NEPTUNE

Nuclear process driven Enhancement of Proton Therapy UNravEled

WP2

R. Faccini Univ. “La Sapienza” and INFN Rome

PROJECT GOAL

Evaluate impact of ^{19}F and ^{11}B on particle therapy

GOALS OF WP2 (IMAGING)

RM1

Evaluate bio-distribution of tracers

Talks from S. Pacifico e N. Protti

Evaluate concentration of samples

NA,PV

Evaluation of bio-distributions of tracers

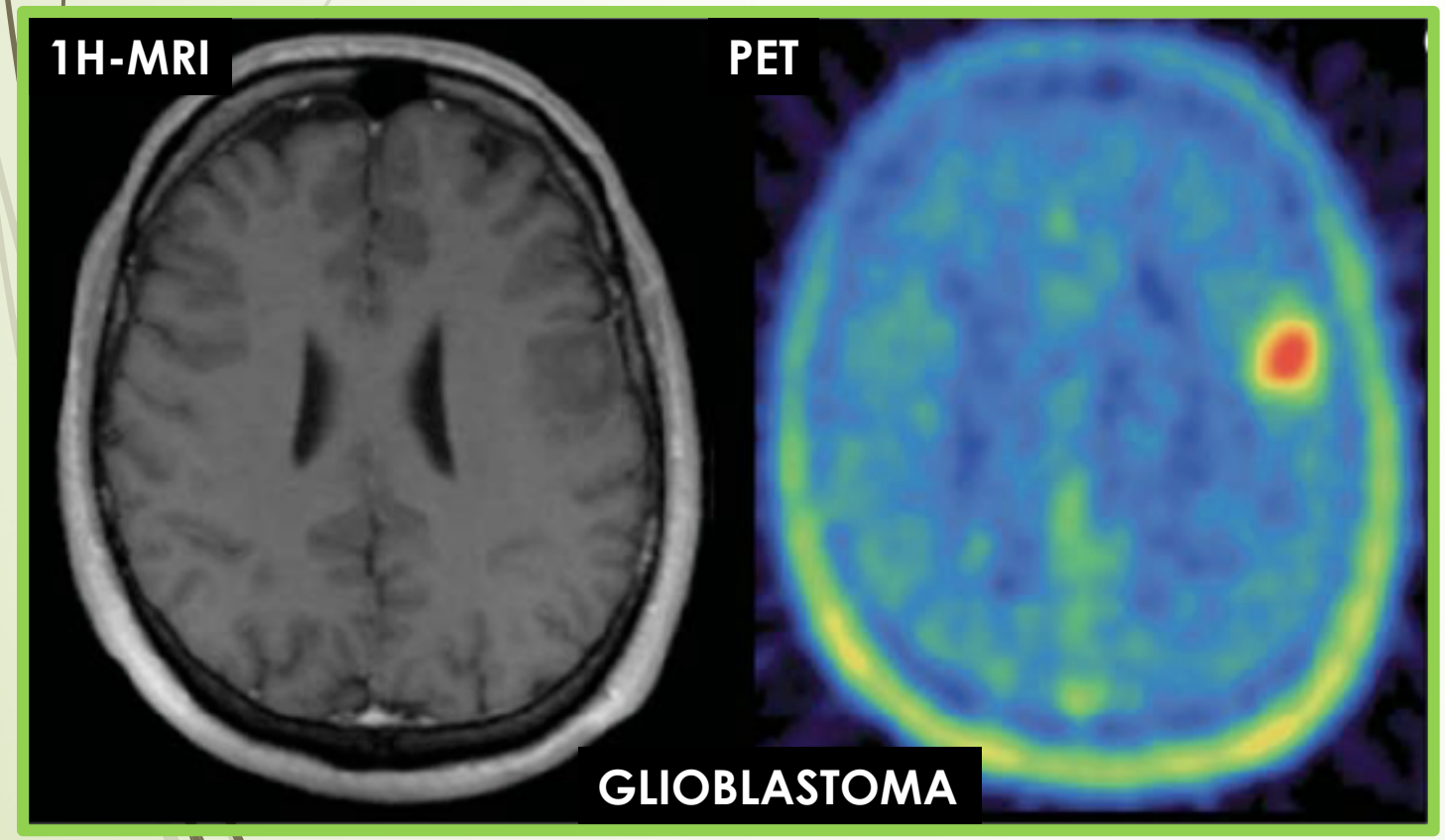
- To apply the potential treatment, we will need to know patient by patient the biodistribution of the tracer.
- Need to detect fluorine (borated compounds have to be tagged with fluorine). Two existing techniques:
  - PET with 18F → too low concentrations
  - MRI with 19F → is the signal high enough?

THIS PROJECT

A) Tests on animals to have samples with the correct concentration
B) Setup a test stand to study and improve, with INFN competences, the signal/noise ratio
C) Study co-registered 19F and 1H images to study the noise correlation and possible algorithms to enhance sensitivity to signal

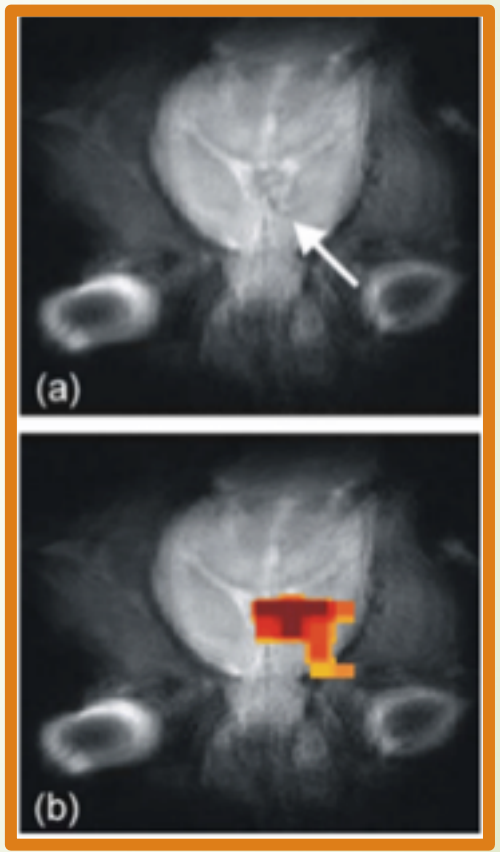
Available techniques: PET/MRI

PET has a worse resolution and tracers more difficult to synthetize/handle but 1H-MRI does not show a signal …



… but:

- gyromagnetic factor of 19F is only 6% away from 1H
- 19F is not present in human body (no physical background)



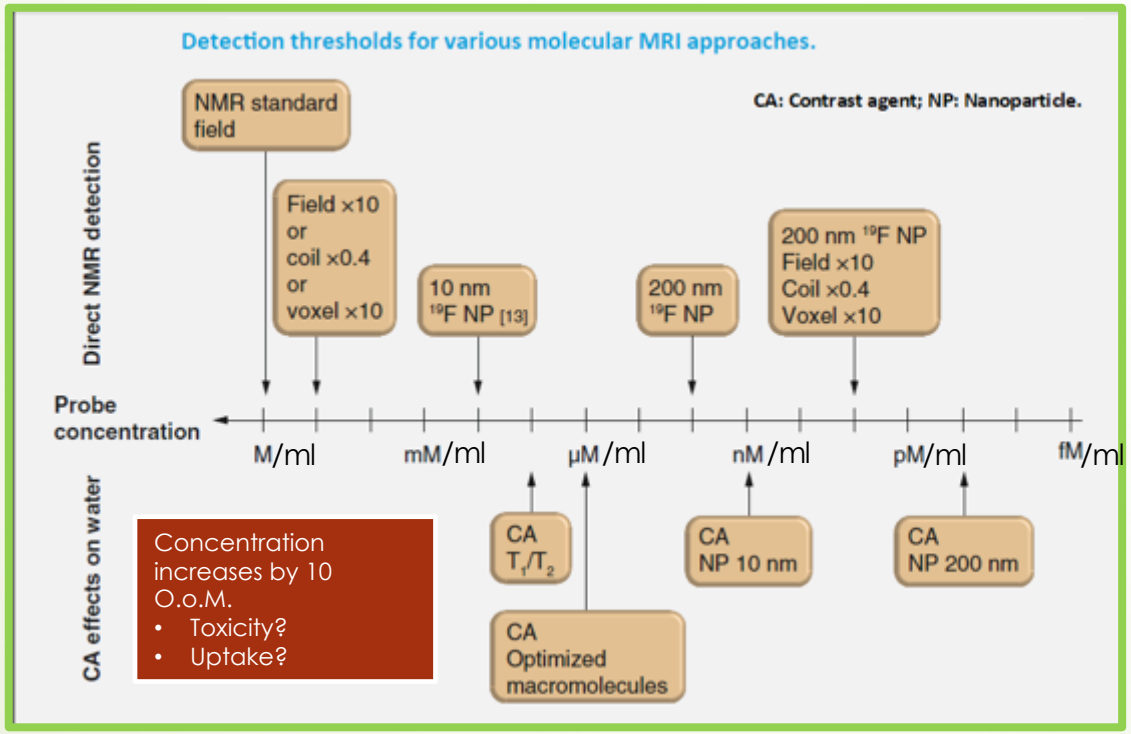
Concentrations and Performances

PET

- Typical PET activity concentrations:
  - Inject ~200MBq FDG (i.e. 3 10^{-12} moles), detect ~ 10^{-16} moles/ml

Cell Lines: PANCREAS(PANC-1)
Tracers: BSH
phenylalanine

MRI



Concentrations required by Particle Therapy:

- 80 ppm
- 0.11 mg/ml
- 10 µM/ml

Expert in pharmaceutical compounds (Dip. Chimica e Tecnologie del Farmaco)

D. Rotili (CTF-Sapienza)
S. Capuani (CNR-ISC)

F. Vulcano (ISS)
L. Milazzo (ISS)
G. Macioce (ISS)

Task 2.1: ex-vivo tests

NMR expert. Two LABS in the Dept. of Physics of Rome

Animal tests experts. All instrumentation and competences at ISS

- Animal tests on PANC-1 model at ISS
- Obtain samples with the correct concentration of 19F for realistic studies
- Estimate:
  - chemical shifts of tracers in realistic environment
  - Concentration of tracers in tumor

Notes:

- We will make use of the **9.4 T small samples NMR** of CNR-ISC installed in the Dept. of Physics of "La Sapienza" (19F coil missing)
- Possibility to test different tracers

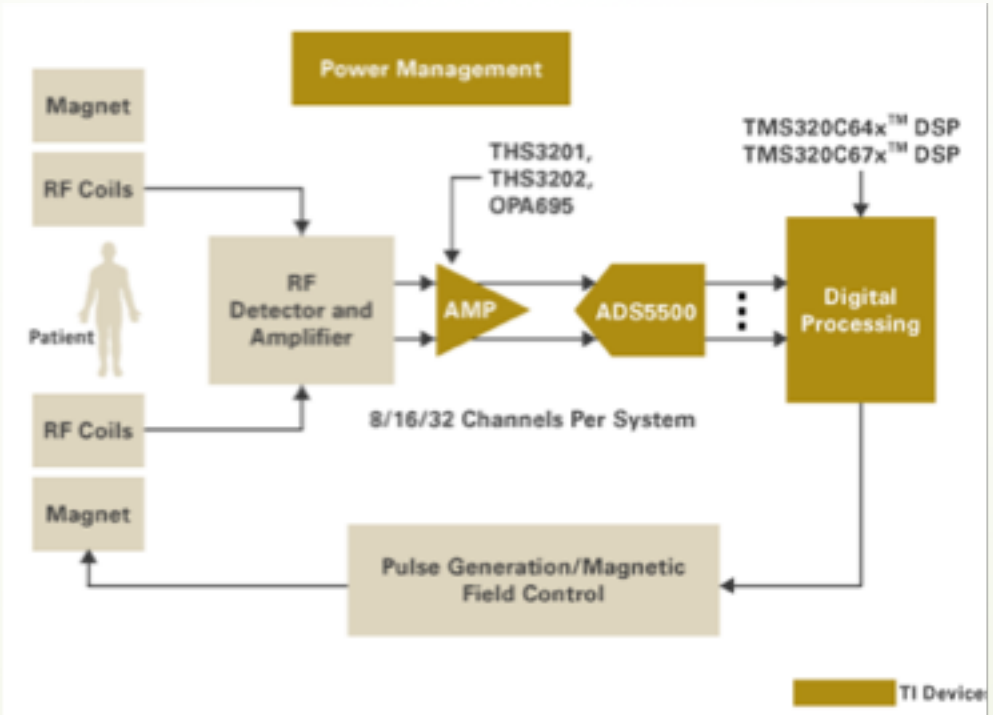
Task 2.2:
HW improvements to ^{19}F-MRI

V. Bocci
P. Fresch
A. Mostacci+L. Ficcadenti
S. Frasca
M. Vignati → A. Cruciani

Tecnologi stabilizzandi

- Achievable concentrations of ^{19}F is ~6 o.o.m smaller than protons
  - Needs to improve signal-to-noise ratio (tumor-non-tumor ratio is intrinsically very large)
  - Need to improve both generation and reception of signal

Gyromagnetic factor
g(1H) = 42.6 MHz/T
g(19F) = 40.1 MHz/T



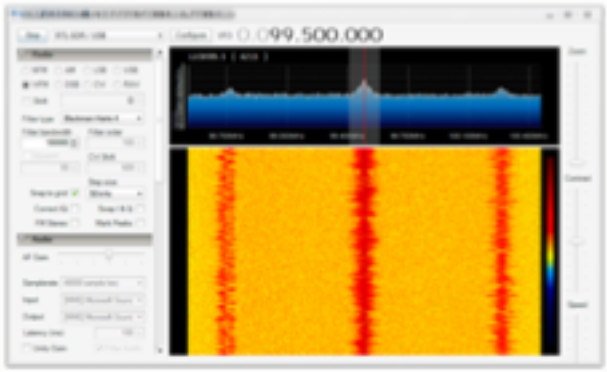
BRUKER is interested in study and, **if NEPTUNE is funded**, is open to a research collaboration → Support in design

Creation of a test stand for 19F-MRI

- First goal (year 1): setup a test stand
  - Starting point: **0,35T NMR scanner** in CNR-LAB in the Dept. Of Physics of »La Sapienza»
  - Expected integrations:
    - **Software Defined Radio RTL readout**
    - **Optimized antenna** for Low signal NMR
- Define benchmark parameters for hardware optimization

Signal characterization and noise reduction

Software-defined radio (SDR) is a radio communication system where components that have been traditionally implemented in hardware (e.g. mixers, filters, amplifiers, modulators/demodulators, detectors, etc.) are instead implemented by means of software on a personal computer or embedded system. While the concept of SDR is not new, the rapidly evolving capabilities of digital electronics render practical many processes which used to be only theoretically possible.



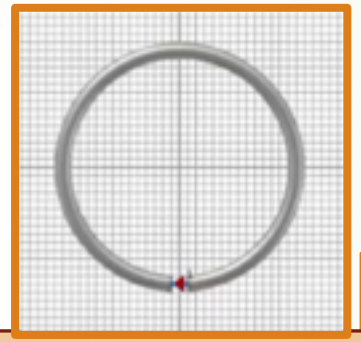
- The use of the SDR technology will allow to test different DSP algorithms and compare their performances in the real clinical environment (V. Bocci & P. Fresch)
- Signal and Background studies will be performed exploiting the competences of VIRGO (S.Frasca) and CALDER (A. Cruciani)

ANTENNA DESIGN

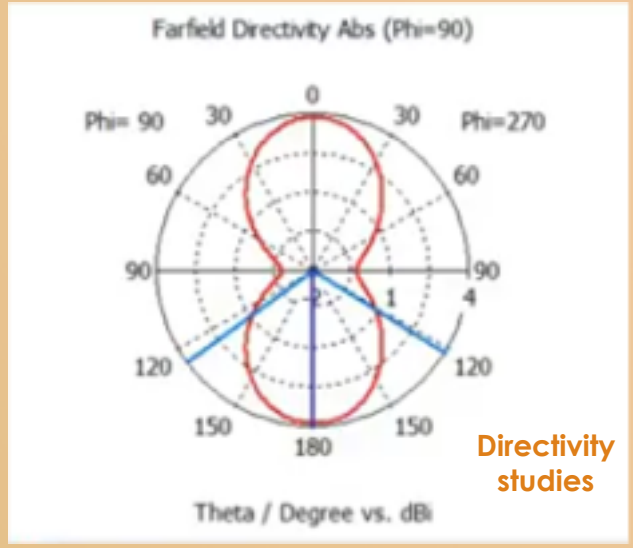
Competences available on antenna optization → expertize in CST

Strategy:

- simulate existing antenna
- Optimize free parameters
- Realize new antenna prototype

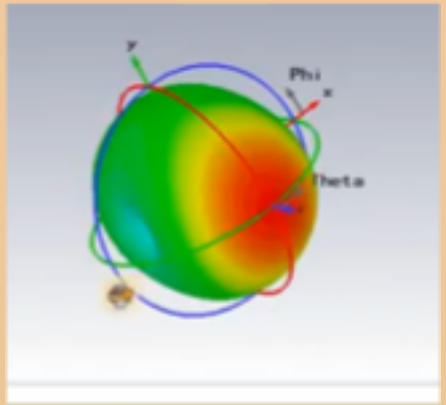


Example with loop antenna

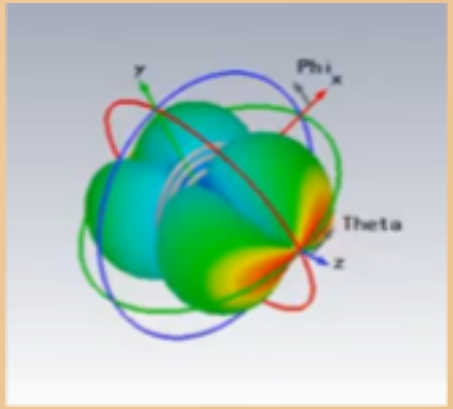


Directivity studies

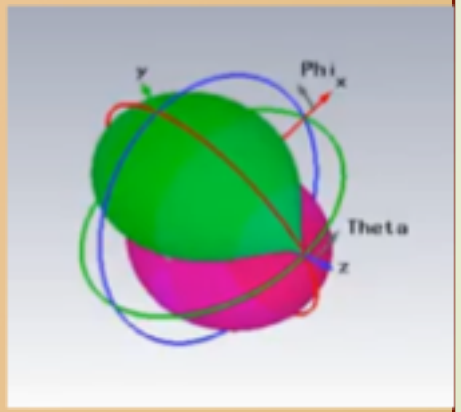
Field Amplitude



Field Theta



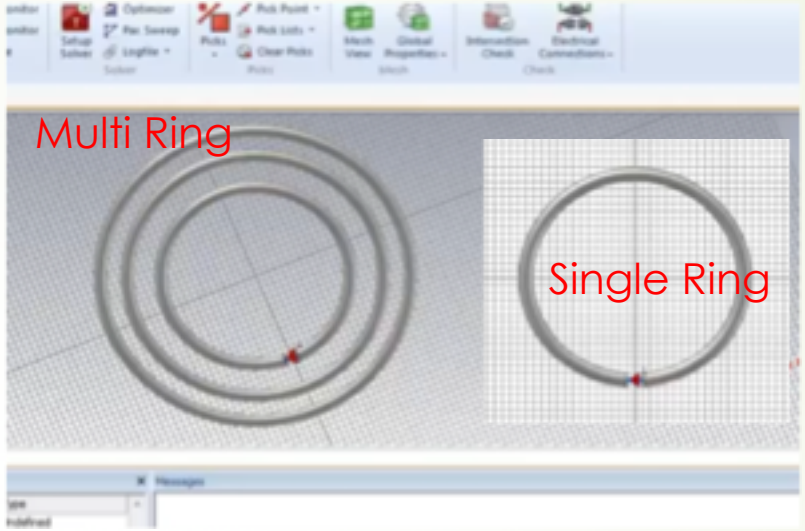
Field Phase

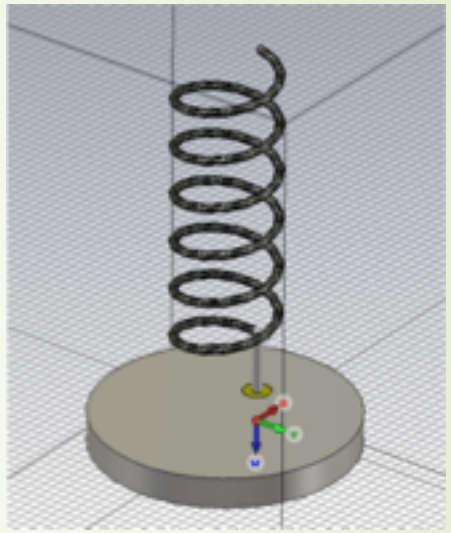


Antenna activity plan:

Choice antenna type:

Helix antenna may be smaller than the loop antenna at the same working frequency;





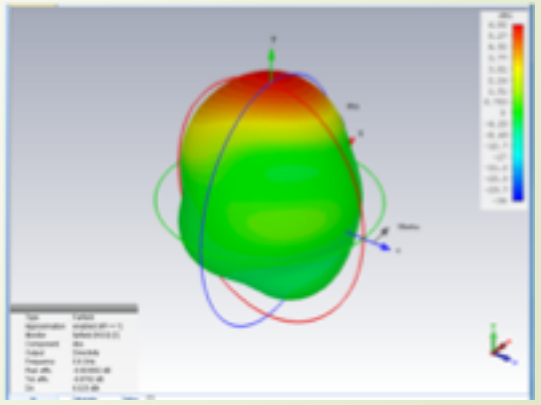
We need to know:

- maximum dimensions of the antenna (available space);
- exact working frequency;
- required amplitude of the radiated field and power on the sample;
- distance from the sample;

Future plan:

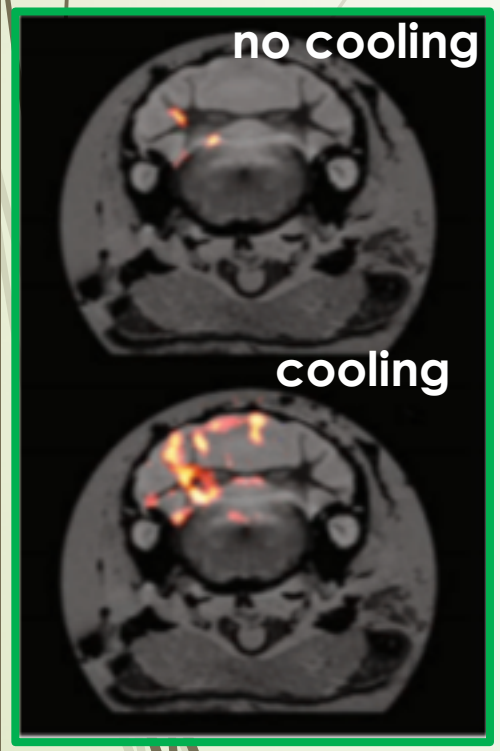
- e.m. simulation using CST;
- realization of the antenna prototype;
- measurements on the prototype in an anechoic chamber;

Helix antenna



M. Vignati → A. Cruciani

Possible improvement: electronics' cooling



- After the first year of system set-up and dimensioning of the system, we (M. Vignati, A. Cruciani) will be able to design a cooling test of the amplifier, to test the impact on the signal-to-noise ratio.
- Typical **Cryogenerator** of required performances

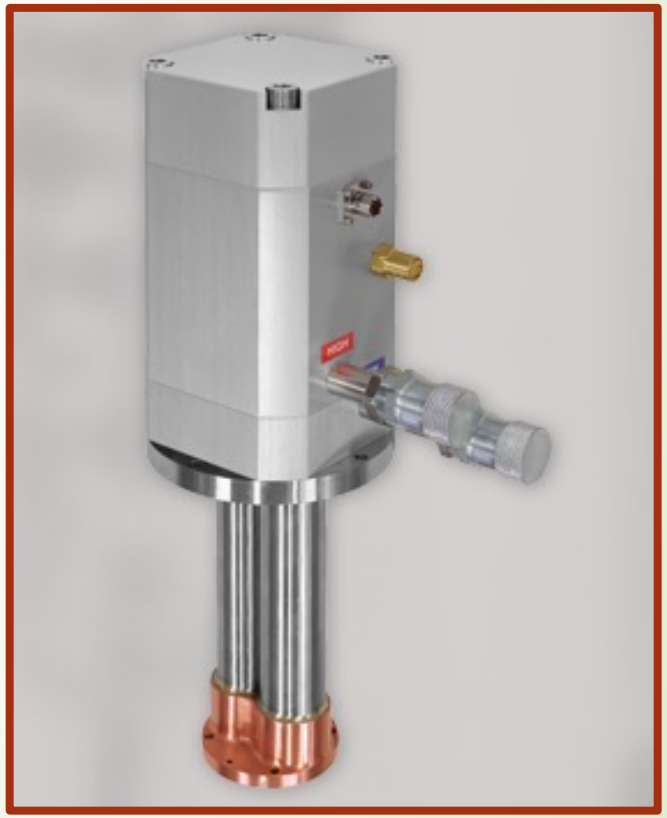
Identified

- Existing study [1] shows that cooling the entire

probe improves definition. How much can we

Improve cooling only the amplifier (easier to

implement)

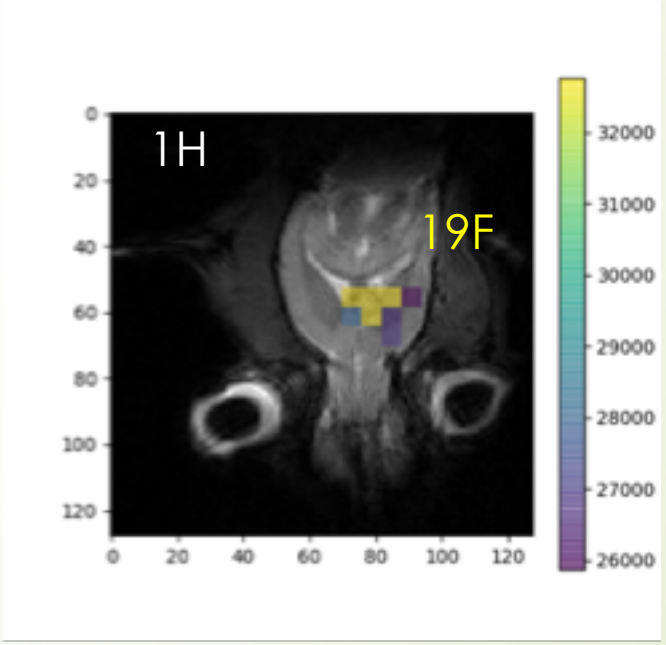


[1] S. Waiczies et al, SciRep 7: *9808 (2017)*

Task 2.4: SW improvements to ^{19}F MRI

S. Giagu
A. Messina
A. Sarti
C. Voena

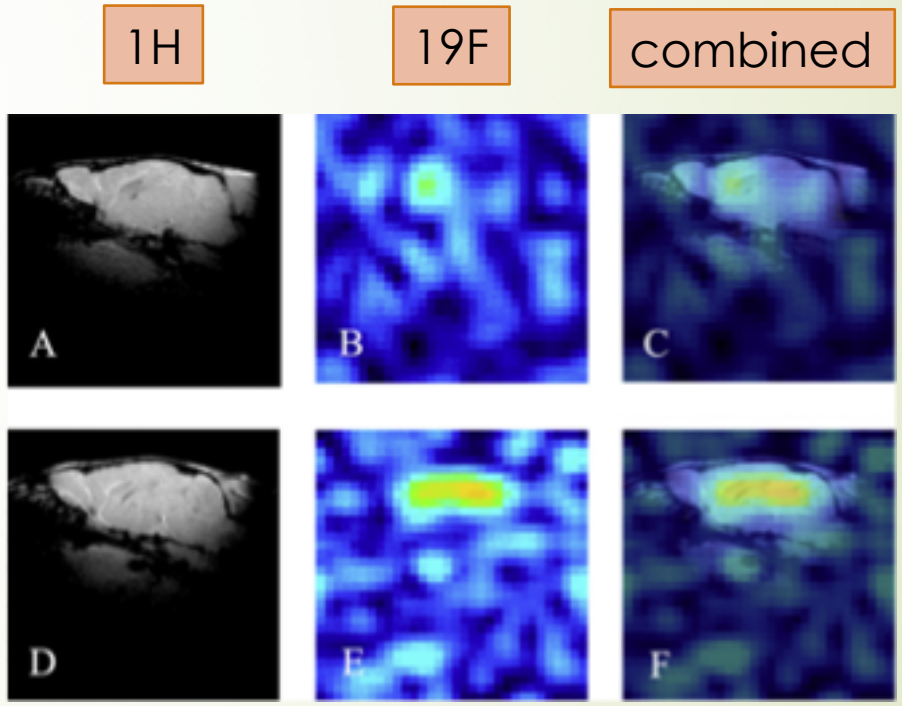
- Currently 19F images are extremely coarse because of low signal and because they concentrate on visual inspection
  - Stastitically rigorous treatment of low signals and texture analysis can allow much more refined images
    - Use of neural networks (autoencoders) as denoisers
  - Test different scanning sequences for 19F imaging resolution
  - Quantification of concentration from image
    - Possible use of deep ConvNet as regression algorithms



Task 2.4: Coregistration of 1H and 19F images

- Currently 1H and 19F images are only superimposed for visual comparison (combination is just product of signals)
  - Study of noise and correlation with 1H image
  - Multivariate analysis for concentration estimate:
    - Study of alignment between images
    - Use the 1H images for segmentation (eventually with neural networks)
    - Estimate of 19F in the identified segments.

Low statistics can be cured with the use of GAN for data augmentation



GANNT 2019

Attivita'	nov-dic 18	gen-mar 19	apr-lug 19	sett-dic 19
Protocollo test animali				
Test su animali (incl setup strumentazione e protocollo)				
Disegno Antenna				
Istallazione SDR (incl. Accordo con Bruker)				
Validazione SDR				
Studio Segnali Analogici				
Studio immagini MRI passate/Valutazione rumore				
Test con 19F MRI ad alta risoluzione				
Applicazione reti neurali a segmentazione, allineamento e de-noising				

Talks

10:40 - 11:00	WP2: Introduction and overview Convener: Riccardo Faccini (ROMA1)	
11:00 - 11:10	WP2: Elettronica e antenne Convener: Mr. Francesco Iaconelli	
11:10 - 11:20	WP2: NMR con F19, stato dell'arte e test su animali	S. Capuani
11:20 - 11:30	WP2: Analisi immagini MRI con 19F	C. Voena
11:30 - 11:45	WP2: Metabolomica cellulare in Neptune via UHPLC-ESI-qQTOF analisi. Convener: Dr. Pacifico Severina	
11:45 - 12:00	WP2: Misura del boro-10 tramite autoradiografia neutronica: imaging della distribuzione e quantificazione in campioni cellulari e tessuti Convener: Nicoletta Protti (PV)	