醫學影像原理與實務

磁振影像與組織特性關聯性

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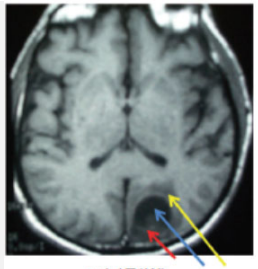
本週學習目標

1. 認識磁振造影對比劑應用
   - 磁振對比劑特性
   - 對比劑血管攝影
   - 對比劑腫瘤造影
2. 了解臨床磁振造影應用
   - 擴散權重與擴散張量影像
   - 非對比劑顯影血管攝影

References:

- Fundamentals of Medical Imaging (2nd Ed.) Chapter 4
- MRI The Basics (4th Ed.)
- MRI in Practice, (5th Ed.)

磁振造影對比劑應用



Effects of Contrast Agents

Edema
Cyst
Tumor

Gadolinium (Gd) 釓

64
Gd
Gadolinium
157.25

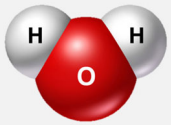
- The most commonly used MR contrast agents are Gadolinium based.
- As an element, Gd is ferromagnetic and highly toxic.
- Metal ions (Gd^{3+}) with free electrons tend to accumulate in tissues with a natural affinity for metals (compete with Ca^{2+}).
  - Membranes
  - Transport proteins
  - Enzymes
  - Osseous matrix
  - Renticuloendothelial system: lungs, liver, spleen, and bone

A cumulative poison !

Gadolinium Chelates (螯合物)

- Chelates have a high affinity for metal ions.
- Gd chelates are paramagnetic and relatively safe.
  - Shorten T1 relaxation time
- Majorly excreted by the renal system.
- In a patient with normal renal function, the biological half-life of Gd chelates is 2 hours.

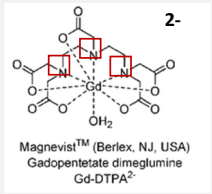
Low relaxation efficiency!!



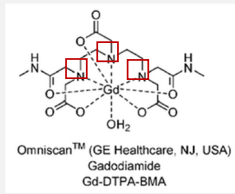
Reduce the T1 relaxation time of nearby water spins !!

Development of Contrast Agent

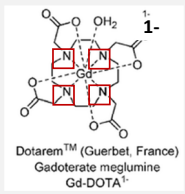
1st generation	2nd generation	3rd generation
Linear ionic	**Linear nonionic**	**Macrocyclic ionic/nonionic**
Products: **Magnevist** (Gd-DTPA)	Products: **Omniscan** (Gd-DTPA-BMA)	Products: **Dotarem** (Gd-DOTA) **ProHance** (Gd-HP-DO3A)



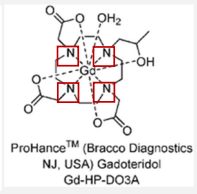
Magnevist™ (Berlex, NJ, USA)
Gadopentetate dimeglumine
Gd-DTPA^{2-}



Omniscan™ (GE Healthcare, NJ, USA)
Gadodiamide
Gd-DTPA-BMA



Dotarem™ (Guerbet, France)
Gadoterate meglumine
Gd-DOTA^{1-}



ProHance™ (Bracco Diagnostics NJ, USA) Gadoteridol
Gd-HP-DO3A

7 July 2017
EMA/424715/2017

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

PRAC confirms restrictions on the use of linear gadolinium agents

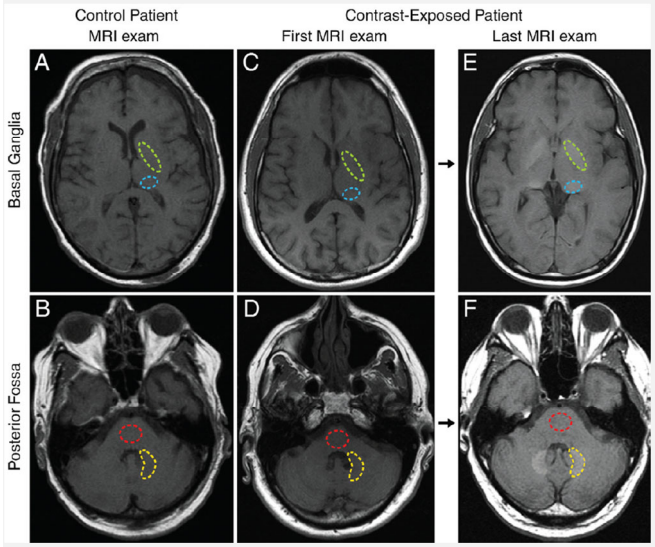
Benefit-risk balance of certain linear gadolinium agents no longer favourable

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has confirmed its previous conclusion from March 2017 that there is convincing evidence of gadolinium deposition in brain tissues following use of gadolinium contrast agents.

No specific conditions linked to gadolinium deposition in the brain have been identified, but the clinical consequences are unknown.

As a result of the review, the PRAC recommends that the intravenous linear agents gadoxetic acid and gadobenic acid should only be used for liver scans in the situations where they meet an important diagnostic need. In addition, gadopentetic acid should only be used for joint scans as the gadolinium concentration in the formulation used for joint injections is very low.

All other intravenous linear agents (gadodiamide, gadopentetic acid and gadoversetamide) should be suspended in line with the PRAC's March 2017 recommendation.



Intravenous GBCA exposure is associated with neuronal tissue deposition in the setting of relatively normal renal function.

globus pallidus (green), thalamus (blue), dentate nucleus (yellow), and pons (red)

Radiology: 275(3):772-782, 2015.

Brand name	Chemical name	Structure	Comments
Magnevist®	gadopentetate (Gd-DTPA)	linear ionic	Oldest agent (FDA approved 1988) with historically largest world-wide market share and clinical experience; below average relaxivity; probable ↑risk NSF
MultiHance®	gadobenate (Gd-BOPTA)	linear ionic	Highest relaxivity of all extracellular gadolinium agents due to transient protein binding; 3-5% hepatocyte uptake; competitive inhibitor for cMOAT drugs (tamoxifen, methotrexate, cisplatin); QT prolongation
Omniscan™	gadodiamide (Gd-DTPA-BMA)	linear nonionic	Low thermodynamic stability; disproportionately ↑risk NSF; may interfere with serum Ca^{++} measurements
Optimark™	gadoversetamide (Gd-DTPA-BMEA)	linear nonionic	Low thermodynamic stability; probable ↑risk NSF; may interfere with measurements of serum Ca, Fe, Cu, and Zn
Dotarem®	gadoterate (Gd-DOTA)	macrocyclic ionic	One of oldest agents with largest market share in Europe; most recent entry (2013) into US market
ProHance®	gadoteridol (Gd-HP-DO3A)	macrocyclic nonionic	Lowest osmolality and viscosity of all agents; below average relaxivity
Gadavist®	gadobutrol (Gd-BT-DO3A)	macrocyclic nonionic	Highest viscosity due to 1.0M formulation (all others 0.5M); above average relaxivity; marketed as Gadovist® outside the US
Eovist® (USA) Primovist®	gadoxetate (Gd-EOB-DTPA)	linear ionic	Designed for liver imaging; ~50% uptake by hepatocytes after initial extracellular phase; joint renal & biliary excretion; very high relaxivity due to size and transient protein binding; may interfere with serum Fe measurements; QT prolongation
Ablavar®	gadofosveset (Gd-DTPA-DCHP) (MS-325)	linear ionic	Highest relaxivity of any agent due to reversible albumin binding; intended for MRA; steady-state blood pool imaging 20 min – 4 hrs after injection; long elimination half-life (16+ hrs); QT prolongation

extracellular interstitial space

hepatic

vascular

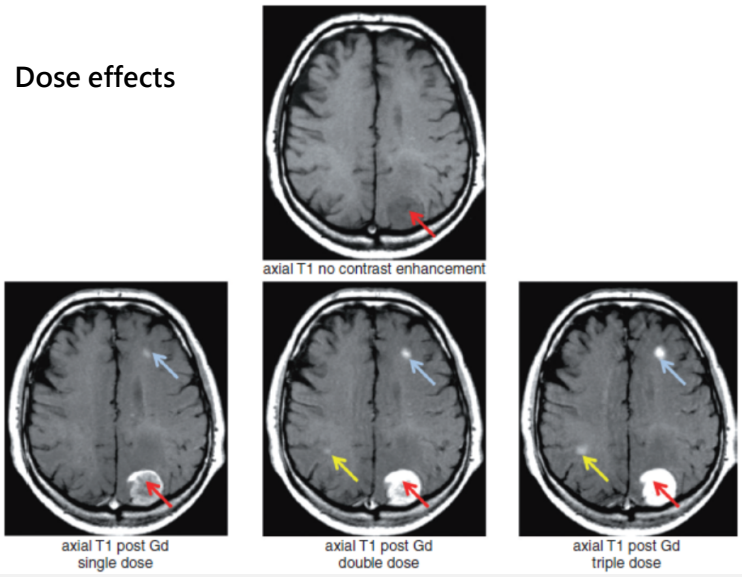
http://mri-q.com/so-many-gd-agents.html

Gadolinium Administration/Dose

- The recommended dosage of gadolinium is 0.1 millimoles per kilogram (mmol/kg) of body weight (0.2 mL/kg).
- The lethal dose, (LD_{50} – the dose required to kill half of the study population) determined in rat studies is between 6 and 20 mmol/kg.
- As dose increases (to a point), the ability to visualize structures and lesions also increases. With standard gadolinium the optimal dose is weight-based.

A fixed dose of contrast agent is unacceptable!

Dose effects



Nephrogenic Systemic Fibrosis

- **Nephrogenic systemic fibrosis (NSF)腎因性全身性纖維化**: patients who suffered from renal insufficiency.
- Normally, approximately 80% of gadolinium is excreted by the kidneys in 3 h and 98% is recovered by feces and urine in one week.
- But it may take longer for patients with NSF.
- Gadolinium is a contraindication and a relative precaution for patients in renal failure.

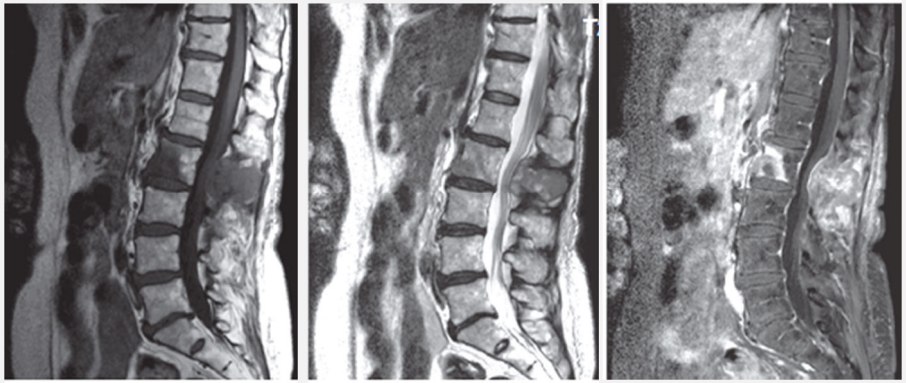
台灣衛生署 2011 年 8 月 4 日公告

- 需至少檢視病人三個月內之 serum creatinine 檢測結果，以了解受檢者之腎功能及是否有急性腎衰竭。
- 不可用於慢性嚴重腎臟疾病或急性腎衰竭之受檢者。
- 必要施行顯影性磁振造影時，謹慎的使用不超過標準劑量(0.1 mmol/kg) 之中或低風險含釓對比劑。
- 兩次顯影性磁振造影需間隔 7 天以上。

2017 中華民國放射線醫學會對比劑手冊

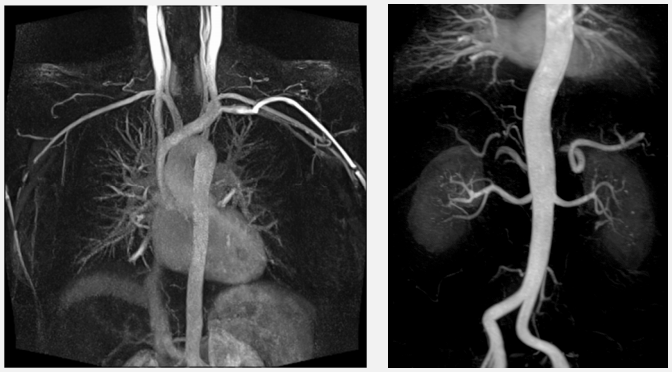
Lumbar Spine with Bone Metastases

T1-weighted image | T2-weighted image | T1W+C with fat saturation



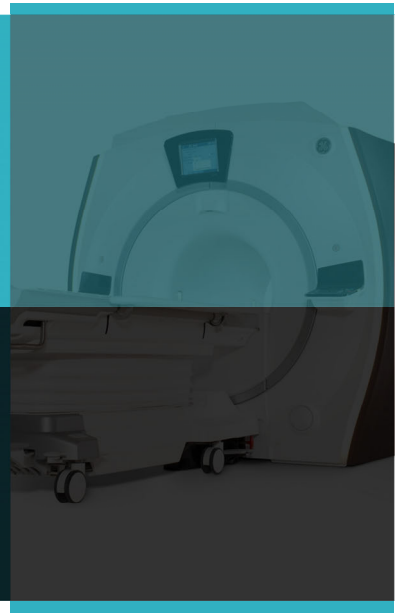
Contrast-enhanced MR Angiography

Time-resolved CE-MRA (Courtesy Siemens) | Single-phase CE-MRA



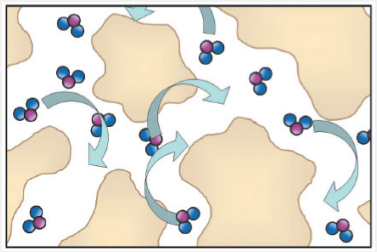
https://mriquestions.com/contrast-enhanced-mra.html

臨床磁振造影應用

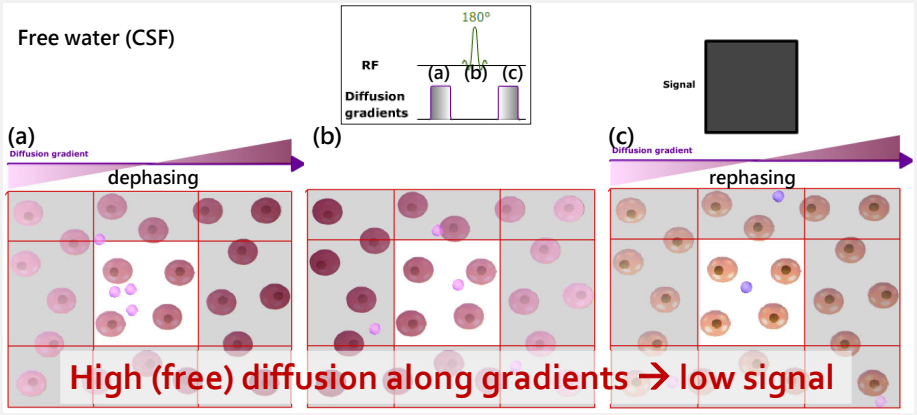


MR Diffusion

- MR Diffusion is a term used to describe the movement of molecules in the **extra-cellular space** due to random thermal motion.
- This motion can be restricted by boundaries such as **ligaments, membranes, myelin, and macromolecules**.

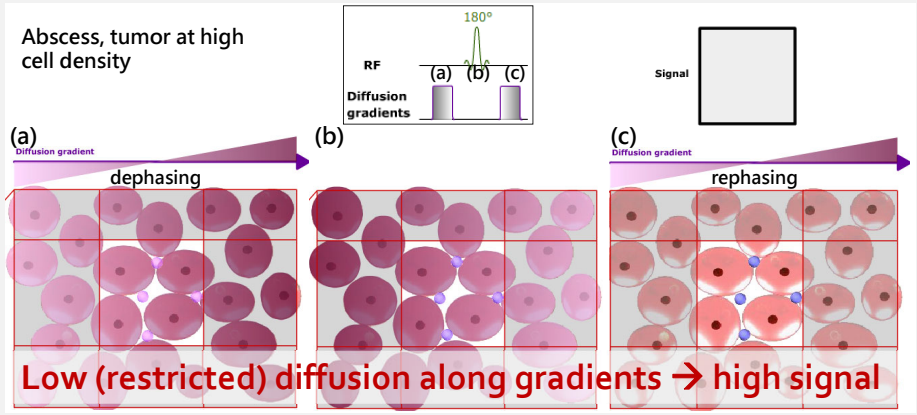


Diffusion gradient and motion



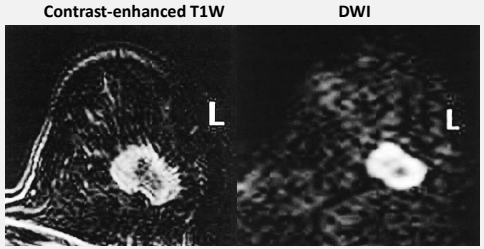
IMAIO 2014, http://www.imaios.com/en/e-Courses/e-MRI/Diffusion-Tensor-Imaging/diffusion-principles

Diffusion gradient and motion



IMAIO 2014, http://www.imaios.com/en/e-Courses/e-MRI/Diffusion-Tensor-Imaging/diffusion-principles

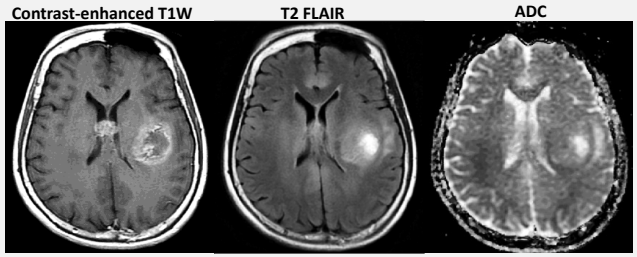
Tumor imaging



Invasive ductal carcinoma

b=600~700

Kuroki, 2004.

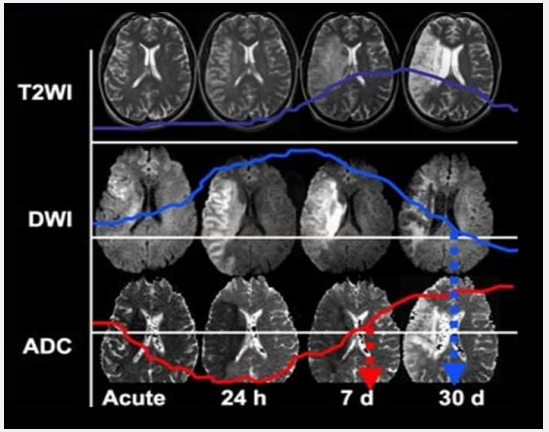


Glioblastoma

b=900~1000

DWI/ADC of Ischemic Stroke

- Acute (0~7 days)
  - ADC ↓ (hypo-intensity)
  - DWI ↑ (hyper-intensity)
- Subacute (1~3 weeks)
  - ADC iso-intensity
  - DWI ↑ (hyper-intensity)
- Chronic (>3 weeks)
  - ADC ↑ (hyper-intensity)
  - DWI ↓ (hypo-intensity)

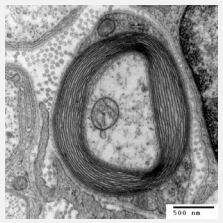


https://www.stroke-manual.com/mri-dwi-in-stroke-diagnosis/

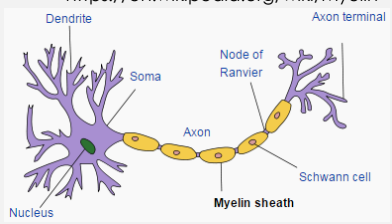
Myelin Sheath on Axon

- Myelin is a fatty white substance that surrounds the axon of some nerve cells, forming an electrically insulating layer.
- It is essential for the proper functioning of the nervous system.

https://en.wikipedia.org/wiki/Myelin

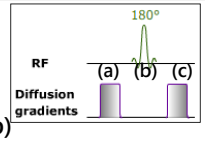


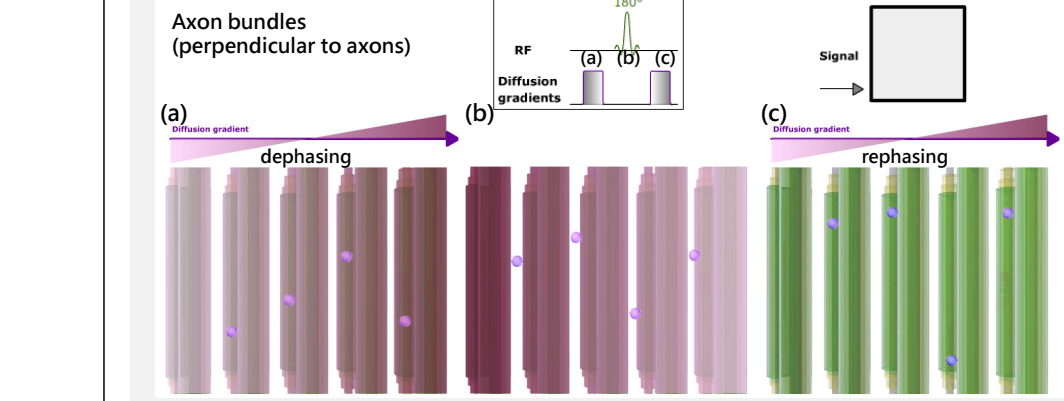
Transmission electron microscopy (TEM)



Diffusion gradient and motion direction

Axon bundles (perpendicular to axons)

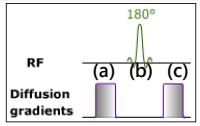




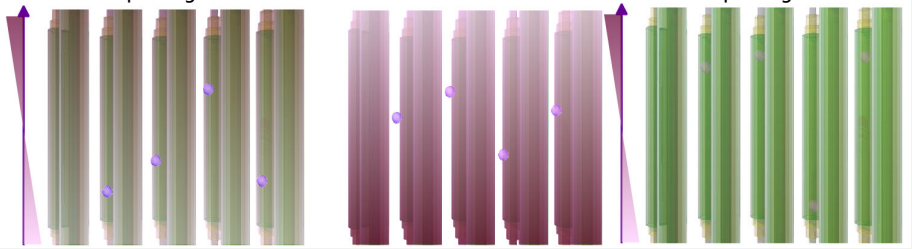
IMAIO 2014, http://www.imaios.com/en/e-Courses/e-MRI/Diffusion-Tensor-Imaging/diffusion-principles

Diffusion gradient and motion direction

Axon bundles
(parallel with axons)



(a) dephasing (b) (c) rephasing



IMAIO 2014, http://www.imaios.com/en/e-Courses/e-MRI/Diffusion-Tensor-Imaging/diffusion-principles

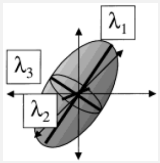
DTI Tractography

The matrix of diffusion tensor

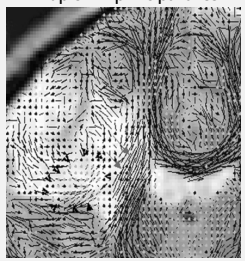
$$\begin{bmatrix} Dxx & Dxy & Dxz \\ Dyx & Dyy & Dyz \\ Dzx & Dzy & Dzz \end{bmatrix}$$

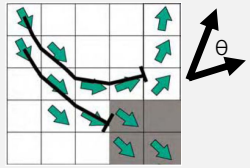
eigenvectors

Three principal axes of ellipsoid model



Map of 1st principal axes



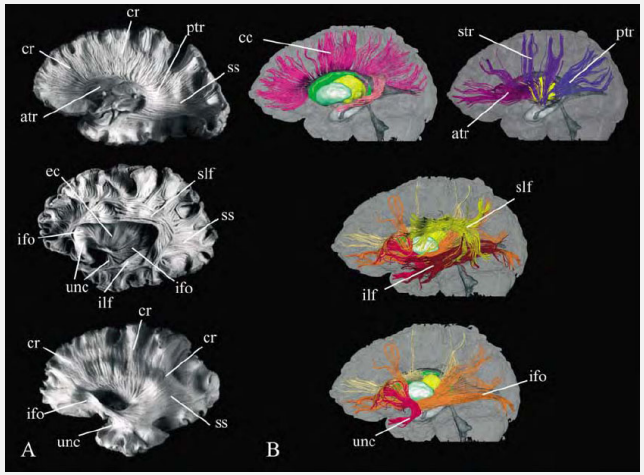


(every voxel is seed)

Fiber Assignment by Continuous Tracking (FACT) algorithm

- Stopping criteria
  - FA lower than 0.2
  - Turning angle larger than 60°

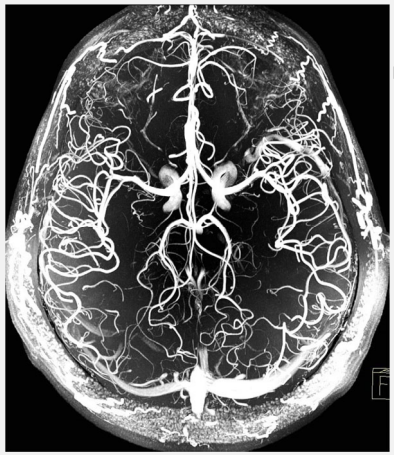
Axonal Fiber Bundles



- Tract
- Fasciculus
- radiation

Mori et al. MRI Atlas of Human White Matter, Elsevier, 2005.

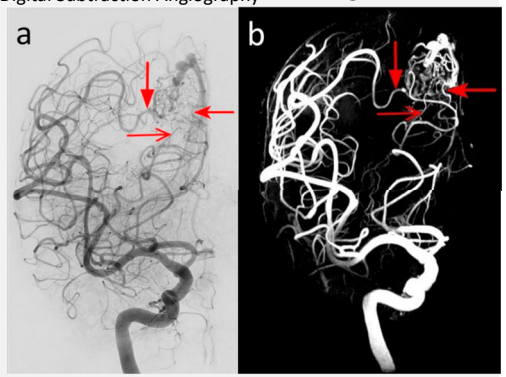
Time-of-Flight MR Angiography



← 7T TOF MRA without contrast agent

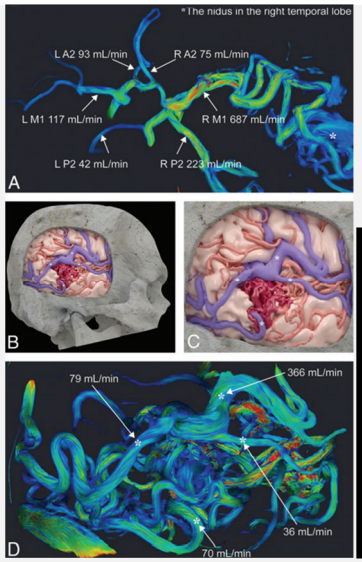
Digital Subtraction Angiography

7T TOF MRA



European Radiology Experimental (2024) 8:68

Phase Contrast MRA



3D PC-MRA of a temporal AVM
AJNR 2021, 42.12: 2138-2145.

4D PC-MRA

https://youtu.be/4nLUWuz5Tr8

重點回顧

- 臨床磁振對比劑主要為釓螯合物(gadolinium chelates)，可縮短組織T1時間。
- 環狀結構相較於線性結構的釓螯合物更為穩定。
- 過往十年已證實對比劑沉積於腦部的現象(gadolinium deposition)，但未見明確臨床症狀。
- 對比劑之使用應確認其必要性，以及病患腎功能。
- 臨床上，對比劑可用於腫瘤攝影、血管攝影、灌流攝影、發炎等應用。
- 磁振造影的臨床技術相當廣泛，例如：擴散權重影像、磁化率權重影像、磁振頻譜分析、功能性造影、心臟動態攝影等。

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