Neptune-WP2
Imaging and Quantification

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S. Pacifico
& **Caserta group**

Goals of WP2 (imaging)

- Evaluate bio-distributions of fluorinated tracers using ^{19}F-MRI
- ^{19}F-MRI performances limited by low SNR ratio
- Possible **hardware improvements** to ^{19}F-MRI
  - low noise RF coil
  - software defined radio technology for signal digitization
  - new pre-amp & cooling

test-stand: 0.35 T scanner

- Possible **sofware improvements** to ^{19}F-MRI
  - use of deep learning to denoise and analyse images
- Choice of fluorinated molecules
  - tests on animals to have samples with correct concentrations

9T spectrometer

Status@ Last Meeting (Feb 2022)

- New antenna

  - antenna test underway

- Sofware Defined Radio system

  - ready to be tested

Quantification with Pavia/Caserta

- Choice of fluorinated moleculed

  - improved NMR protocol for F-BPA developed

Multimodal evaluation of ^{19}F-BPA internalization in pancreatic cancer cells for boron capture and proton therapy potential applications

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- Mice tests

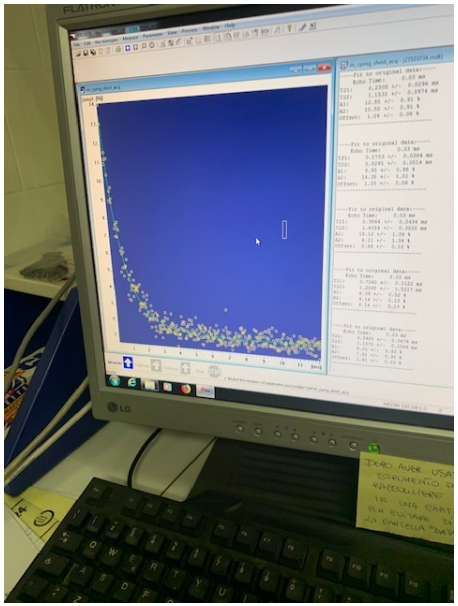
  - first mice tests perfomed. Seen less F-BPA than expected
  - new tests planned at ISS with Xenograft model

- AI based denoiser

  - denoiser developed and tested on proton data
  - exerimental campaign planned at Santa Lucia for ^{19}F images

New Antenna/SDR

- Tests on new antenna on low field scanner performed in ^{1}H-MRI
- Improved electromagnetic shielding
- Signal to noise ratio still lower to that of Brucker antenna
- Q value must be improved (with inductance)
- SDR test can in principle start

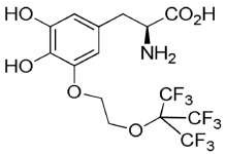


Internalization Measurements with improved protocol

- Reduce resonance line broadening
  => apply better shimming and field locking to the spectromenter to reduce field disomogeneities
  => improve sample preparation i.e."extract" to reduce impact of polar macro-molecules (proteins)
- Use an internal standard (reference molecule mixed with sample)
- PFTP-DOPA (measurements underway)
  => see if enhances F-BPA uptake in PANC-1

perfluoro-tert-butoxy 3,4-dihydroxy-L-phenylalanine

PFTP-DOPA



Internalization fraction

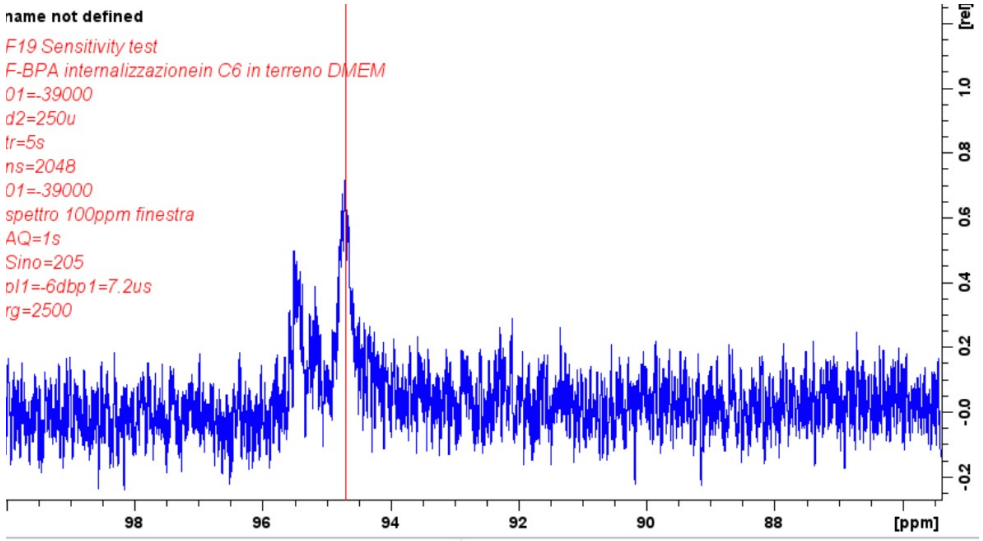
Old measurement 4h pretreatment (published)

$f_1 = 0.5 \pm 0.1$

$f_2 = 0.4 \pm 0.1$

New measurement 4h pretreatment (but 10B)

$f = 0.420 \pm 0.044$



Mice Tests

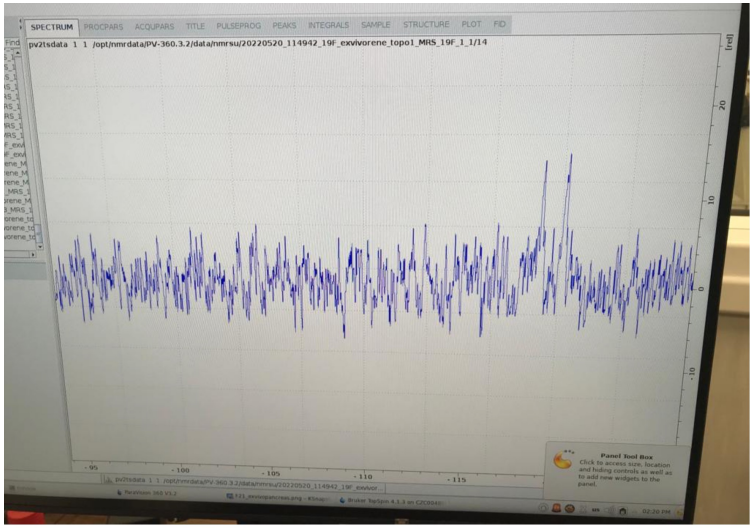
- Reminder: in ex-vivo tests with ortothopic PANC model see less F-BPA than expected (both in MRS and neutron autoradiography) @ 13.6 mM administrated

- New in-vivo test at ISS with animal scanner (7T) in localized NMR spectroscopy

  - no signal in the tumor
  - some signal in kidney

- Sent to Pavia samples for neutron autoradiography
  - analysis underway

- Calibration measurements planned with scanner

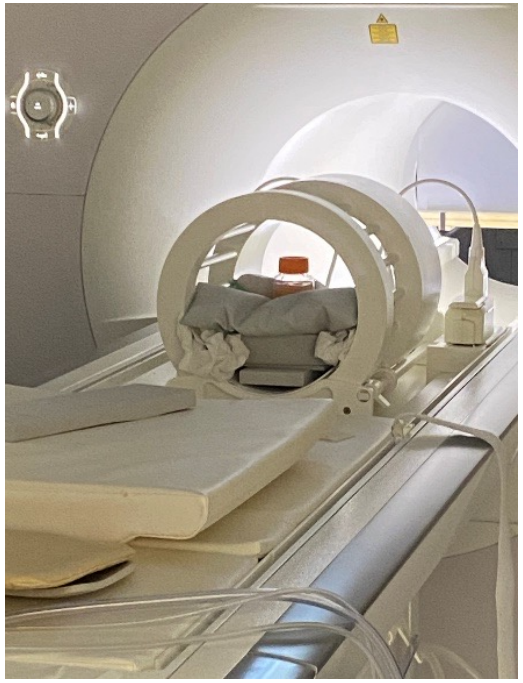


^{19}F Imaging @Santa Lucia

- Goal: take ^{19}F images to optimize acquisition protocol and apply denoiser

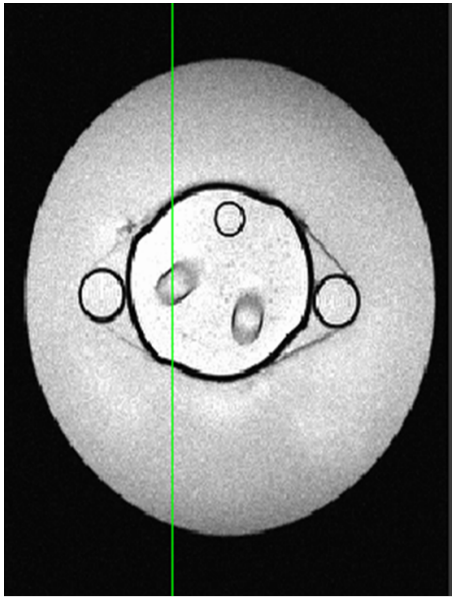
- Phantom (d=6 cm, h=10 cm)
  - three eppendorf-type tubes (d=1 cm, h=4 cm) F-BPA 13.6mM
  - external compartment with F-BPA 1.4 mM
  - two external falcon (d=1,5 cm, h=12 cm) with 13.6 mM to help frequency tuning

3T scanner



Phantom

^{1}H-MRI of phantom



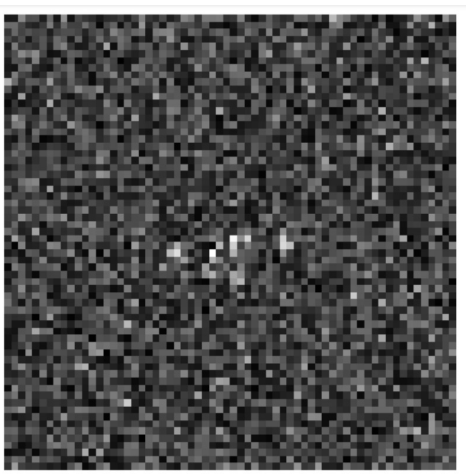
^{1}H-MRI

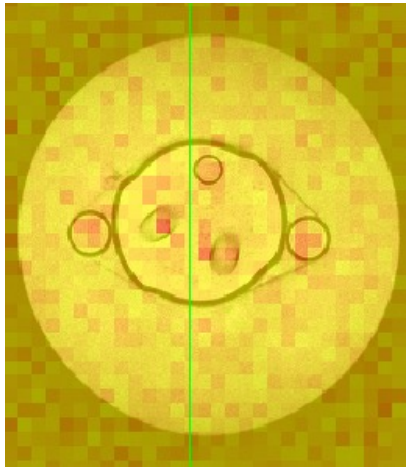
Data Acquisition

- Data acquired in two configurations

Configuration 1) 2 images of 1 hours and 20 each

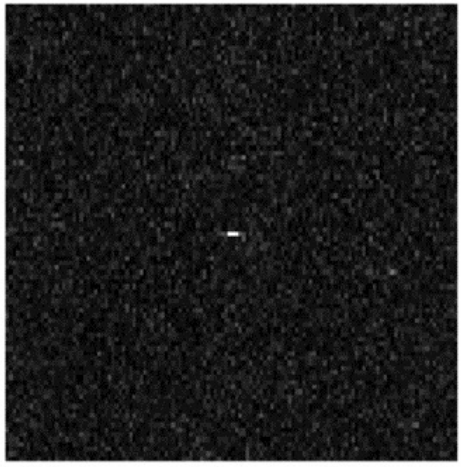
- gradient-echo ^{19}F sequence
- 1024 transients each averaged.
- voxel volume = 5x5x5 mm^3
- FOV = 64×30 mm2,
- Slice Thickness = 5 mm





Configuration 2) 3 images of 3 hours and 59 minutes each

- 2048 transients
- voxel volume 2,5x2,5x4 mm^3,
- FOV = 320×120 mm2
- Slice Thickness = 5 mm (4 mm+1 mm gap)



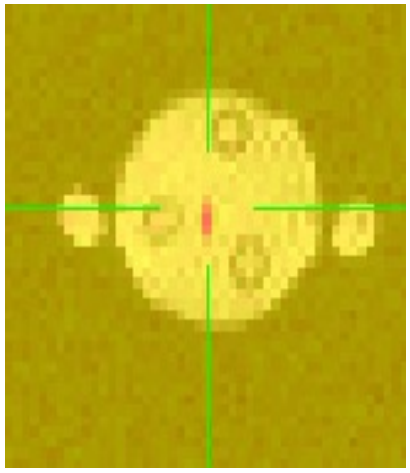
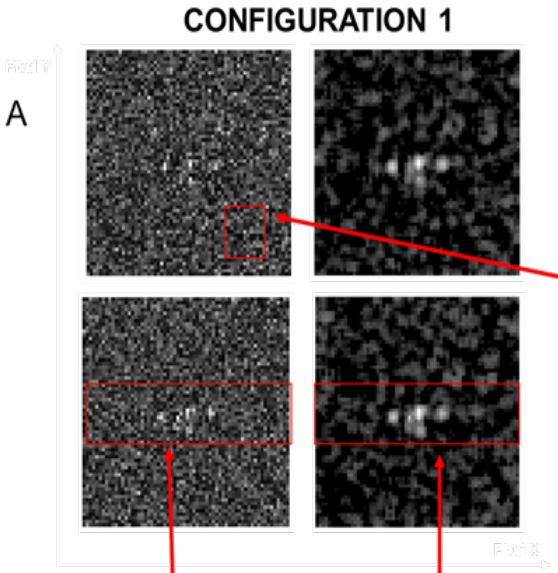
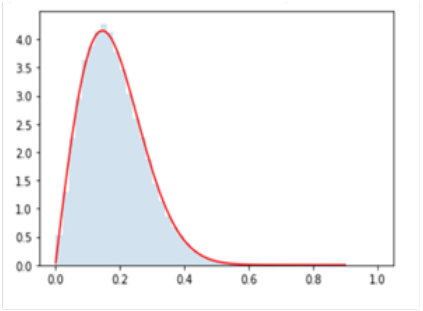


Image Analysis (I)

Original images

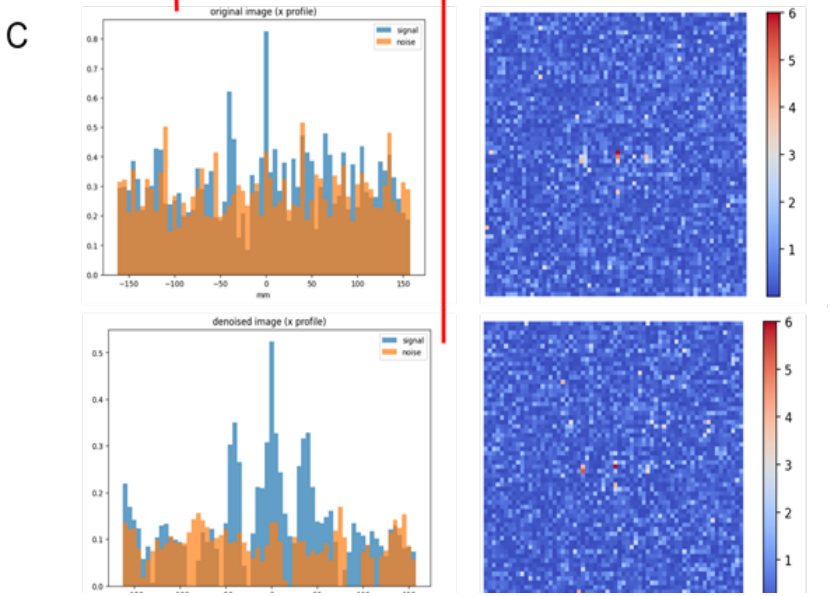


Denoised images
with non-local-mean algorithm



Noise
distribution
(Raleigh)

Intensity
distribution
projected
on x axis



-log(pvalue)
associated to the
significance of each
pixel with respect
to the background hypothesis

$$Pvaule = \int_M^{\infty} A \frac{x}{\sigma^2} e^{\frac{-x^2}{2\sigma^2}} dx$$

$$I(x) = -log_{10}\left(\frac{Pvalue}{A}\right)$$

$$= -log_{10}(e^{\frac{-x^2}{2\sigma^2}})$$

Image Analysis (II)

Original images

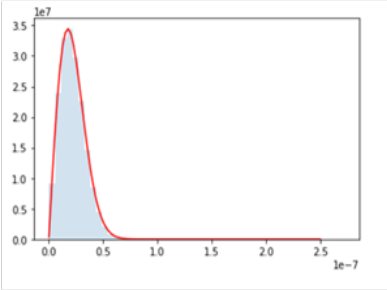
CONFIGURATION 2

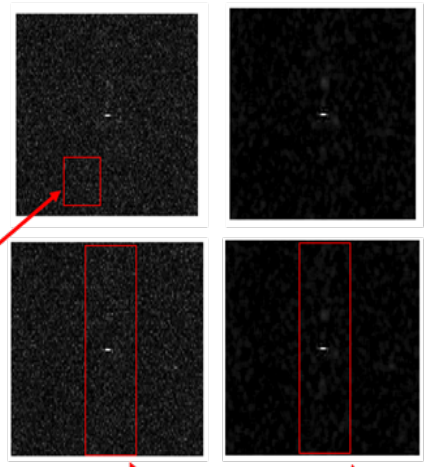
F

Denoised images with non-local-mean algorithm

Noise distribution (Raleigh)

E





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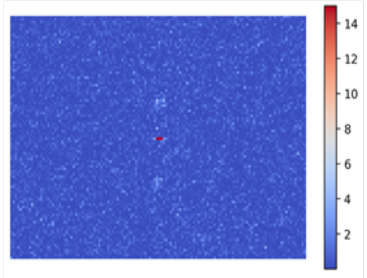

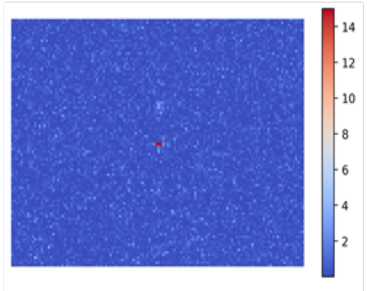

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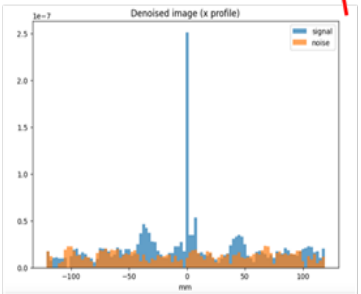


-log(pvalue) associated to the significance of each pixel with respect to the background hypothesis

$$Pvaule = \int_M^{\infty} A \frac{x}{\sigma^2} e^{\frac{-x^2}{2\sigma^2}} dx$$

$$I(x) = -log_{10}\left(\frac{Pvalue}{A}\right)$$

$$= -log_{10}(e^{\frac{-x^2}{2\sigma^2}})$$

Intensity distribution projected on x axis

Neural Network Based Denoiser

- Neural Network based denoiser was trained on low SNR ^{1}H-MRI images of knees

  - they are images with anatomical "structures" different from ^{19}F-MRI images (spots)

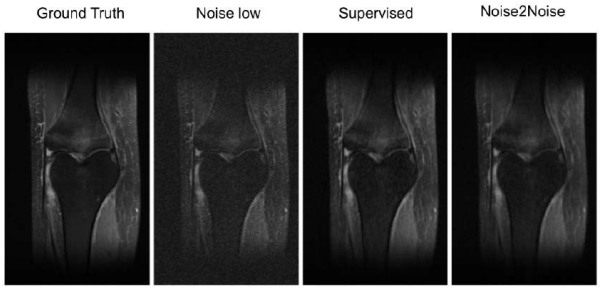
- We decided to re-train the network with a more suitable sample

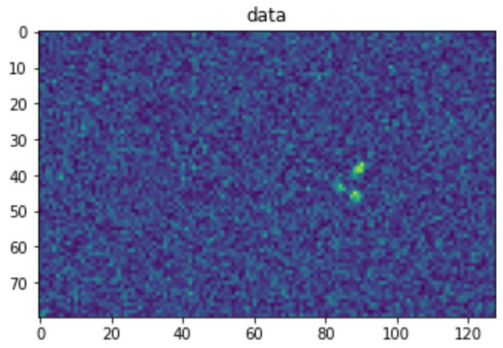
- New training sample: ^{1}H-MRI low SNR phantom rotated many times during acquistion

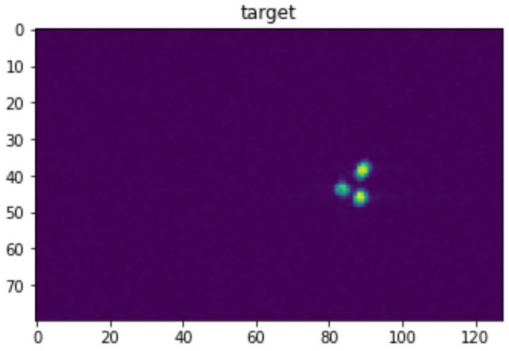
- We retrained the network, but found some overfitting given that the training sample contains correlated images

- We are planning to build another traning sample with independent images

1H-MRI knees







Summary and Perspectives

- New low noise antenna: working, but we need to improve Q value to get adequate performances
- SDR: we don't know if we will manage to finish this part
- Quantification measurement: new protocol gives results for the internalization fraction of F-BPA in PANC @13.6 mM consistent with the published one, with an improved error
  - we are testing enhancement of PFTP-DOPA on F-BPA uptake (but on c6 cellular line)
- Mice tests: on-going.
- Imaging: we are validating the Neural Network based denoiser on a ^{19}F- sample in collaboration with Santa Lucia