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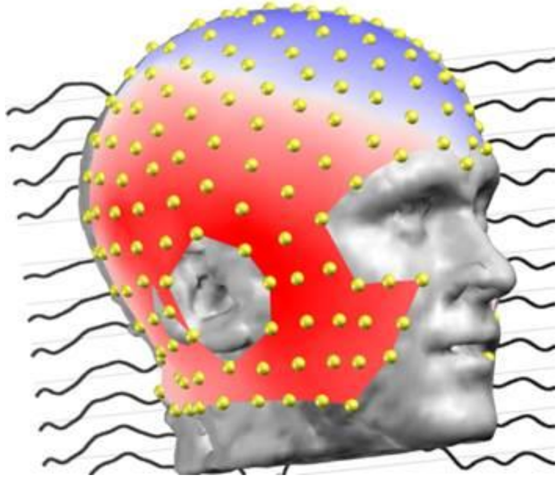
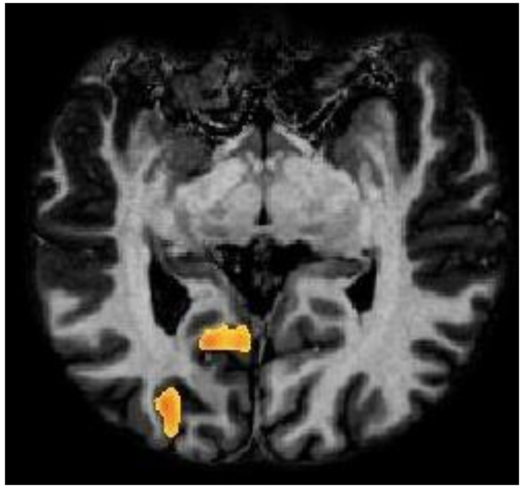
BRAIN AND BEHAVIOUR LABORATORY



The path toward Ultra-High Field



Frédéric GROUILLER

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April 14th, 2020

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A brief History of MRI

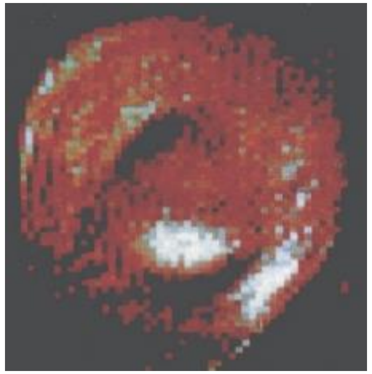
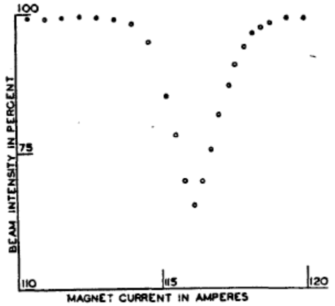
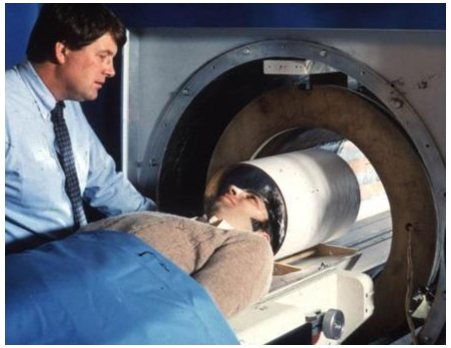


Image of human finger from Mansfield (1977) at 0.35T in 23 minutes

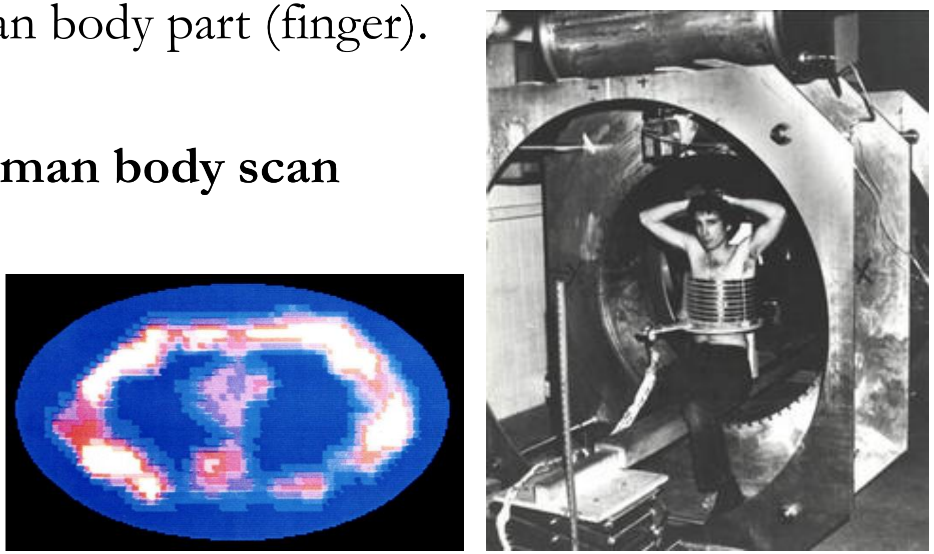
- 1938: Isidor Rabi discovered **Nuclear Magnetic Resonance** (NMR)
- 1973: Paul Lauterbur applied magnetic field gradients to obtain a 2-dimensional image (**spatial encoding**) of water tubes.
- 1977: Peter Mansfield used a magnetic field gradient for **slice selection** and obtained the 1sr image of a human body part (finger).
- 1977: Raymond Damadian acquired the **first human body scan**
- 1983. 1st whole-body 1.5T MRI
- 2003: 1st clinical 3T MRI
- 2017: 1st clinical 7T MRI



Resonance in LiCl from Rabi, 1938



First whole-body 1.5T (1983)



First whole-body image obtained by Damadian in 1977 (5 hours of acquisition)

MRI Field Strength

Hoult & Lauterbur, Journal of Magnetic Resonance, 1977:

«Whole-body MRI would not be possible above 10MHz (0.24T)»

0.3T — 1T — 3T — 7T — B_0

Low Field | Mid Field | High Field | Very High Field | Ultra High Field

Siemens Terra , 7T,

Iseult, 11.7T,
Neurospin, Paris, 2019

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Ultra-High Field MRI scanners

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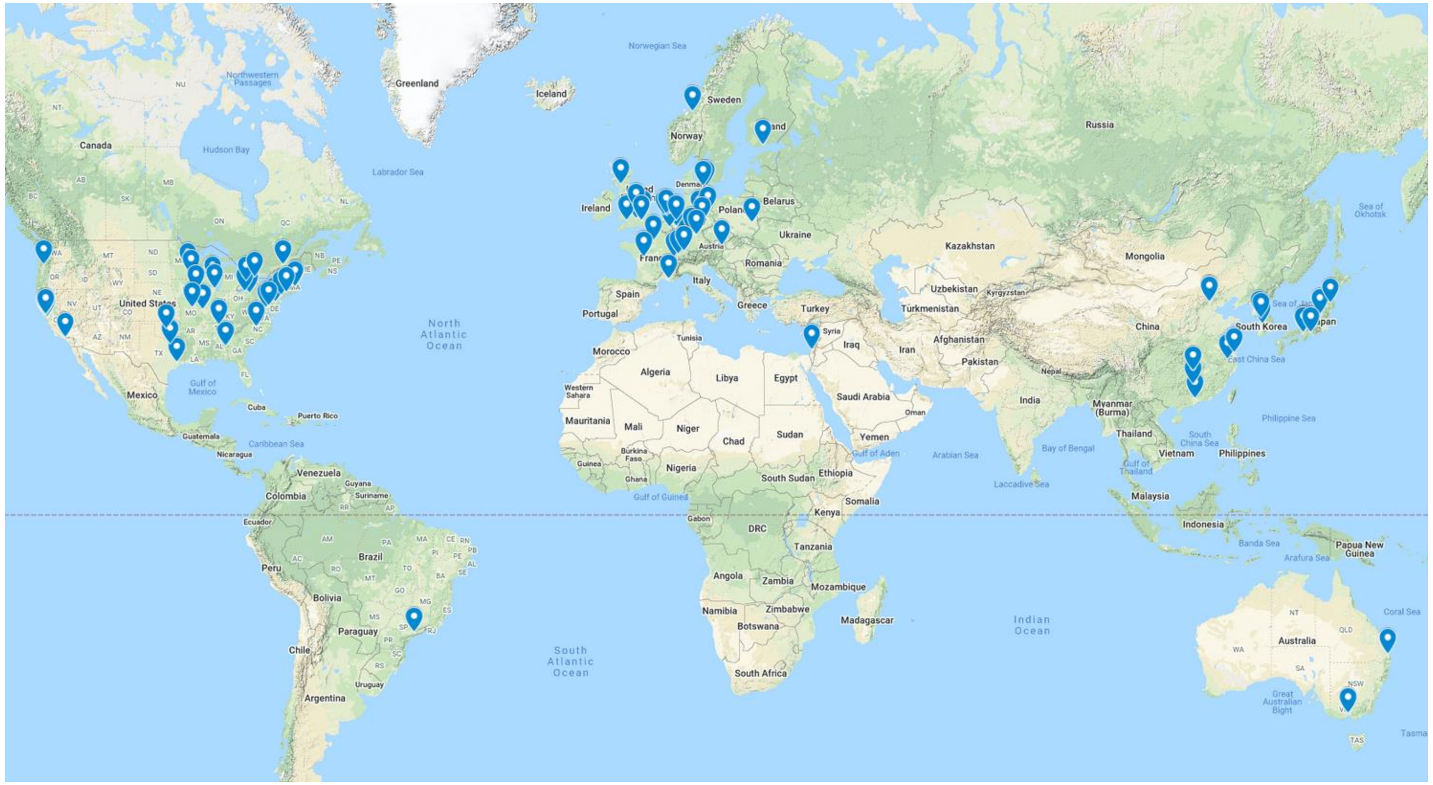

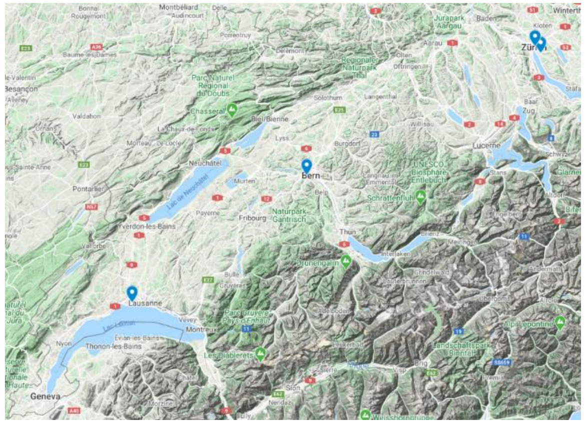

Today: 96 Ultra-High MRI scanners worldwide

- 7T MRI: 87 scanners (80% Siemens), 34 new installations in the last 2 years
- >7T MRI: 9 scanners (9.4T, 9.7T, 10.5T, 11.7T)

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From 3T to 7T

3T		7T
		
7.35 tons	**Weight**	25 tons
186 cm	**Length**	297 cm
31 m^2	**Min. Room Size**	50 m^2

Why moving toward higher magnetic field?

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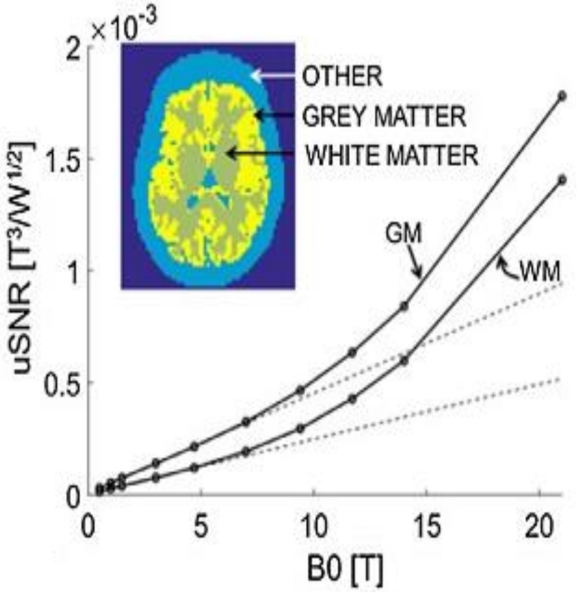
- Increase of **SNR** with magnetic field:

$$SNR \propto \rho_0 \frac{\gamma^2 \hbar^2 I(I+1)}{3kT} B$$

=> increase of spatial resolution and/or decrease of scan time

- Modification of **relaxation time**:
  - ✓ Increase of T_1
  - ✓ Decrease of T_2 and T_2^*
- Increase of **magnetic susceptibility** (internal magnetization of the tissue)
- Increase of **chemical shift** (differences between resonance frequencies of molecules)



Ladd et al., Progress in Nuclear Magnetic Resonance Spectroscopy, 2018

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Effects of magnetic field

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- **Stronger attractions of magnetic objects**:

  => potentially more dangerous

  => MR-conditional devices at 3T might be unsafe at 7T (eye-tracker, respirator, …)

- More restrictions with **implanted devices**: pacemaker, prostheses, stent, sterilet, ….

- **Adverse effects**: dizziness, nausea, metallic taste, claustrophobia, …

What about radiofrequency ?

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Radio Frequency waves used in MRI have to be trasnsmitted at **Larmor Frequency**:

$\boldsymbol{\omega = \gamma B_0}$ avec γ the gyromagnetic ratio (for H_1, γ=42.58MHz/T)

B0	1.5T	3T	7T
Larmor Frequency (ω)	63.87 MHz	127.74 MHz	298.06 MHz
Radio-Frequency Wavelength (λ)	470 cm	235 cm	100 cm

Larmor frequency is the speed of precession of the spins under the influence of the magnetic field

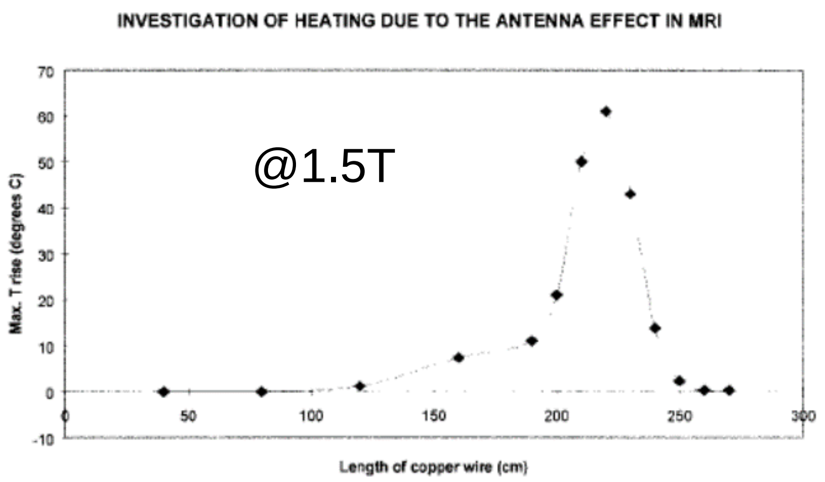
Wavelength is the distance between 2 repetitions of the waves (inversely proportional to the frequency)

=> All the radio-frequency devices have to be design to deal with this frequency (RF power amplifier, RF transmission, MRI coils)

Radio Frequency: Antenna effect in the wires

B0	1.5T	3T	7T
Larmor Frequency (ω)	63.87 MHz	127.74 MHz	298.06 MHz
Radio-Frequency Wavelength (λ)	470 cm	235 cm	100 cm

- Lengths of the wires (ECG, EMG, ….) can be considered as radio-frequency antenna
- The wires will capture RF waves and will extract power from them
- Resonant antenna: standing wave due to reflection in the wire
- Resonance is achieved when the antenna (wire) is approximately half the wavelength long (~50cm at 7T)

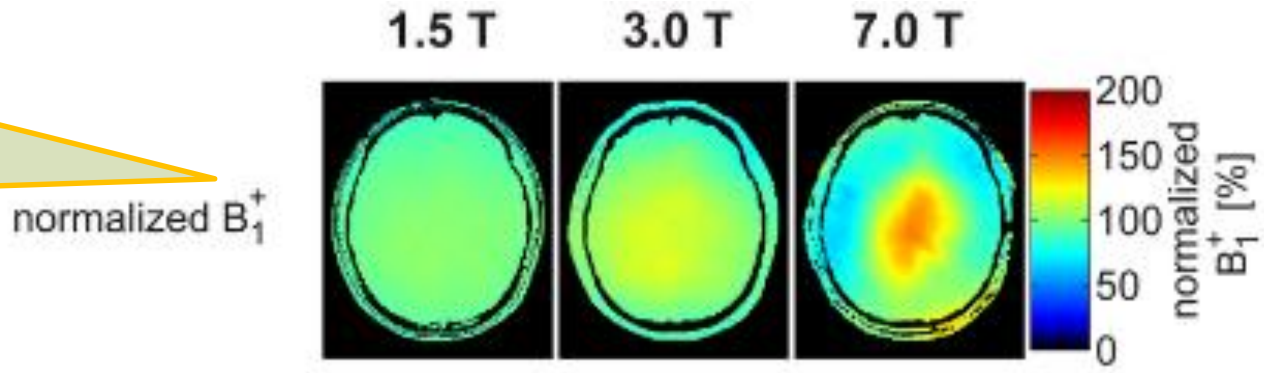


Dempsey et al., JMRI, 2001

=> It has to be seriously considered at 7T and lengths of wires should be carefully selected (avoid 50cm wires should be avoided)

Radio Frequency Field Inhomogeneity

Radio Frequency field is written B_1.
B_1^+ stands for the transmitted RF field and B_1^- stands for the received RF field.

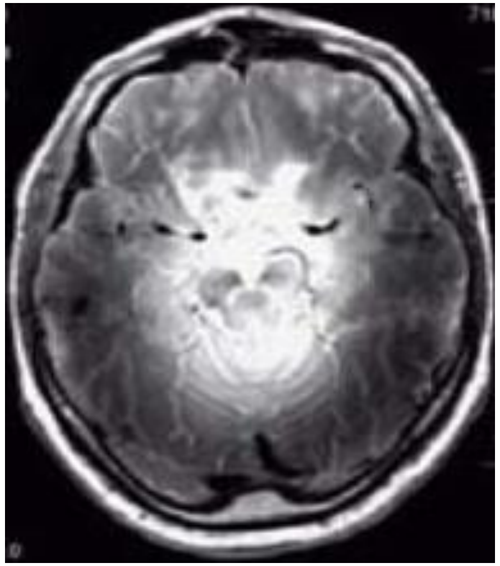


Dieringer et al., Plos One, 2014

- In order to obtain uniform signal, radio frequency field (B_1) have to be transmitted homogeneously over the brain

- At 7T, Radio Frequency wavelength is close to the size of the head leading to an inhomogeneous penetration of the radio frequency field into the brain.

- **Correction of the RF Field inhomogeneity is required**

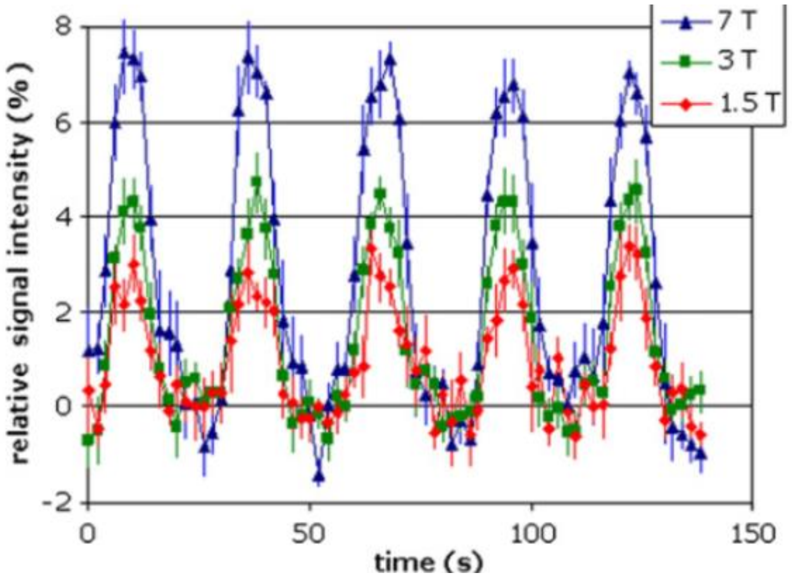


Example of B_1 inhomogeneity

BOLD signal changes at UHF

- **Double benefit:**
  - higher SNR
  - increased sensitivity to tissue susceptibility

- **Interest:**
  - increase spatial resolution
  - reduce scanning time by decreasing the number of trials



Van der Zwaag et al., Neuroimage, 2009

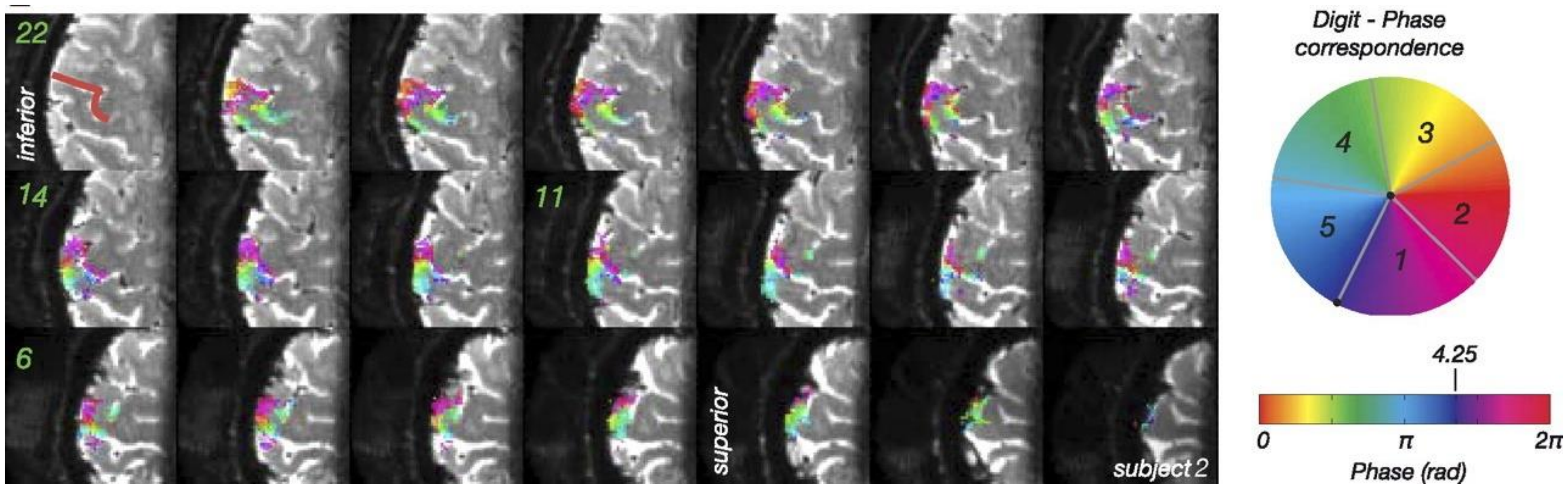
- **But:**
  - also more sensitive to susceptibility artefacts
  - physiological noise (respiratory and cardiac activity) is also proportional to signal intensity

Applications of BOLD fMRI at UHF

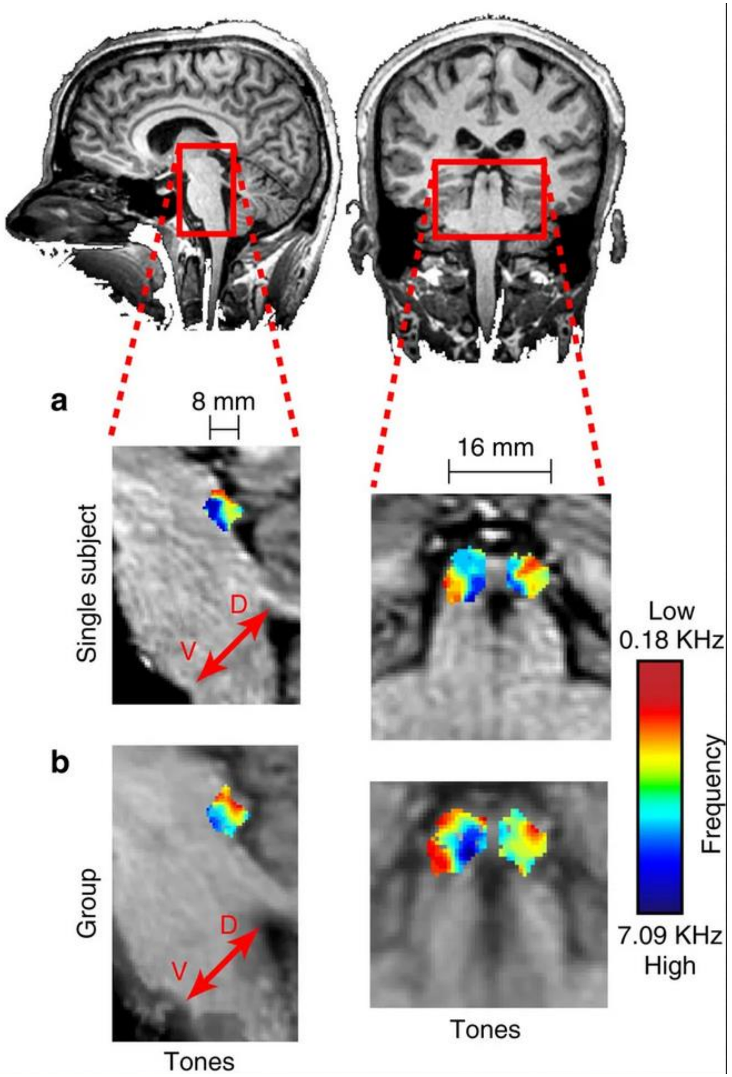
High-resolution fMRI

- Somatotopy: localisation of somatosensorial area corresponding to each digit, voxel size = 1mm isotropic

- Tonotopy: tonotopic maps in human inferior colliculus, voxel size = 1.5mm isotropic



Sanchez-Panchuelo et al., Journal of Neurophysiology, 2010



De Martino et al., Nature Communications, 2013

Applications of BOLD fMRI at UHF

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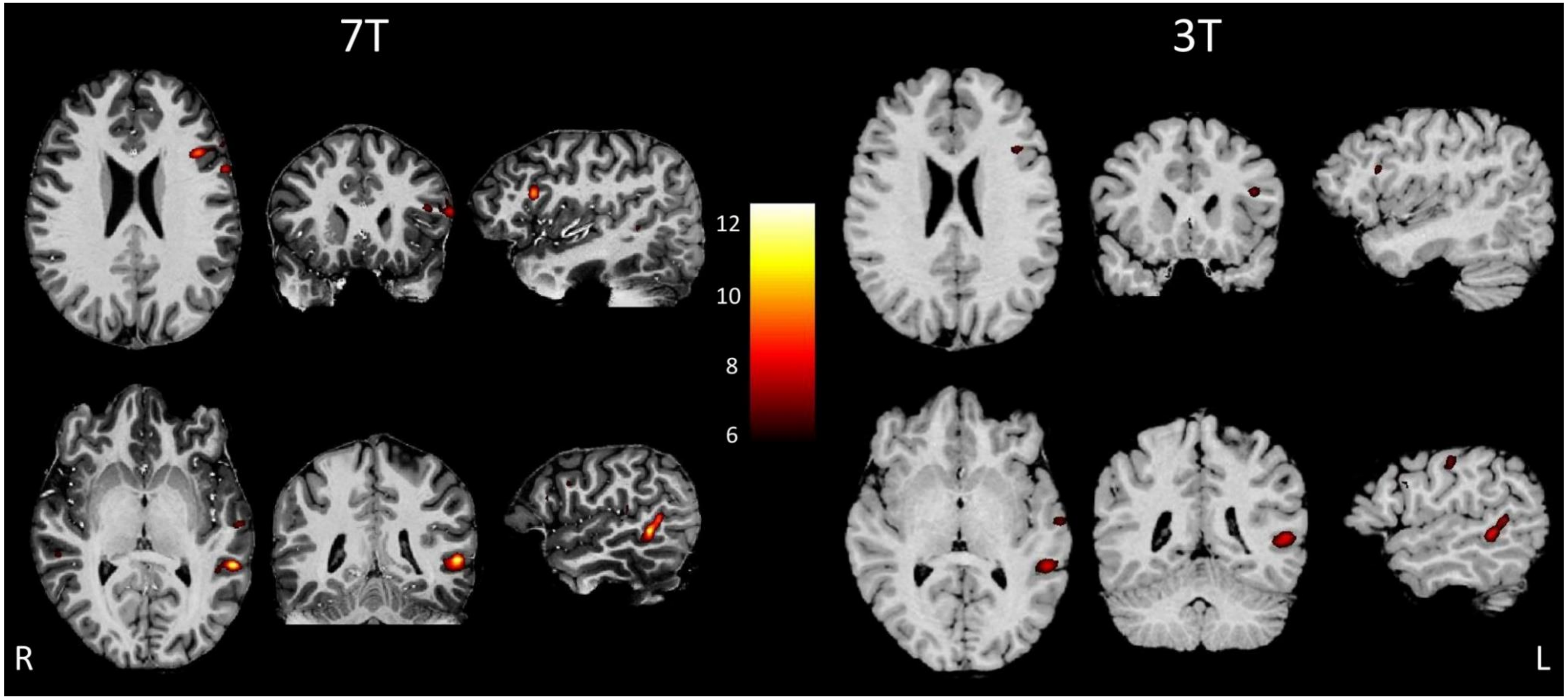
Presurgical mapping of language cortex

- Language fMRI at 7T (1.5mm isotropic) for the presurgical localisation of Broca (left inferior frontal) and Wernicke (left temporal) areas

- Same Language fMRI protocole at 3T in the same patient demonstrated a very good reproducibility between 3T and 7T.



Grouiller et al., Magnetic Resonance Materials in Physics, Biology and Medicine, 2016

Susceptibility Mapping at UHF

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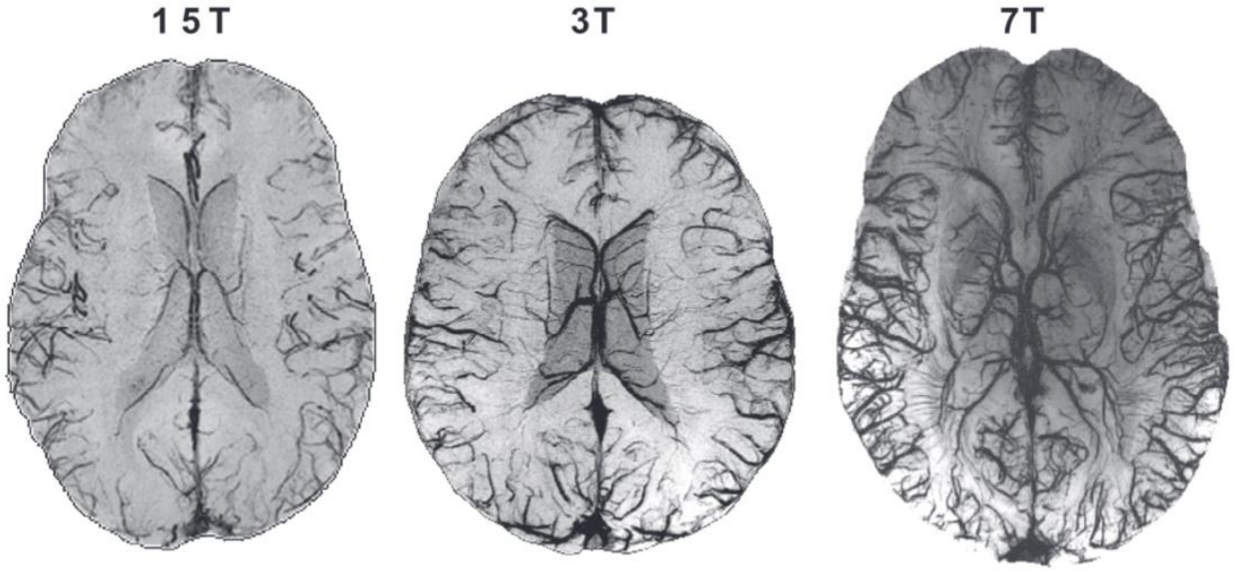
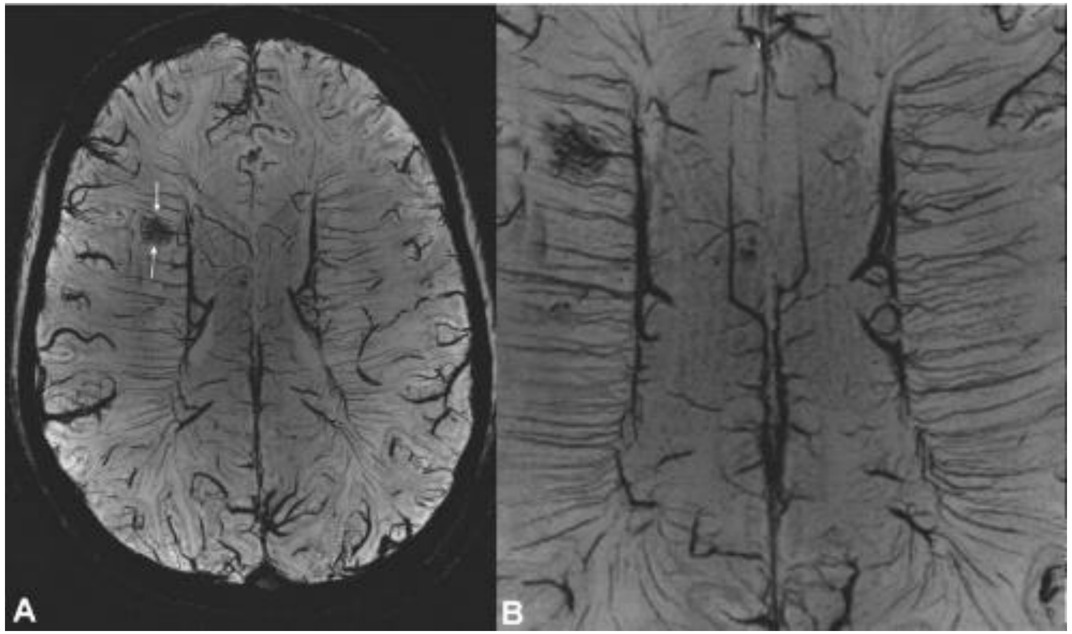
- **Susceptibility Weighted Imaging** also benefits from the increased magnetic susceptibility at UHF.
- Magnitude and Phase images are combined to generate susceptibility maps.
- Phase changes that originate from susceptibility changes are directly proportional to field strength and echo tim



Ladd et al., Progress in Nuclear Magnetic Resonance Spectroscopy, 2018

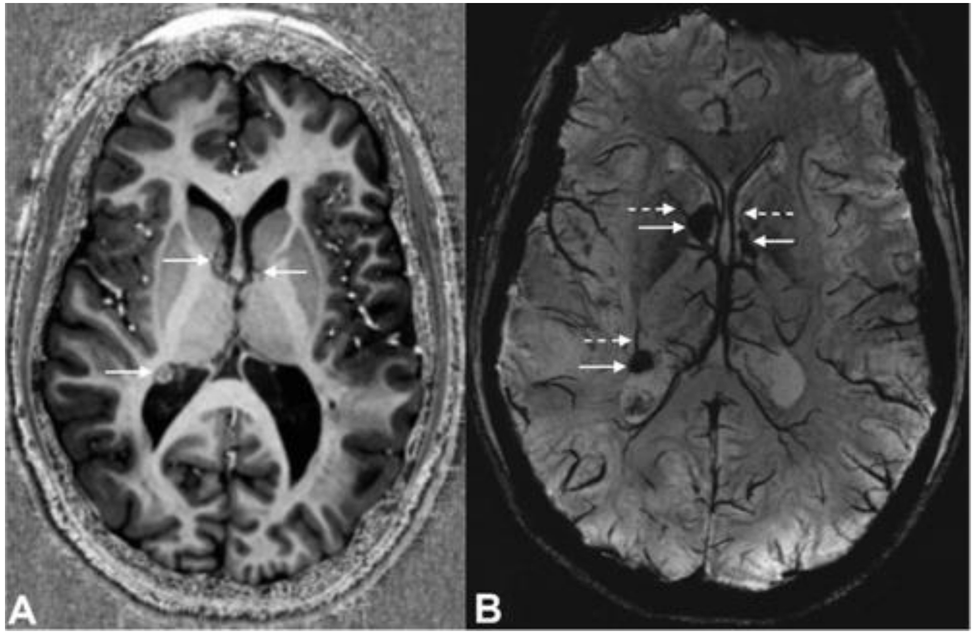
Susceptibility Mapping at UHF

SWI (0.4x0.4x1mm) (A) Small, irregular, and enlarged vessels in this patient with a capillary telangiectasia. (B) Remarkable depiction of the normal transmedullary veins.



Vargas et al., Journal of Neuroimaging, 2017

Patient with tuberous sclerosis. (A) Lesions are hardly visible in structural image. (B) Tubers of different size associated with tortuous veins (dotted arrows).



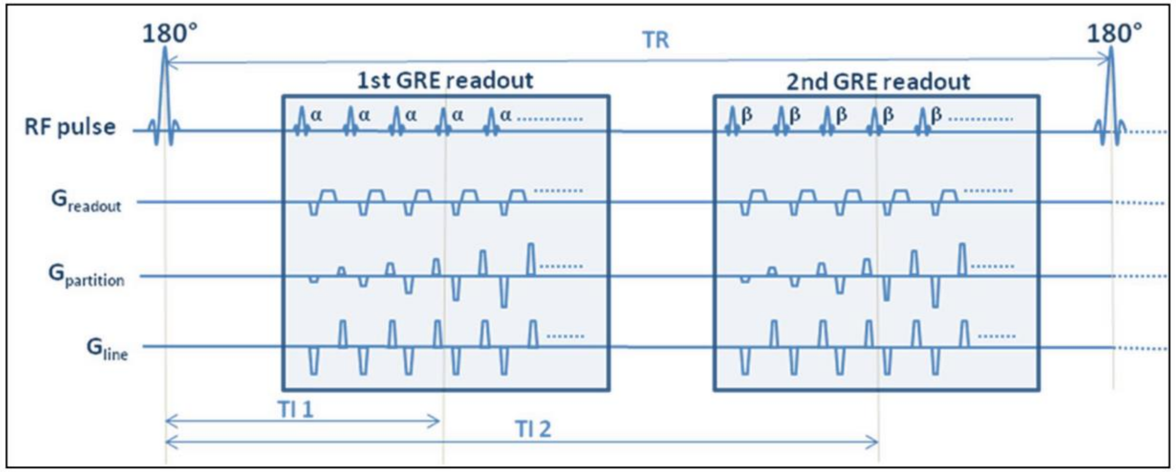
Pittau et al., Journal of Neuroimaging, 2018

⇒ SWI can be used to detect microhemorrages, calcifications, iron accumulation ad visualization of vascular structure.

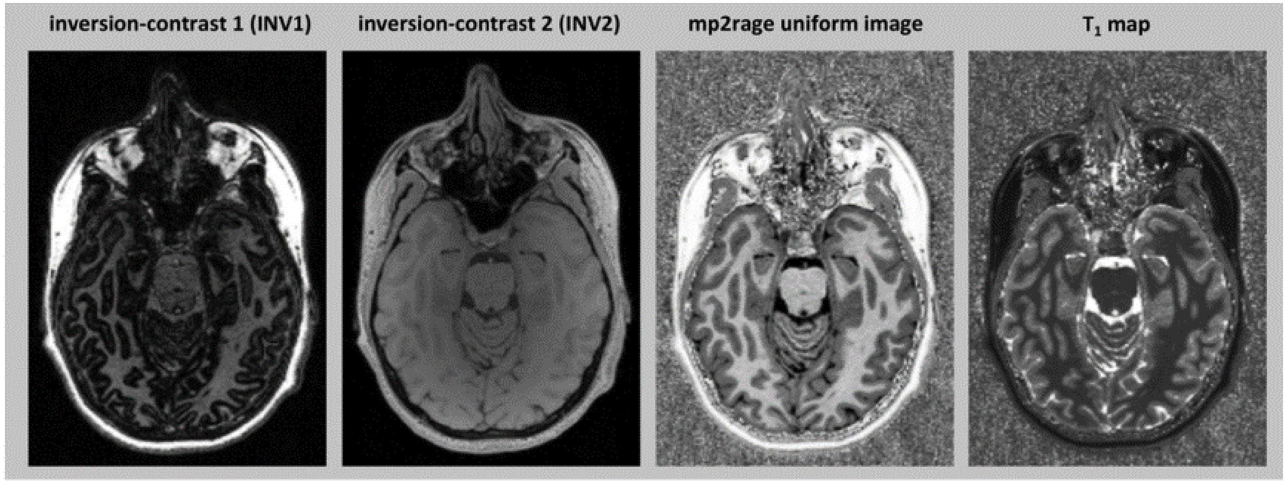
⇒ Abnormal vasculature associated with a lesion might be easier to see than the lesion itself.

Structural Imaging at UHF

- Large spatial inhomogeneities in transmit B_1 field at UHF severely impair image quality.
- Modification of classical MPRAGE sequence in order to obtain 2 images at 2 different inversion time (TI): **MP2RAGE**.
- By combining the 2 images, it is possible to obtain a bias field corrected T_1-weigthed image and a T_1 map.



Marques et al., Neuroimage, 2010

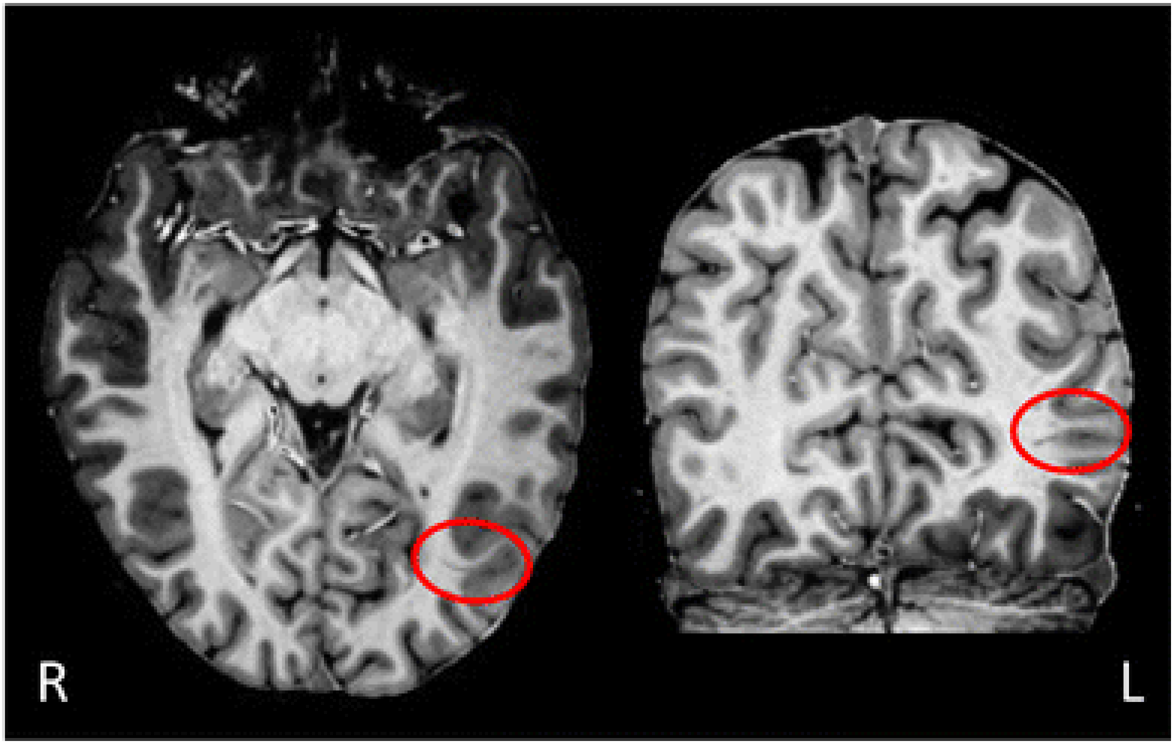


$$MP2RAGE = \frac{GRE_{TI1} GRE_{TI2}}{GRE_{TI1}^2 + GRE_{TI2}^2}$$

Structural Imaging at UHF

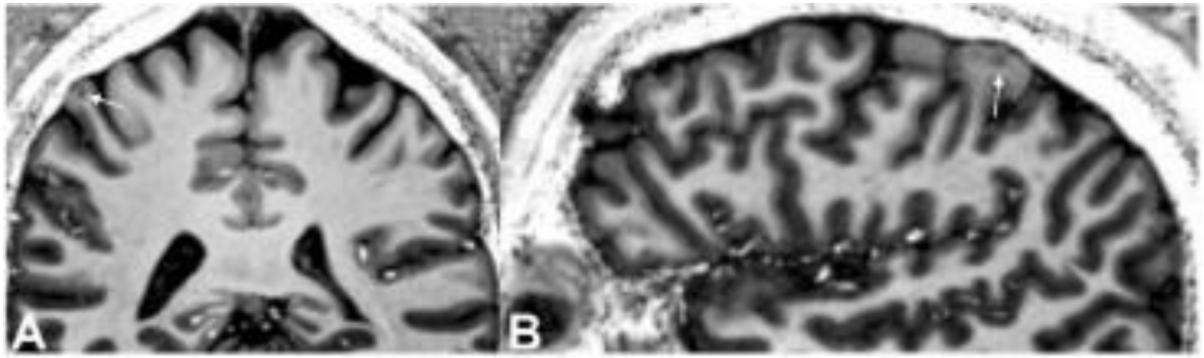
MP2RAGE at 7T

- Patient with left temporal focal cortical dysplasia invisible at 3T.
- Lesion is visible with MP2RAGE at 7T (0.6mm isotropic)



Grouiller et al., Magnetic Resonance Materials in Physics, Biology and Medicine, 2016

- Presence of a small, well-delineated round lesion (arrows) in MP2RAGE at 7T (0.6mm isotropic).
- Postsurgical histopathology confirmed the presence of a right postcentral ganglioglioma.



Pittau et al., Journal of Neuroimaging, 2018§x

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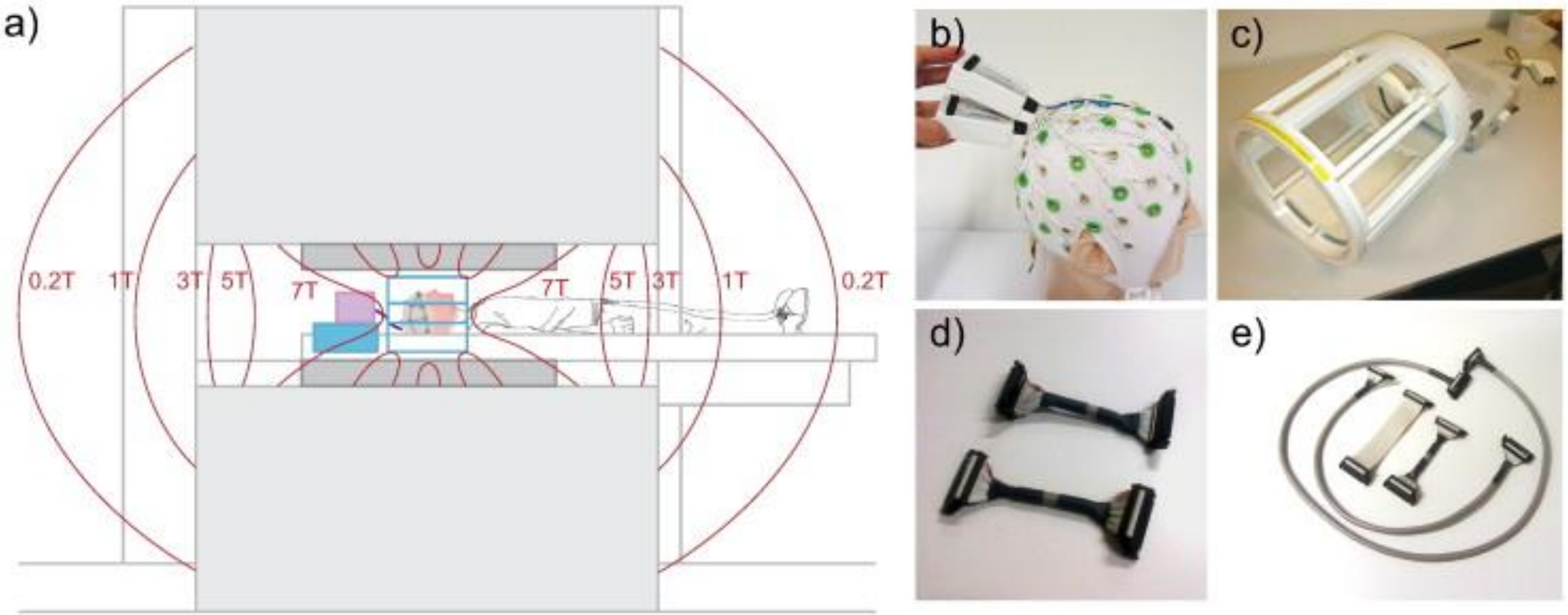
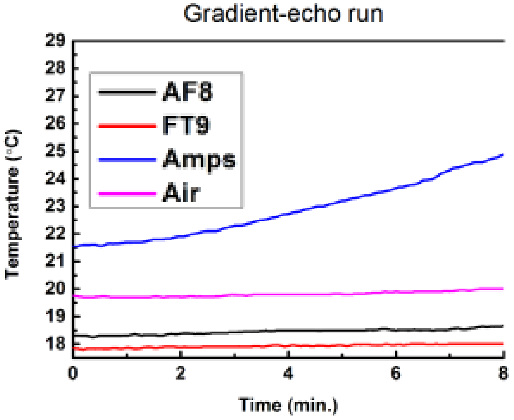
EEG-fMRI: Experimental design optimisation

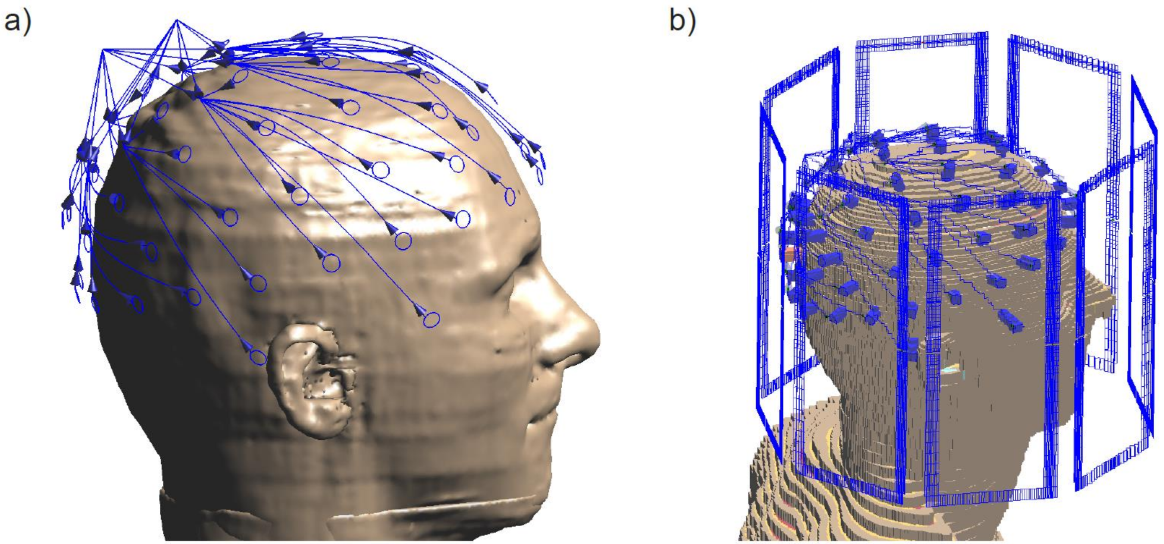


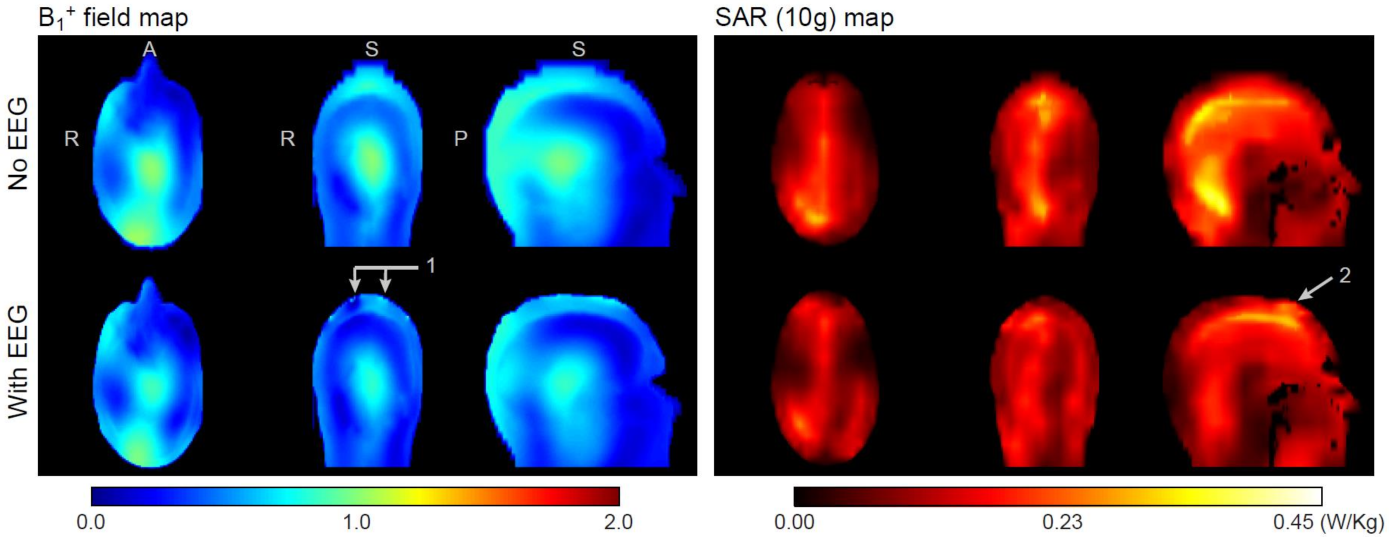


- reduction of the wires length (between cap and amplifier connectors) and replacement of flat wires by bundled wires
- validation with phantom: EEG noise decrease, no temperature increase

Jorge et al., Neuroimage, 2015

Safety: Electromagnetic simulations



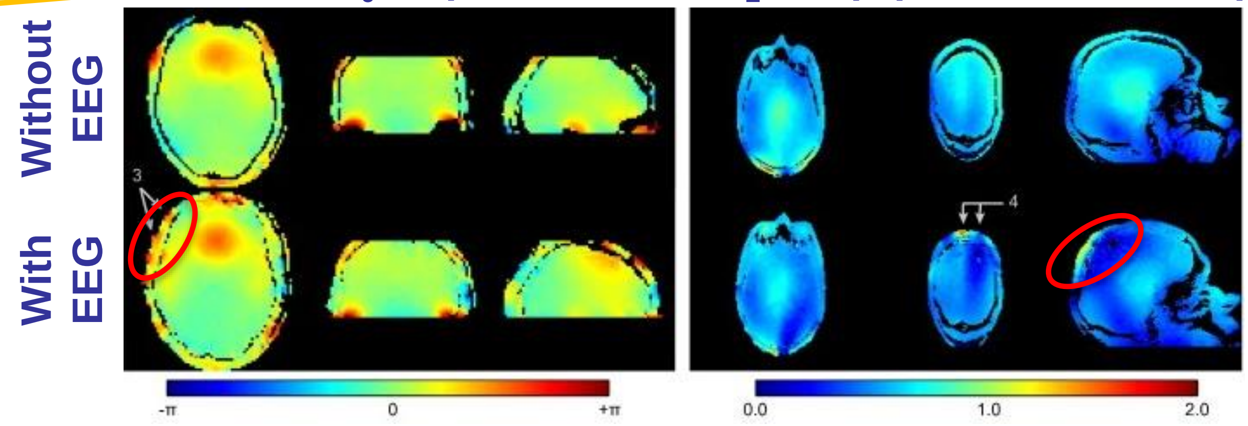


- electromagnetic simulation (SEMCAD X)
- model of realistic human head with 64 ring electrodes, resistance and leads
- 8 channels head array

Jorge et al., Neuroimage, 2015

Image quality: functional images

B_0 map is a map showing the homogeneity of the static magnetic field (B_0)



Jorge et al., Neuroimage, 2015

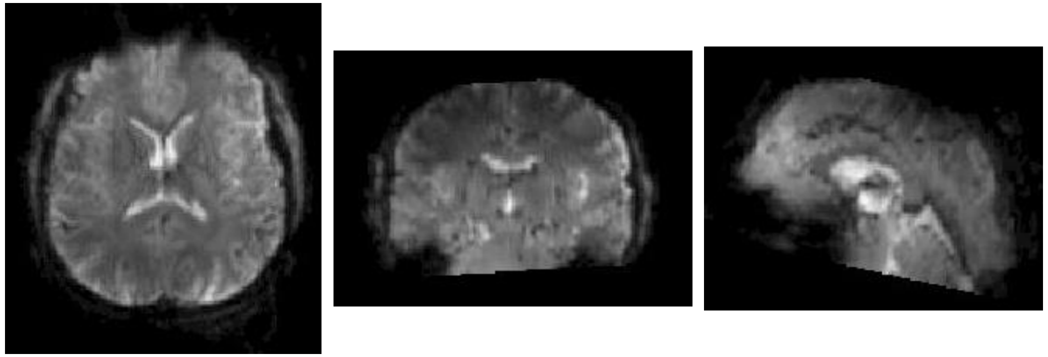
B_1^+ map is a map showing the transmission of the radio-frequency field (B_1), + stands for transmission (- for reception)

Presence of EEG materials induces:

- **local susceptibility effect (B_0)** causing signal drops and geometric distortion (mostly limited to the scalp)

- **disruption or shielding effect (B_1)** reducing the signal-to-noise ratio

fMRI (GE-EPI) with EEG



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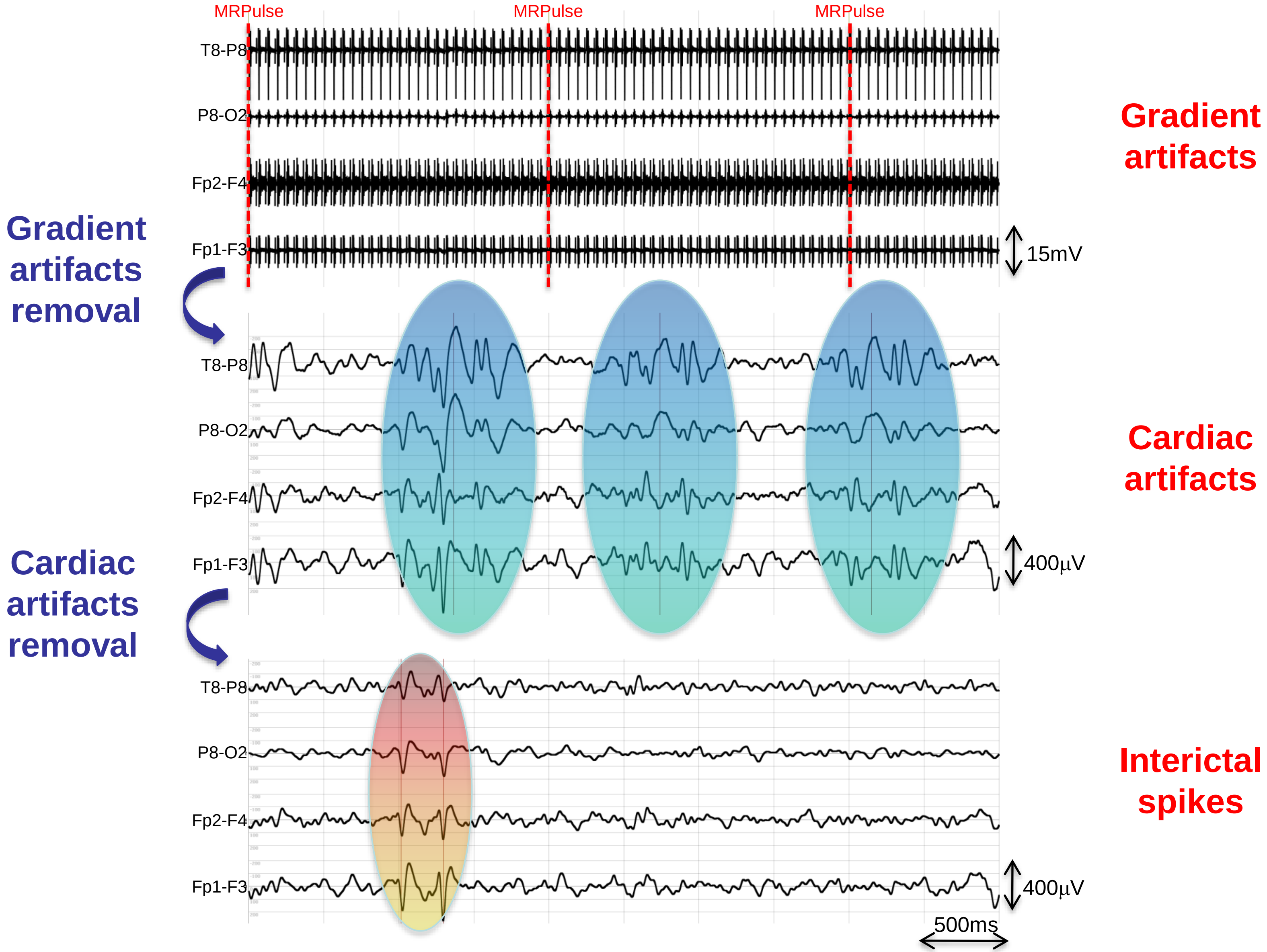
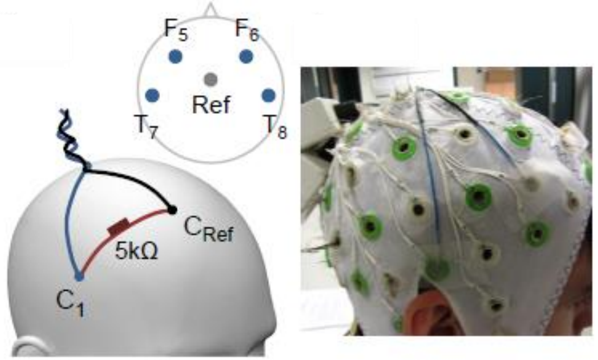
EEG Artifacts removal

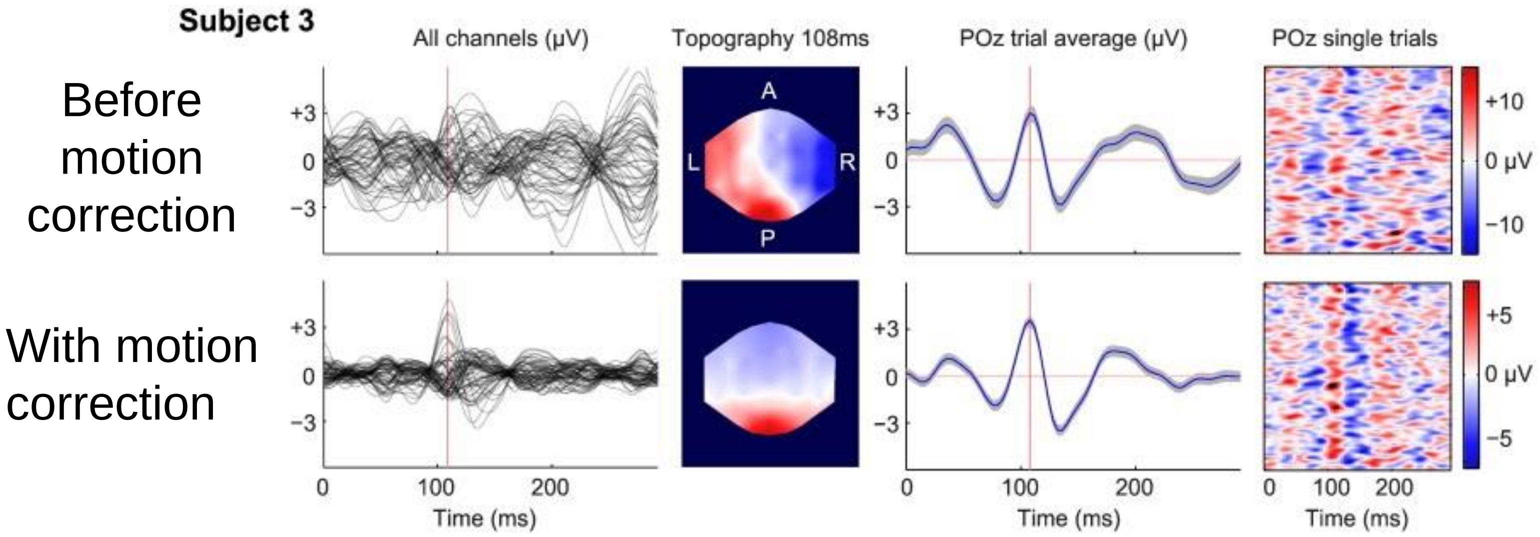


- After gradient artifacts and cardiac artifacts removal, spontaneous or evoked neural activity can be detected in EEG
- Be careful to preserve EEG quality. It is often better to have some artifacts residuals than removing too much signal of interest

Motion artifacts removal

- Motion artifacts are **large**, **unpredictable** and **proportional with B_0**
- Non-permanent modification of the EEG cap:
  4 EEG channels are by-passed to measure motion
- Adaptive filtering to remove motion
- Visual Evoked Potentials in 6 healthy subjects at 7T
- 62% increase in VEP trial-by-trial consistency





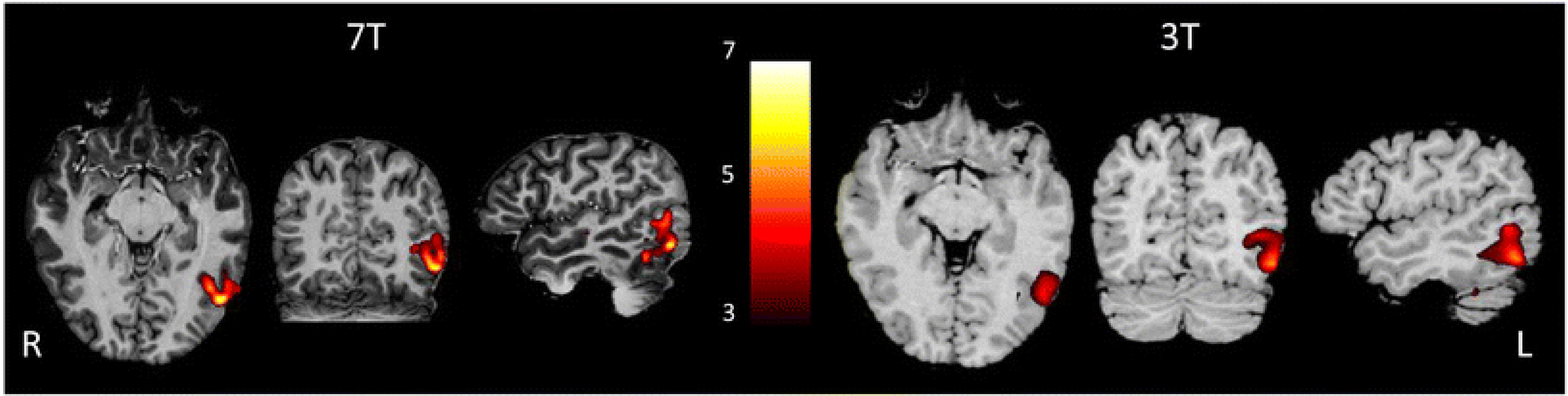
Jorge et al., Neuroimage, 2015

EEG-fMRI at Ultra High Field: comparison with 3T

EEG-fMRI in a patient with left temporal focal cortical dysplasia

=> Activations at 7T are **more precise and stronger**

=> Localization of activations are **reproducible** between 3T and 7T



Grouiller et al., Magn. Res. Mater. Phy., 2016

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Perspectives

Bimodal connectivity-based neurofeedback using simultaneous EEG-fMRI

- **Aim:**
  - EEG and fMRI neurofeedback are used successfully to regulate brain activity in different disease
  - Simultaneous EEG-fMRI is a compelling method to study the functioning of the human brain using the complementarity of electrical and hemodynamic signals.

- **Aims:**
  - Develop new powerful algorithms to process the EEG acquired simultaneously with fMRI **in real-time** based on our previous work at 7T.
  - Demonstrate that EEG neurofeedback can be run simultaneously with fMRI acquisition at 3T and 7T.
  - Combine simultaneous EEG and fMRI neurofeedback in order to increase its efficiency especially in the context of emotion regulation.

- **Perspectives:** Applications of these algorithms for real-time epilepsy mapping or to perform bimodal neurofeedback in other neurological or psychiatric diseases.

- **Funding:** obtained from Swiss Science Foundation (3 years, 452'796 CHF)

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Perspectives

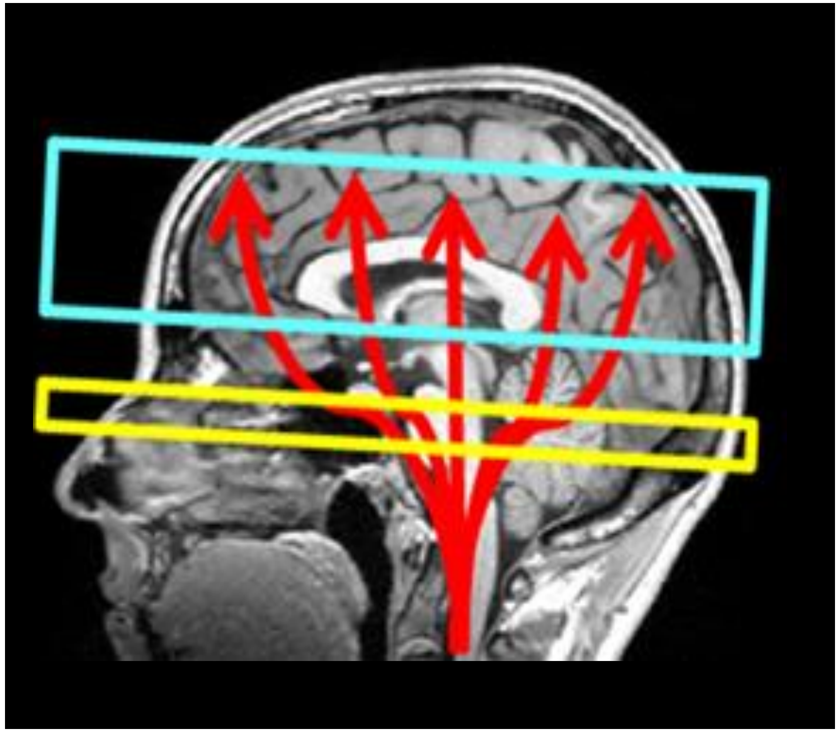
Arterial Spin Labelling (ASL)

Aim: measure of brain perfusion quantitatively and non-invasively (without contrast agent)

Labelling: Inversion of spin magnetization of the arterial blood before entering in the region of interest (labelling plane perpendicular to the carotids) thanks to a radiofrequency pulse.

Transit time: time between labelling of the blood and acquisition, During this time, the labelled blood diffuse into the capillaries (post-labelling delay ~ 1600ms)

Acquisition: usually EPI acquisition



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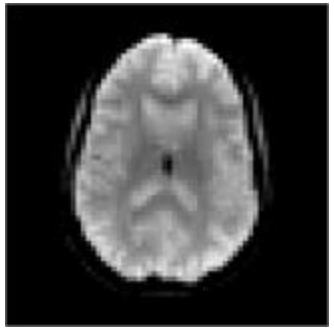
Perspectives

Arterial Spin Labelling (ASL)

CONTROL IMAGE



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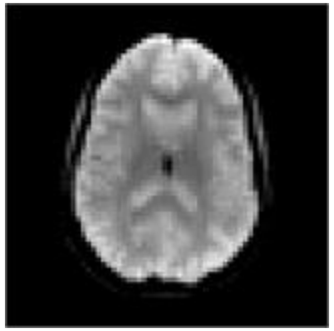
LABELLED IMAGE



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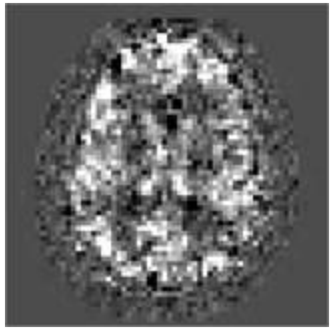
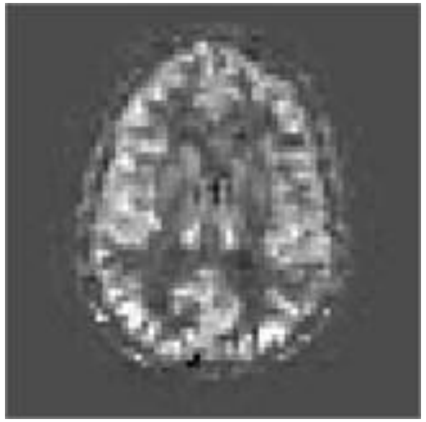


Perfusion Map:

- Succession of control and labelled images.
- Labelled images are composed of signal from labelled blood and from static signal from tissue.
- With the subtraction of labelled and control images, only the signal from labelled blood is kept.
- Signal to Noise Ratio is very weak (0.5-1% at 3T) => multiple repetitions and averaging required.

After 4 minutes (~20-30 repetitions)



Perspectives

Arterial Spin Labelling (ASL) at UHF

- **Multiple benefit:**
  - higher SNR
  - increased T_1 relaxation time

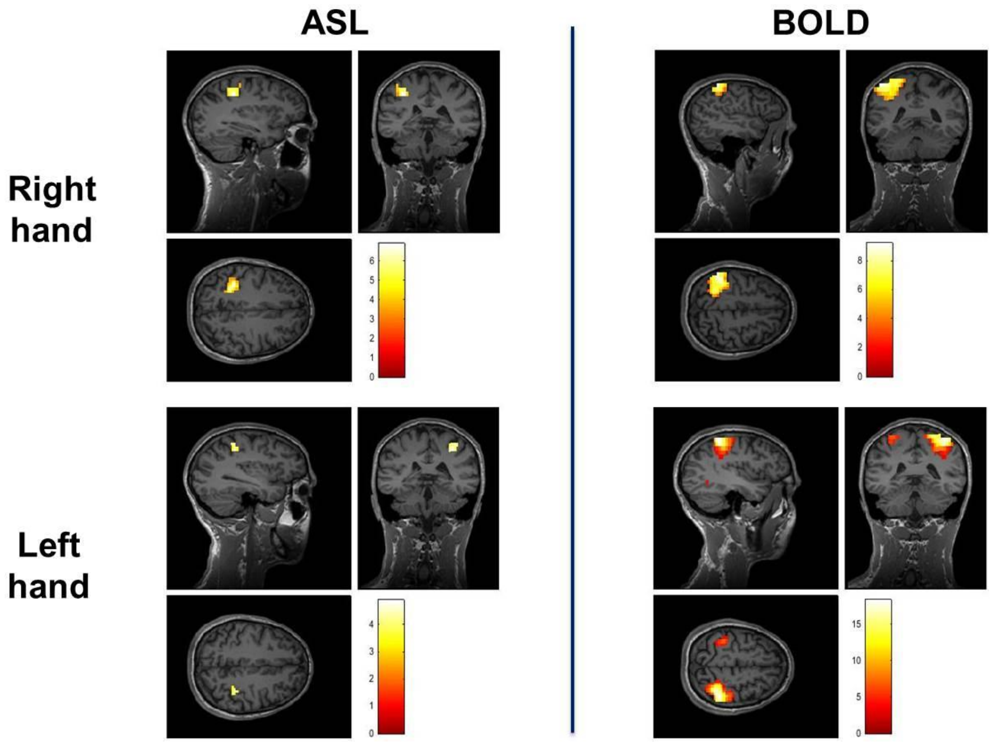
- **Choice of the post-labelling delay:**
  - wait enough for a complete perfusion of the brain (1800 ms in healthy subjects, 2000 ms in patients)
  - SNR decrease quickly in time: blood is used as endogenous tracer and signal decrease with longitudinal relaxation (T_1)

- **Variation of T_1 with magnetic field strength:**
  - T_1 blood = 1500 ms at 1.5T
  - T_1 blood = 1650 ms at 3T
  - T_1 blood = 2100 ms at 7T

Perspectives

Quantitative functional brain mapping using Arterial Spin Labelling as alternative to BOLD

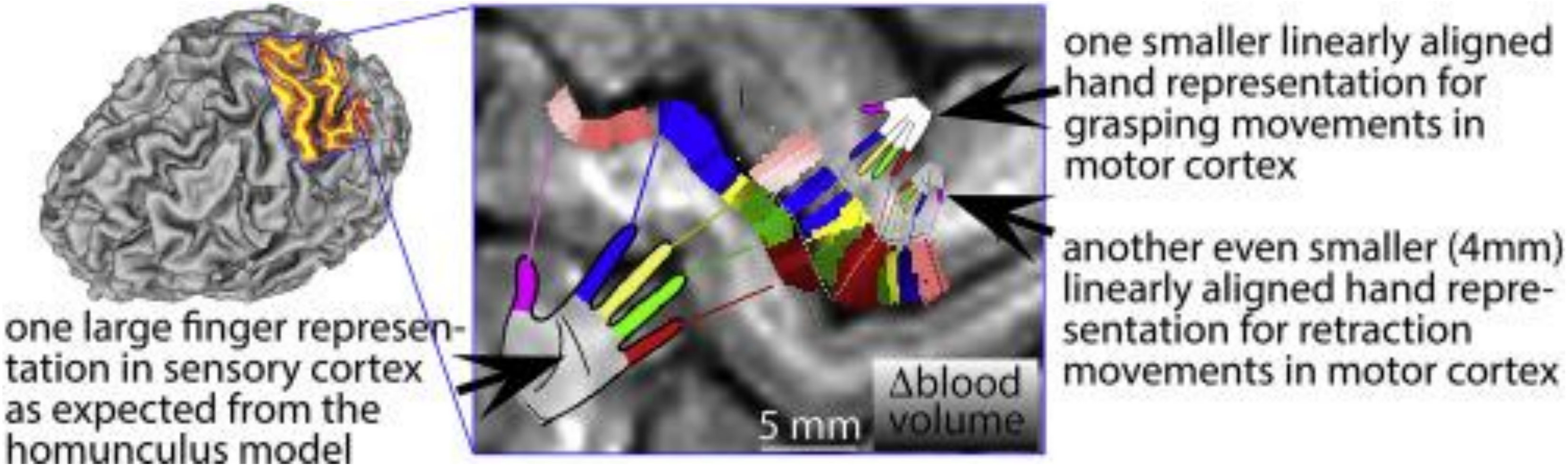
- <u>Rationale</u>:
  - Functional ASL is an alternative imaging technique that allows for a **direct quantitative measure of Cerebral Blood Flow**.
  - More specific than BOLD but less sensitive due to a very low SNR.
  - SNR of fASL at Ultra-High Field is drastically improved
- <u>Aims</u>:
  - Compare BOLD and functional ASL specificity and sensitivity using Dual-Echo pcASL.
  - Develop a robust pipeline for functional ASL analysis
  - Application of this method to patients with potential alteration of neurovascular coupling (brain tumours, stroke, neurovascular diseases, epilepsy, …)



Preliminary results comparing BOLD and functional ASL of the motor cortex at 3T using a Dual-Echo pcASL sequence

Layer specific fMRI

- **Rationales:**
  - fMRI spatial resolution can be more precise than 1mm using Ultra High Field MRI.
  - Conventional algorithms to preprocess the sub-millimetre fMRI are suboptimal (normalisation, motion correction)



Huber L. et al., Neuroimage, 2019

- **Aims:**
  - Optimization of sub-millimetre fMRI sequences.
  - Multi-echo fMRI to separate BOLD from motion and physiological noise.
  - Development of a new surface-based pipeline to analyze sub-millimeter fMRI.

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Conclusions

BBL BRAIN AND BEHAVIOUR LABORATORY

Characteristic	Trend as B_0 ↑	Pro	Con
SNR	↑	Higher resolution, shorter scan time, X-nuclei feasible	None
SAR	↑	None	Fewer slices, smaller flip angle, longer TR, longer breathhold
Physiological side-effects	↑	None	Dizziness, nausea, metallic taste
Relaxation times	T1 ↑[a]	TOF, ASL, cardiac tagging	Longer scan time
	T2 ↓[b]		DWI, DTI
	$T2^*$ ↓	SWI, BOLD	
RF field uniformity	↓	Parallel reception Parallel transmission	Position-dependent flip angle, poor inversion, unexpected contrast
Susceptibility effects	↑	BOLD, SWI, $T2^*$	Geometric distortions, intravoxel dephasing
Chemical shift	↑	Fat saturation, CEST, MR spectroscopy	Fat/water and metabolite misregistration

Ladd et al., Progress in Nuclear Magnetic Resonance Spectroscopy, 2018

- **SNR increases** with magnetic field => higher resolution decreased scan time
- **B_0 and B_1 are less homogenous** and required correction (shimming and post-processing)
- **Susceptibility effect** is increased: good news for BOLD-fMRI and SWI but also more susceptibility artefacts and motion-related artefacts
- **T1 increases**: great opportunity for ASL
- **Chemical shift** increases: interesting for MR spectroscopy