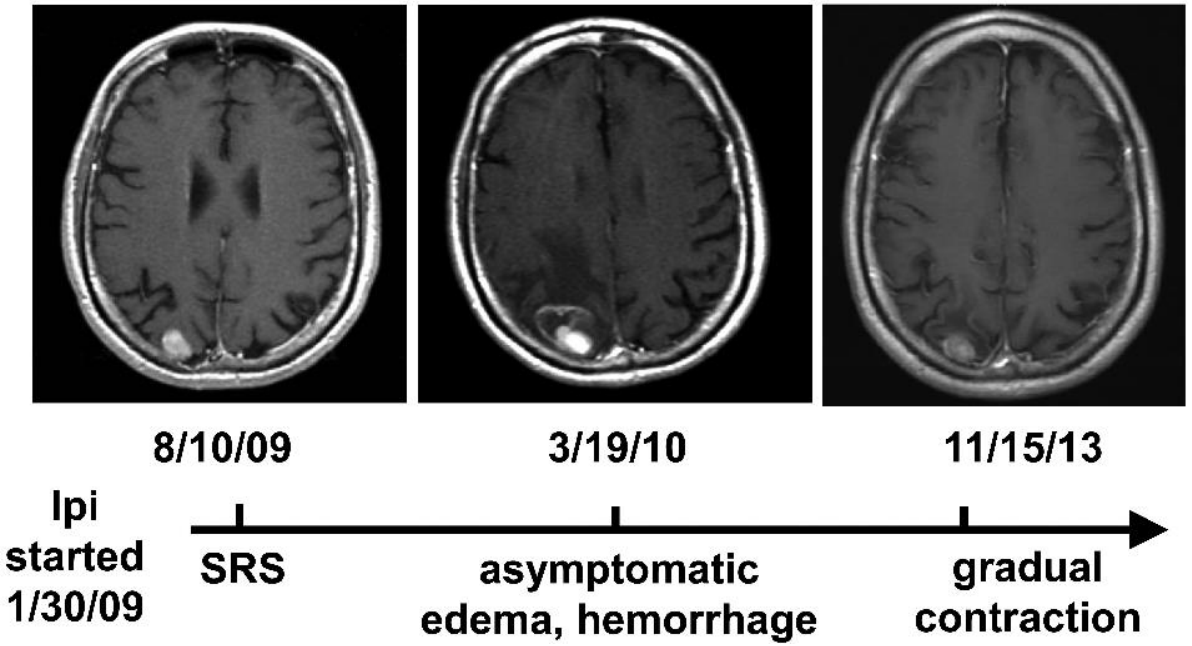
Transformation hémorragique

35 à 40 % de transformation hémorragique (SRS + Ipilimumab) (1) (2)

séries rétrospectives

PROGRESSION OU PSEUDO-PROGRESSION ?



(1) Mathew et al, Melanoma research, 2013
(2) Kiess et al, IJROBP, 2015

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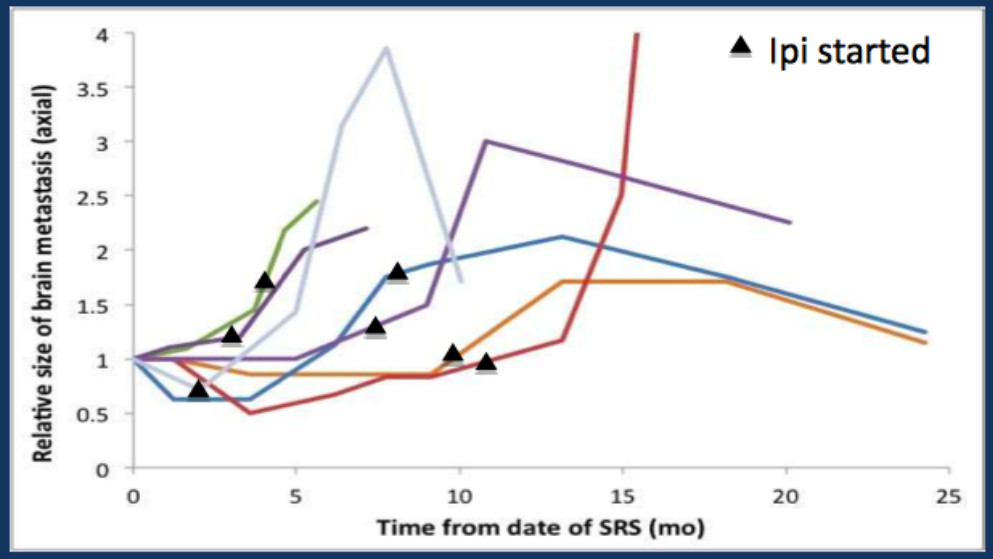
Transformation hémorragique

Prudence chez les patients sous inhibiteur de checkpoints !!!!!!!!!!!!!!!!!!



- Increase in tumor size to >150% seen in 50% of BMs treated during or before Ipi
  - vs 13% of BMs treated after Ipi
  - 11 lesions resected
    - 5 had 100% tumor necrosis

Kiess et al, IJROBP, 2015
(Communication orale ASTRO 2016)

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Evaluation post thérapeutique

Tumeurs "bénignes" :

Méningiome

Adénome

Neurinome

- IRM tous les 6 mois durant les 2-3 premières années puis tous les ans
- Généralement peu de modification volumétrique

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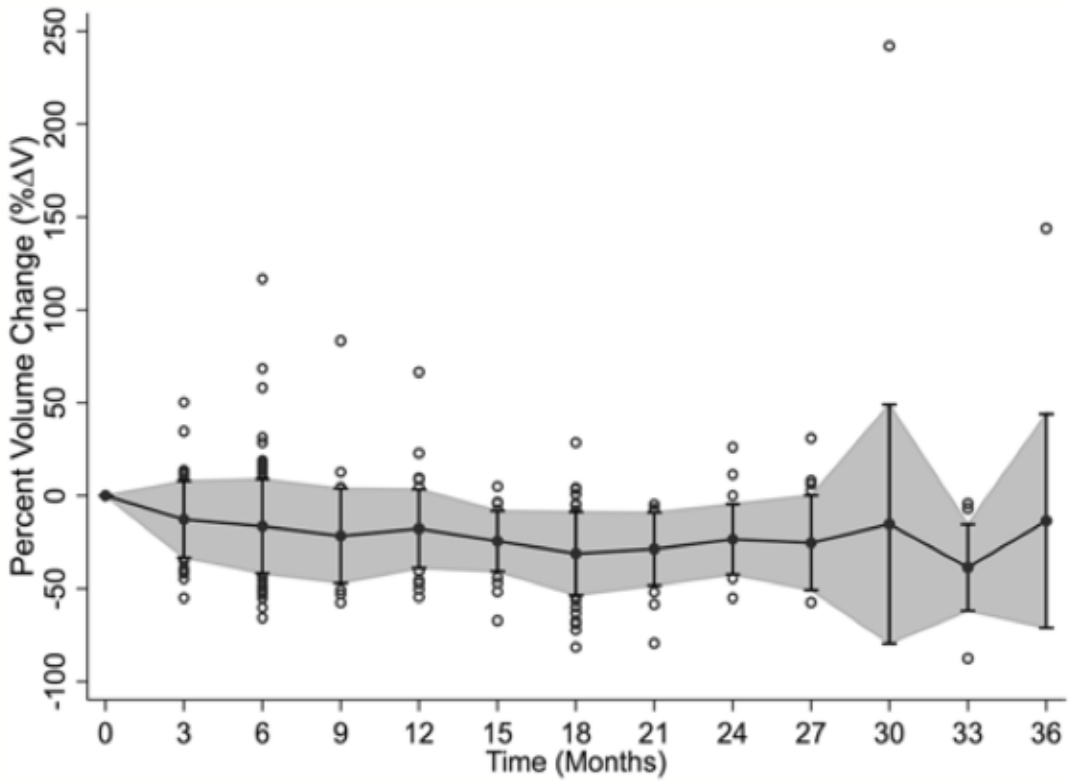
Evaluation post-thérapeutique

252 patients traités par GammaKnife en dose unique



Harrison et al, Journal of Neurosurgery, 2015

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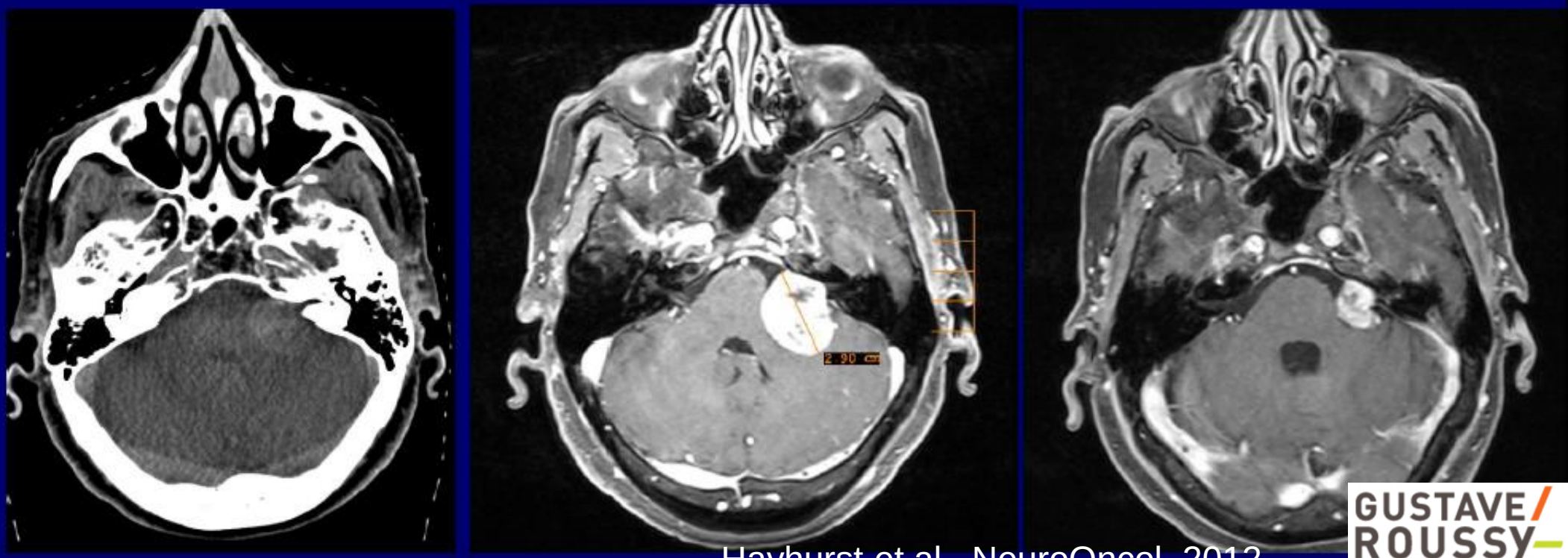
Neurinome

- **Pseudoprogression fréquente en particulier dans la 1ère année (6-25 % des cas)**
- **Parfois volumineuse et symptomatique**

- 2008 2009 2013



Hayhurst et al., NeuroOncol, 2012

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Evaluation post thérapeutique

Ré-irradiation des gliomes

Evaluation post thérapeutique

- **Survie sans progression < 6 mois …**

- **Risque de radionécrose sous-évaluée par un suivi court (souvent aux alentours de 10%)**

Table 4. Patient outcomes from published reports on the use of salvage stereotactic radiotherapy for recurrent World Health Organization Grade 4 glioma compared with the results from the current study

Study	*n*	Median OS (mo)	Median OS from SRS (mo)	Median PFS from SRS (mo)	Median KPS
Hall *et al.* (13)	26	18	8	—	70
Combs *et al.* (4)	32	22	10	5	80
Kong *et al.* (11)	65	23	13	5	100
Biswas *et al.* (14)	33	17	7	4	—
Cho *et al.* (12)	42	—	7	—	70
Fogh *et al.* (15)	105	23	11	—	—
Gutin *et al.* (+BVZ) (34)	20	—	13	7	90
Current study (+BVZ)	33	47	11	5	80
Current study (−BVZ)	16	25	4	2	80
Current study (all)	49	35	9	5	80

Cuneo et al, IJROBP, 2011

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Conclusion

Evolution des lésions après radiochirurgie

- 500 métastases, 120 patients, radiochirurgie (18-24 Gy)
- 1/3 des lésions : augmentation transitoire

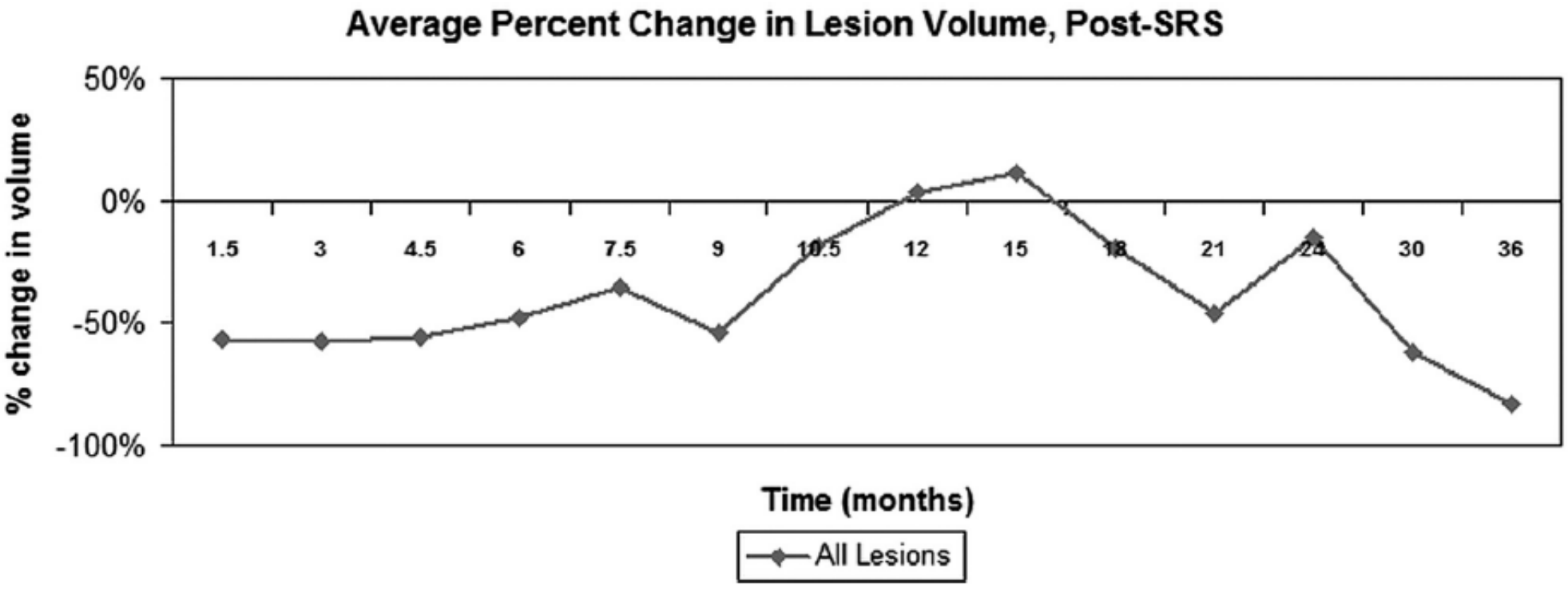

Fig 2. Average change in lesional size with time, relative to initial treatment volume, all lesions. Lesions decreased or remained stable in size for the first 9 months post-SRS. Subsequently, they increased in size until approximately 18 months post-SRS, at which point they began to decrease in size once again.

Patel et al, Am J NeuroRadiology, 2011

Conclusion

1- Soyez prudents avant de tirer des conclusions

2- Avertissez les patients de l'éventualité de cette "fausse progression"

3- Regardez <u>toute</u> l'IRM avec attention : Nouvelles lésions ?

4- Maniez les CTC avec parcimonie : Dose minimale efficace !

Merci pour votre attention !