

nATT

Status report

ROS measerements
in-vivo measurements

Piergiorgio Cerello

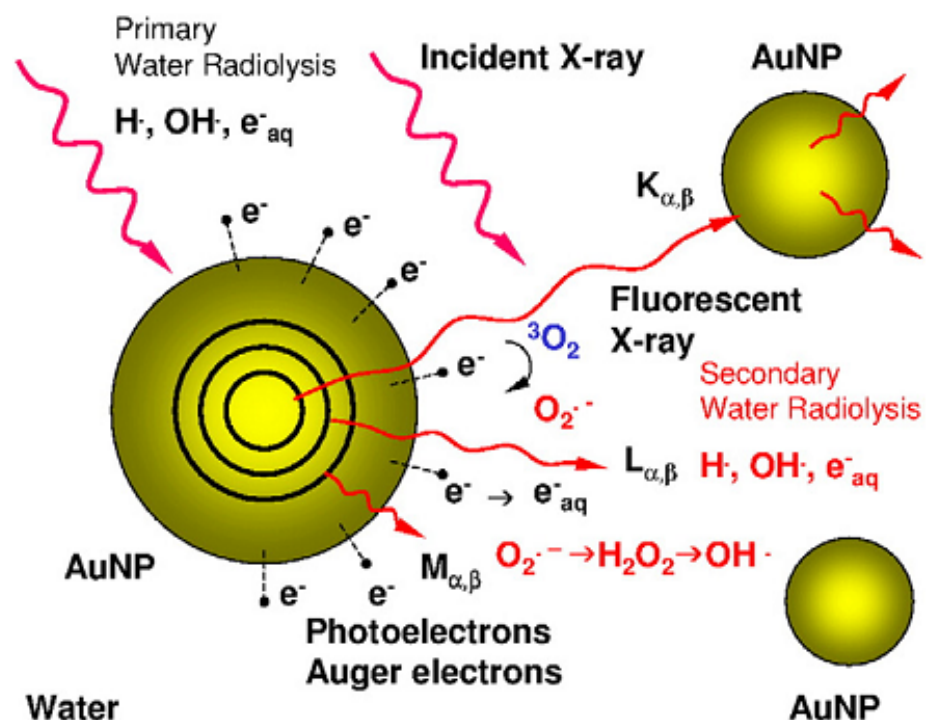
INFN – Sezione di Torino - cerello@to.infn.it

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ROS measurements

Studio della produzione di radicali

Enhancement da GNP:  **ROS?**



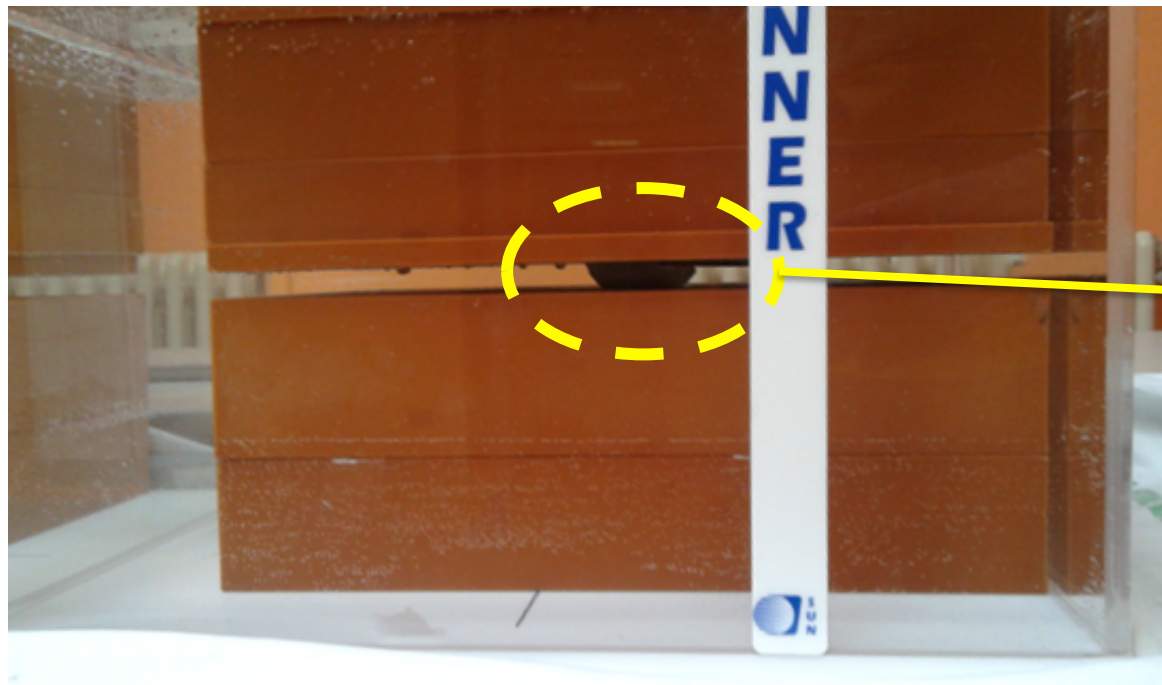
Non esiste in letteratura una misura quantitativa sulla produzione di ROS generati da nanoparticelle, nelle condizioni standard dei trattamenti radioterapici.

Produzione di ROS

Radiolisi dell' acqua

LINAC da **6 MV**, spettro di fotoni continuo con $E_{\max} = 6\text{MeV}$ (presso Ospedale Mauriziano).

Condizioni analoghe a quelle cellulari: composizione campione → prevalentemente **acqua**
(Tampone fosfato – **PBS ph 7,4**)



GNPs in PBS



DPBF in PBS



Quale protocollo?

Cosa:

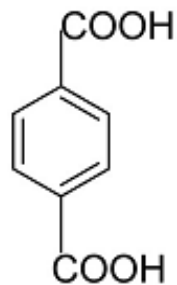
Produzione di **ROS** vs **Concentrazione GNP** e **Dose**

Come:

<i>Probe</i>	<i>Radicale</i>	<i>Misura</i>
DPBF	O_2 e $O_2^{\cdot-}$	Assorbanza
TPA	OH^{\cdot}	Fluorescenza
DHE *	$O_2^{\cdot-}$	Fluorescenza
*[non ancora utilizzato]		

Sodio Tereftalato - TPA

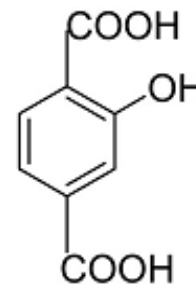
TPA
non fluorescente



+ OH[•]



(OH[•])TPA
fluorescente



$\lambda_{\text{excitation}} \approx 310 \text{ nm}$; $\lambda_{\text{emission}} \approx 430 \text{ nm}$

- ❖ Solubile in acqua,
- ❖ Non è fotosensibile.

Preparazione dei campioni

È necessario usare elevate concentrazioni poiché la quantità di **OH** radicali prodotta è elevata a causa della *radiolisi dell'acqua*.

→ **Vorremmo vedere tutti i radicali OH!** ←

Le concentrazioni di **TPA** usate sono **1,5,10,15,20 mM**.

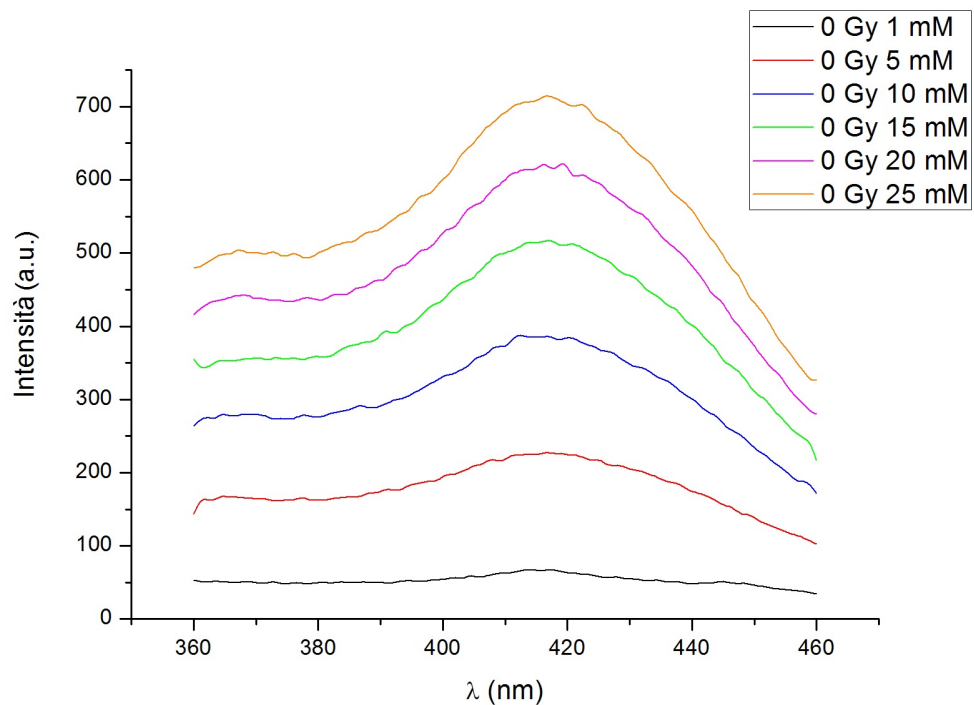
Le **GNP**, utilizzate finora, presentano una concentrazione di **10 μ M**.

La concentrazione di TPA, e quindi i radicali prodotti, è **10³** più grande della concentrazione di GNP.

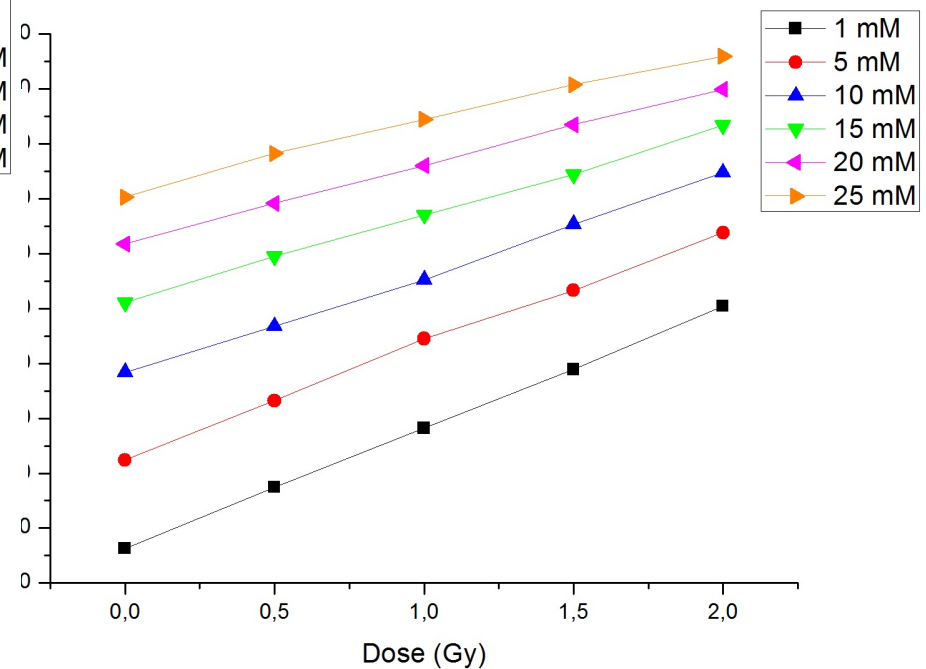
Devo stabilire qual è il contributo dato dalle GNP.

Ottimizzazione concentrazione TPA

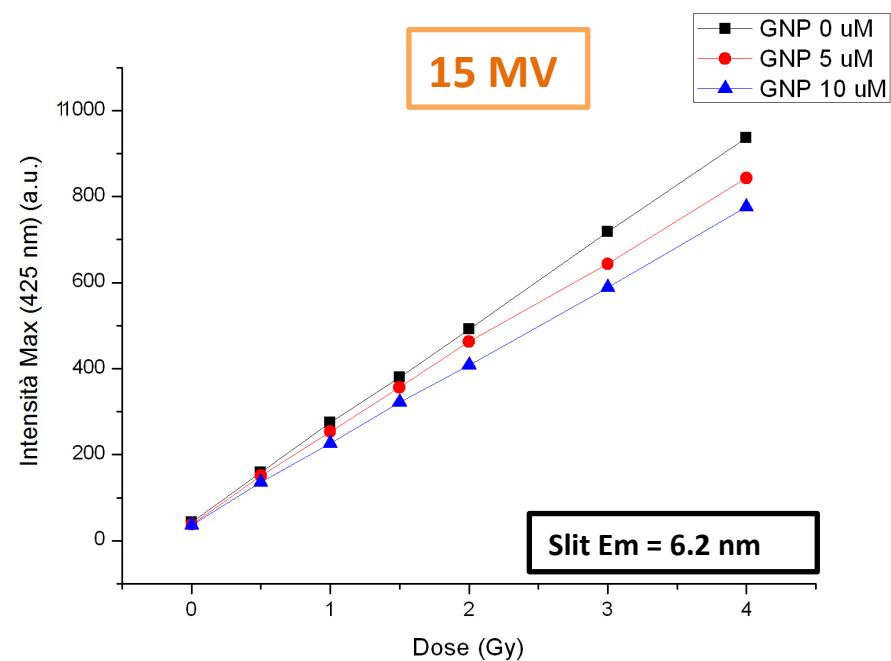
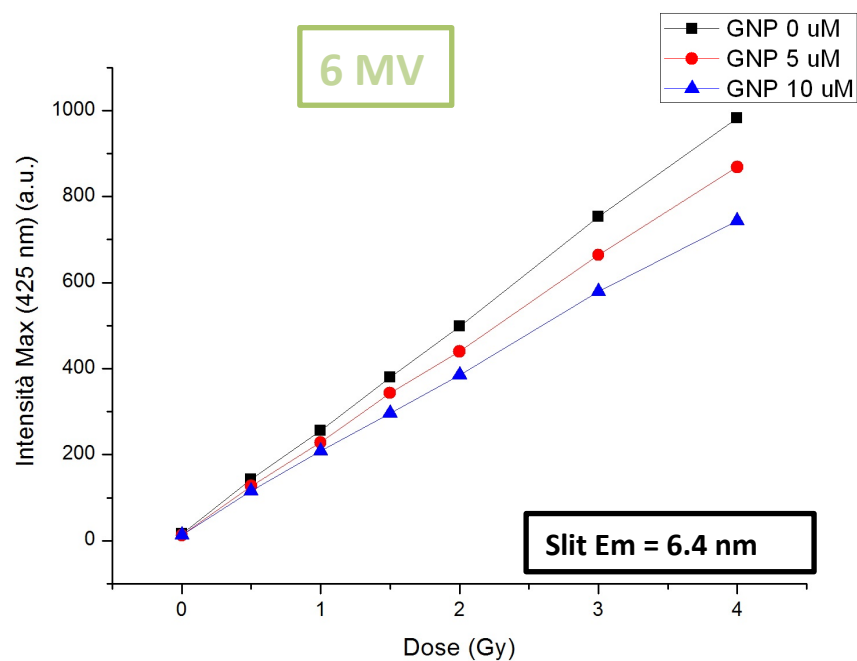
Senza irraggiamento



Irraggiamento 6 MV

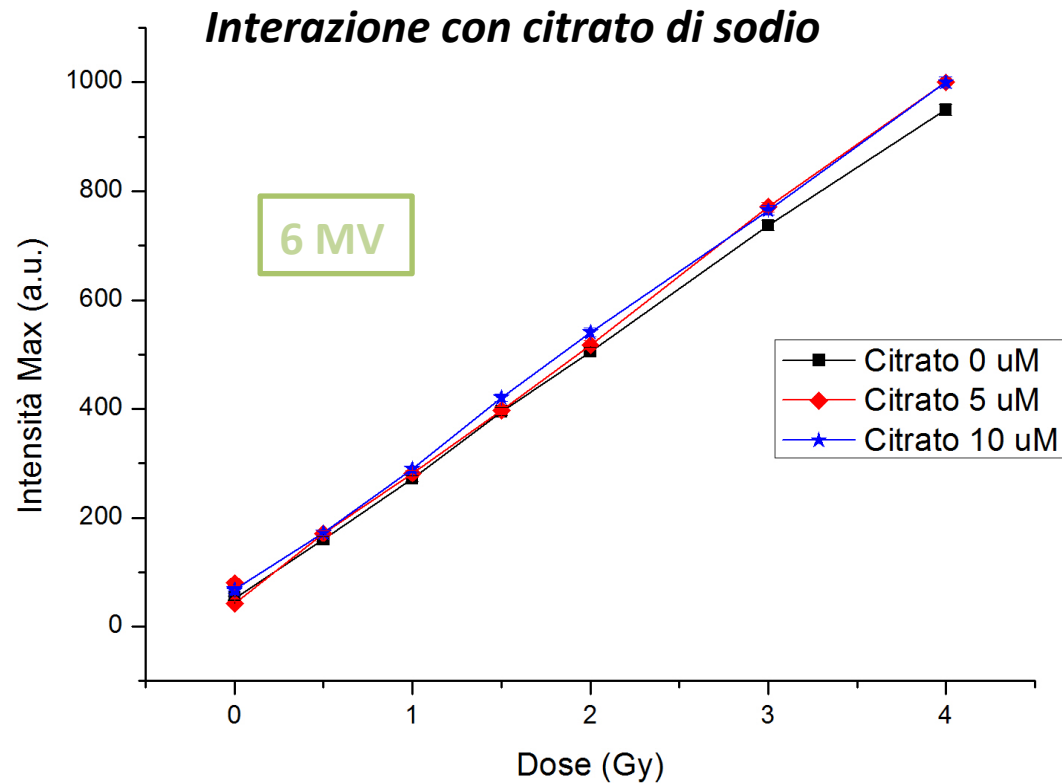


[OH•] vs Dose vs [GNP]



Ipotesi # 1: interazione chimica (*adsorbimento*) tra GNP e TPA?

Correzione per adsorbimento

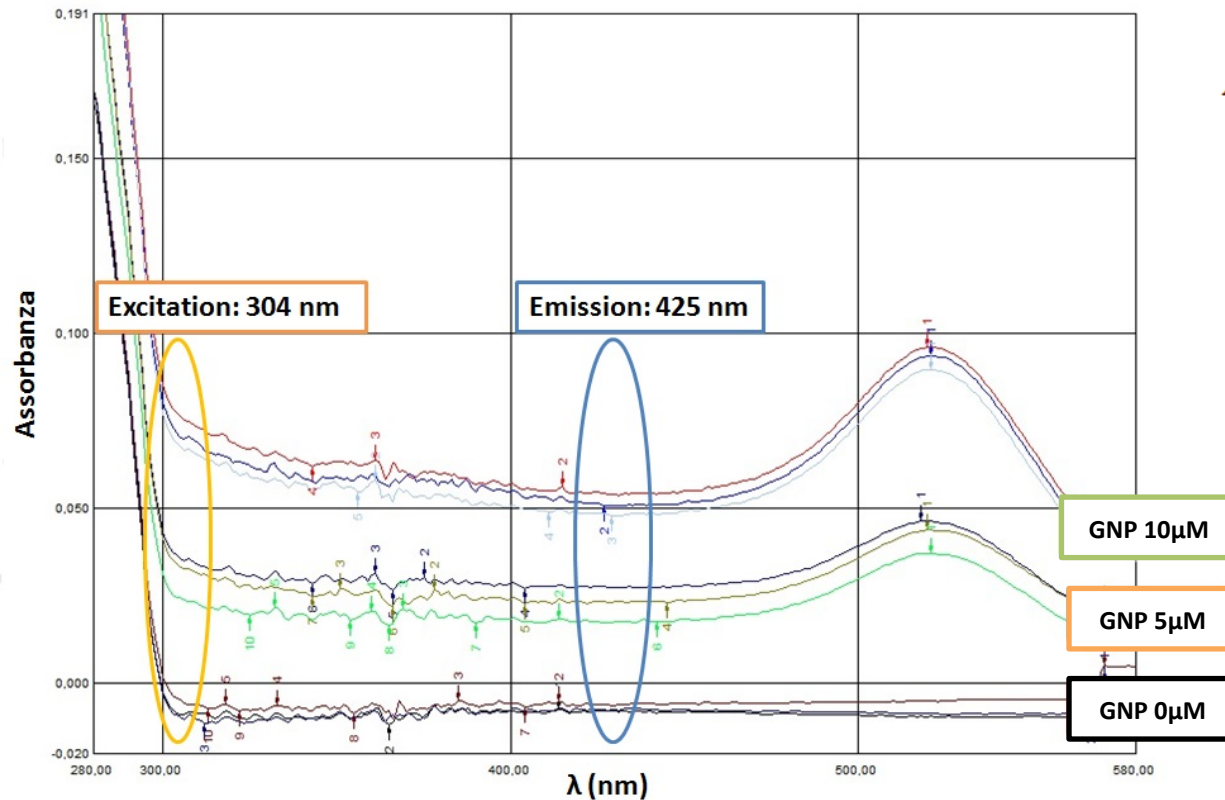


Incremento ~ 5%

Ipotesi # 2:

le GNP *assorbono* la luce di fluorescenza del TPA?

Correzione per assorbanza



$$A = \epsilon \cdot x \cdot C$$

Eq. Lambert-Beer

$$T = \frac{I}{I_0}$$

Trasmittanza

$$A = \ln\left(\frac{1}{T}\right)$$

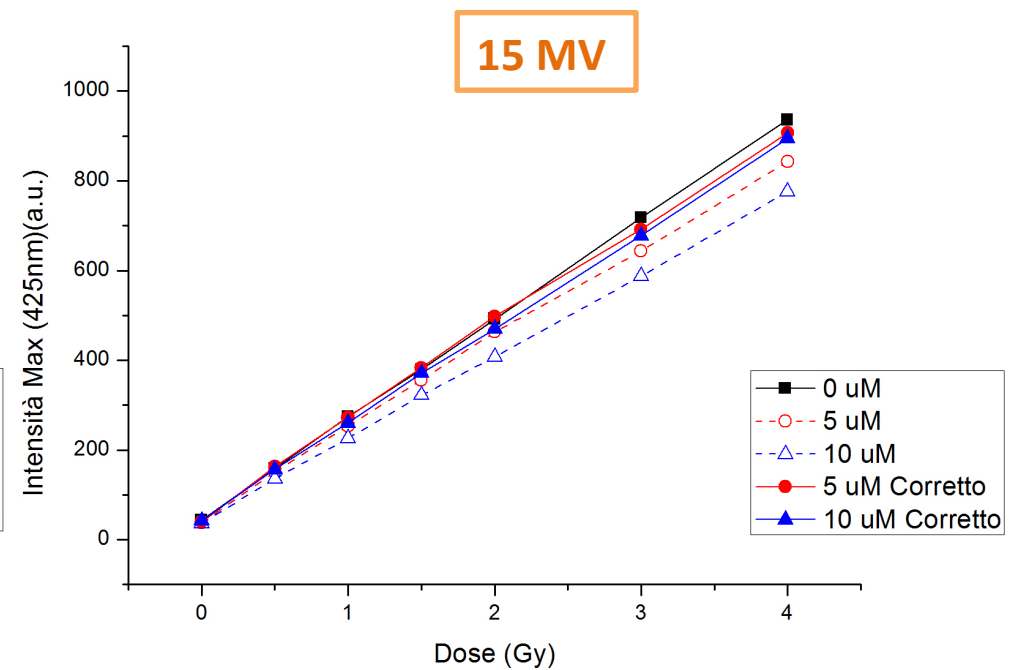
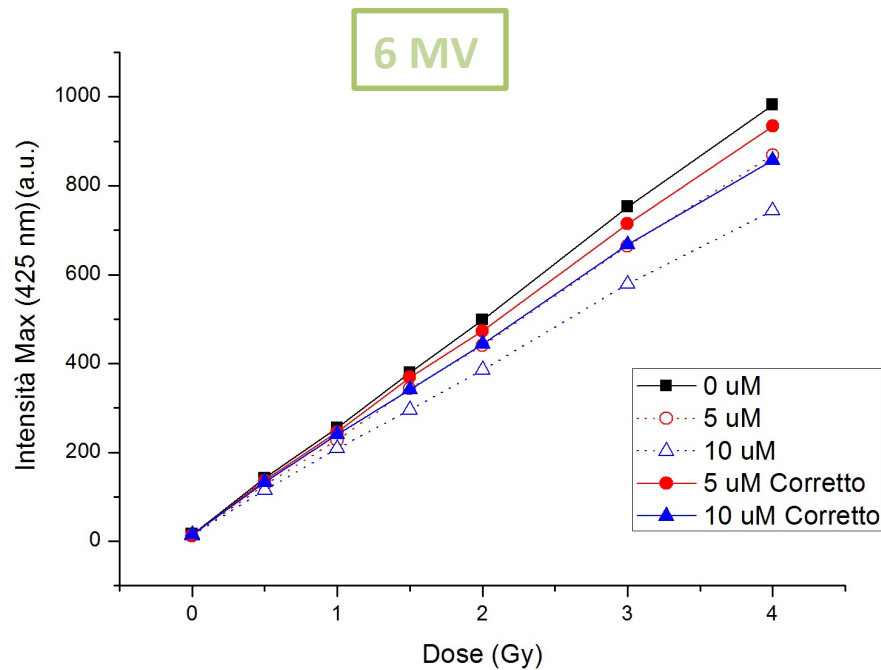
$$I = I_0 e^{-A}$$

$$I = I_0 e^{-\mu x}$$

$$A = \mu x$$

$$I_0 = \frac{I}{e^{-A}}$$

Correzione per assorbanza

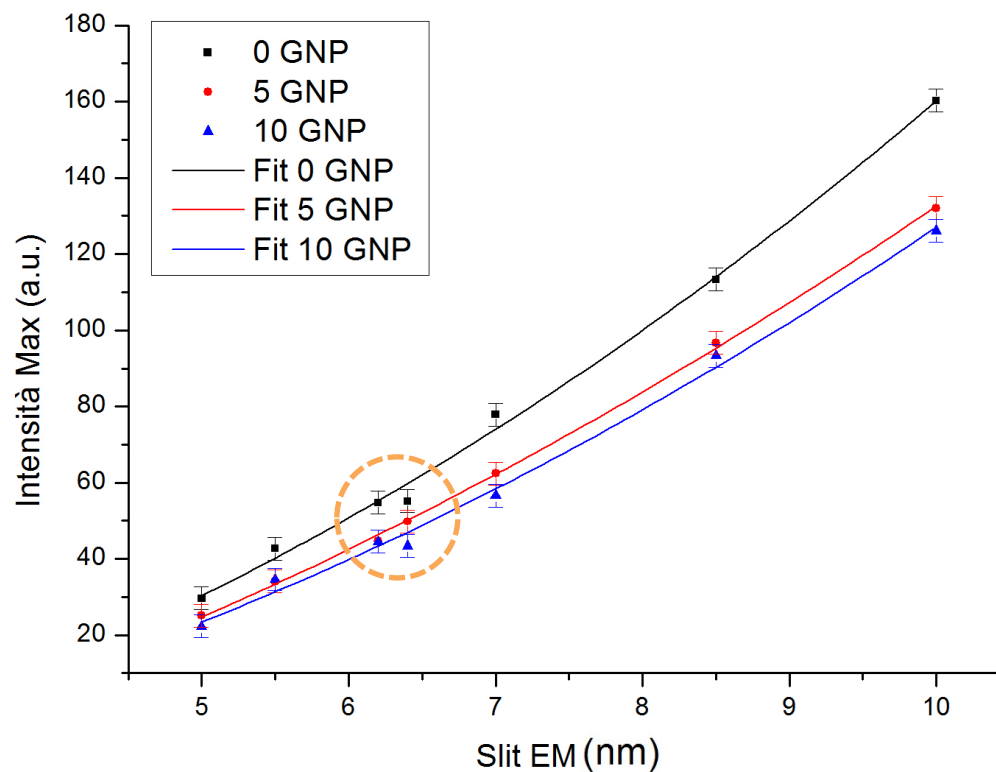


Ipotesi # 3: le GNP *diffondono* la luce di fluorescenza del TPA?

Correzione integrata

✓ [TPA] = 1 mM

✓ Dose = 0 Gy

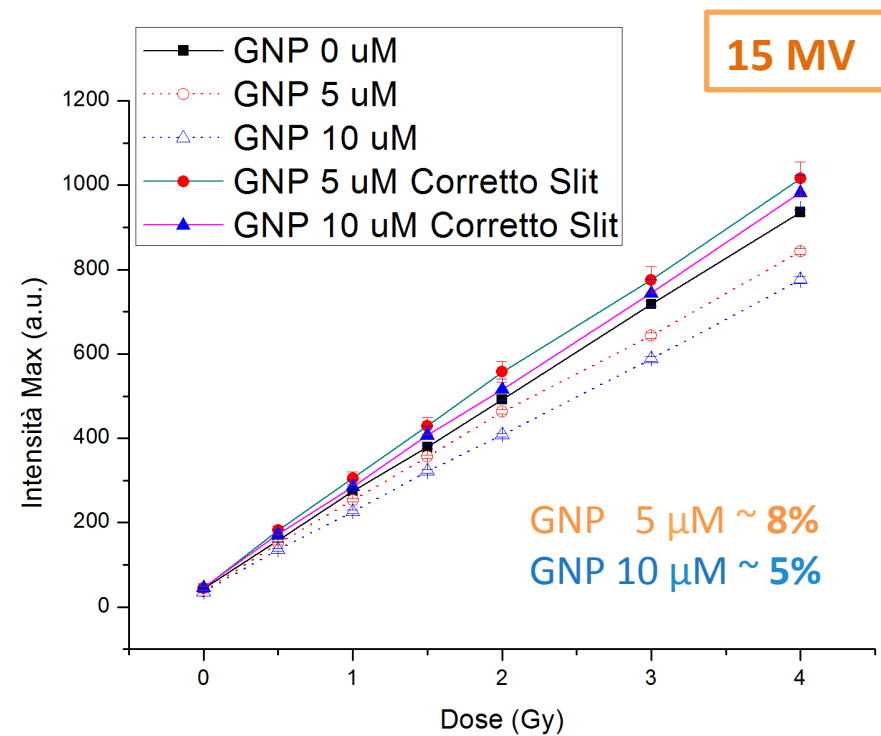
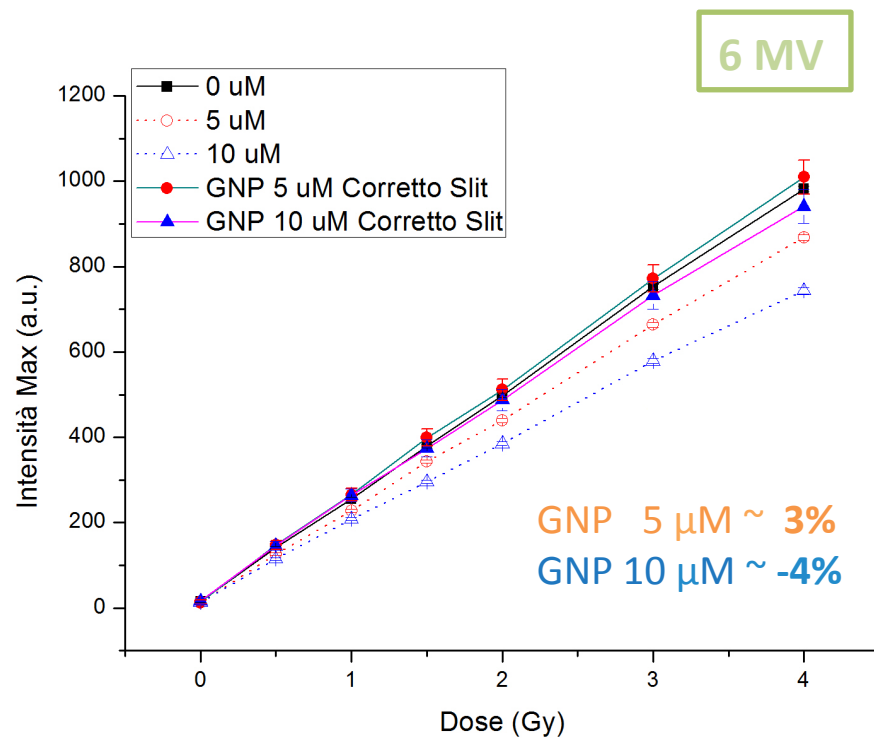


$R^2 (0 \mu\text{M}) = 0,9949$

$R^2 (5 \mu\text{M}) = 0,9989$

$R^2 (10 \mu\text{M}) = 0,9926$

Correzione integrata



Some remarks...

Qualità dei dati:

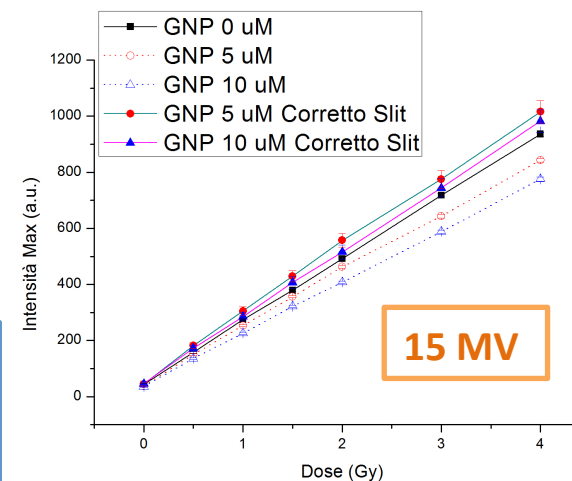
- protocollo di misura riproducibile
- I dati a 6 e 15 MV sono coerenti;
- Analisi dettagliata dei fattori di correzione.

Significato dei risultati:

- Enhancement da GNP limitato < 5 - 8 % (15 MV);
- Incremento danno per effetti locali?

Prospettive:

- Misure con elettroni;
- Definizione di un protocollo per misurare il radicale $O_2^{\bullet-}$ basato sul **DHE**.



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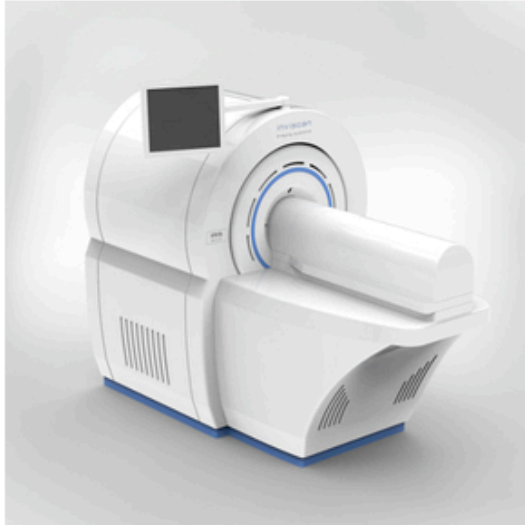
in vivo measurements

microPET/CT imaging system

IRIS PET/CT

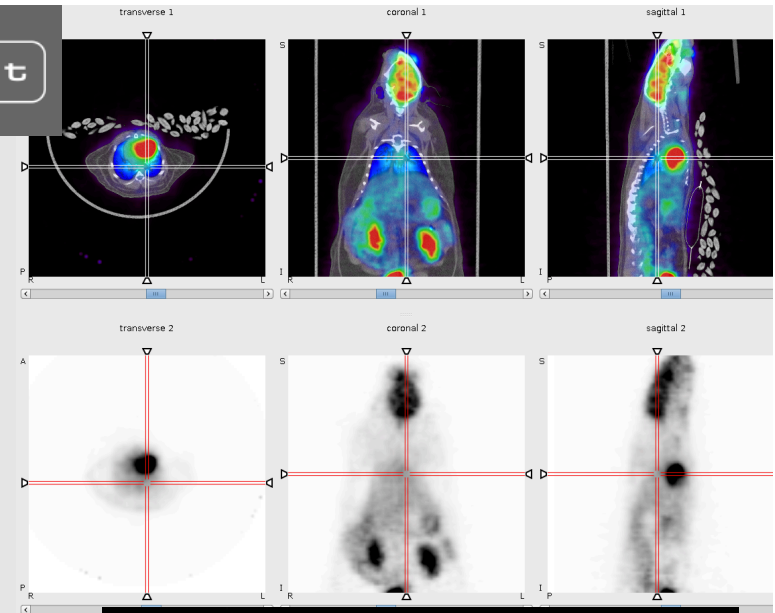
combined PET and CT scanner for mice

2014



Applications

PET/CT Oncology
Cardiac imaging
Brain imaging
New tracer development
Inflammation
Dynamic imaging
Gated imaging

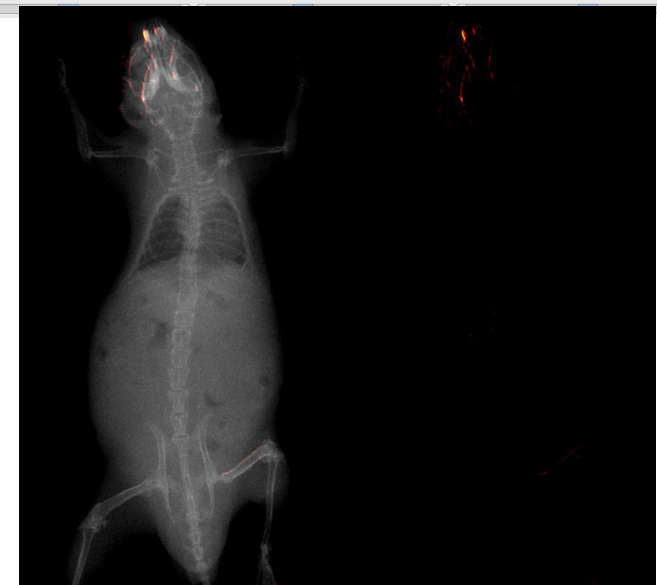


Specifications PET:

Sensitivity = 9.8% [250 keV - 750 keV]
Spatial resolution = 1.1 mm (MLEM)
Axial FOV = 94 mm
Trans-axial FOV = 80 mm
Energy resolution = 14%
Timing resolution = 1.4 ns

Specifications CT:

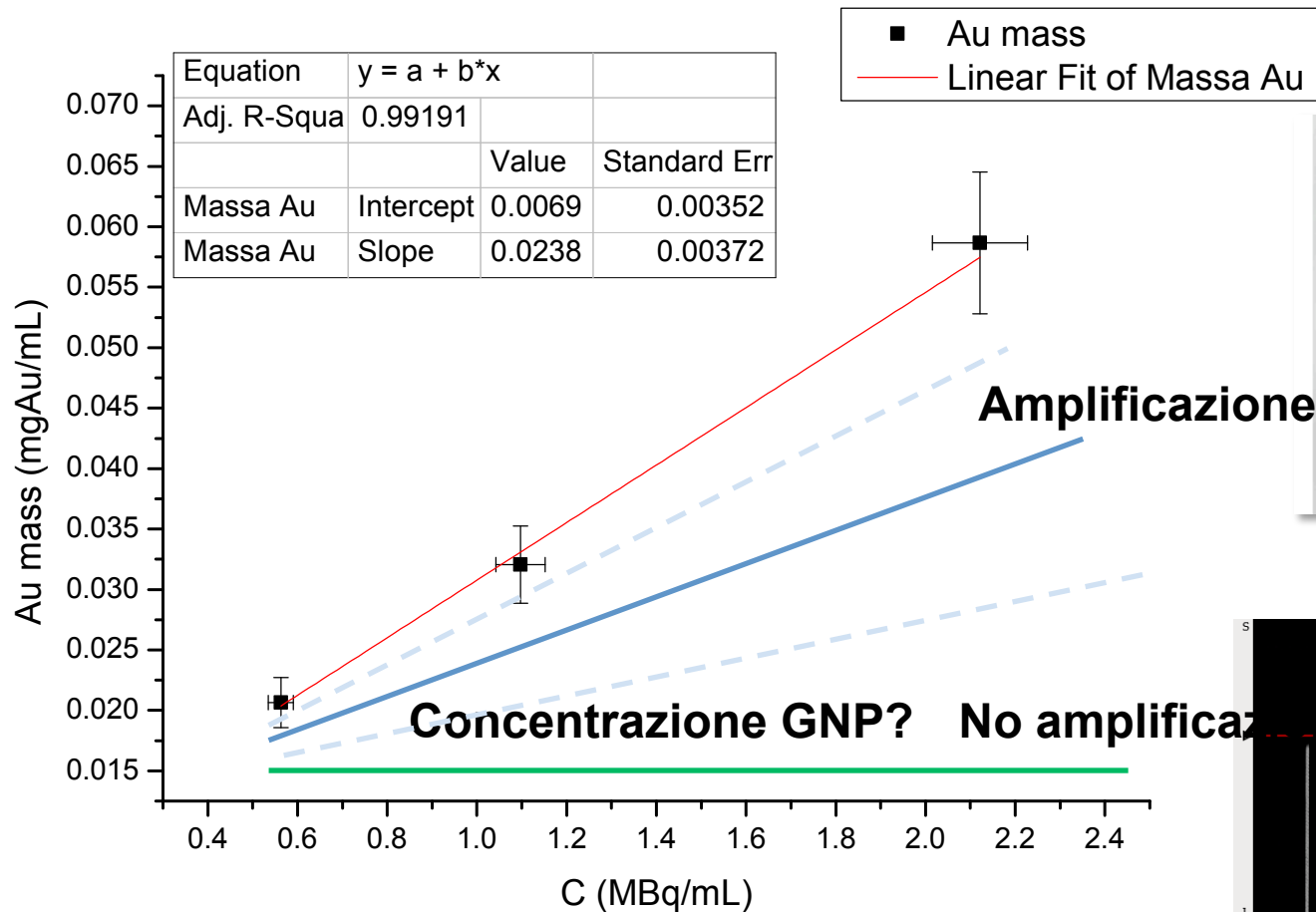
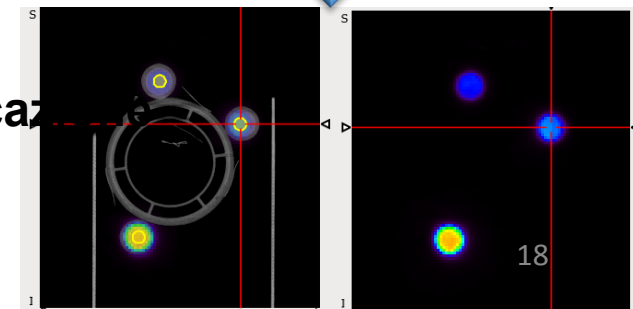
Fast scan time = 20 sec.
Low dose = 20 mGy
Resolution = 5 lp/mm
Axial FOV = 90 mm
High resolution scan time = 1 min.
Max rate = 86 fps



Studio in vivo



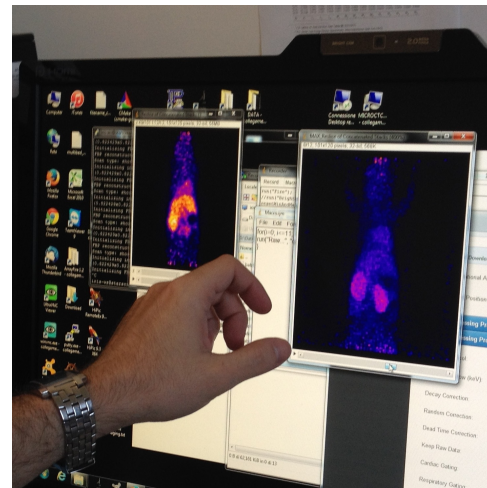
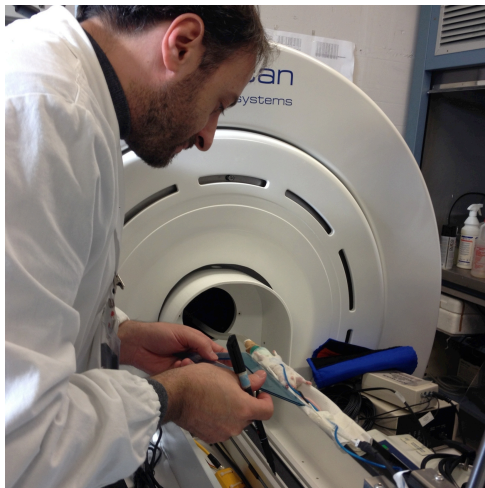
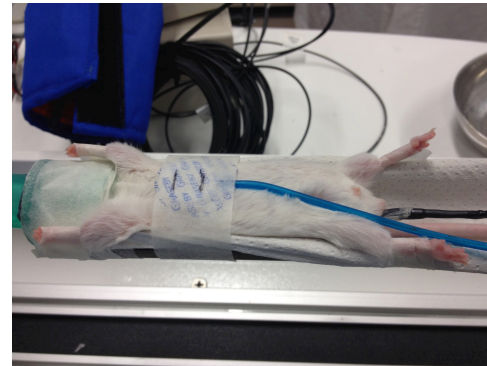
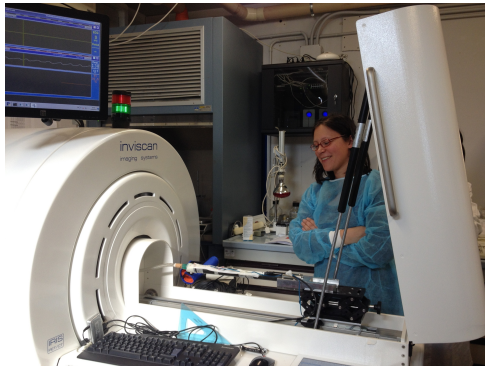
Pisa - CNR: Studio in vivo con ^{18}F - FDG - GNP e ^{18}F - RGD - GNP



in vivo measurements



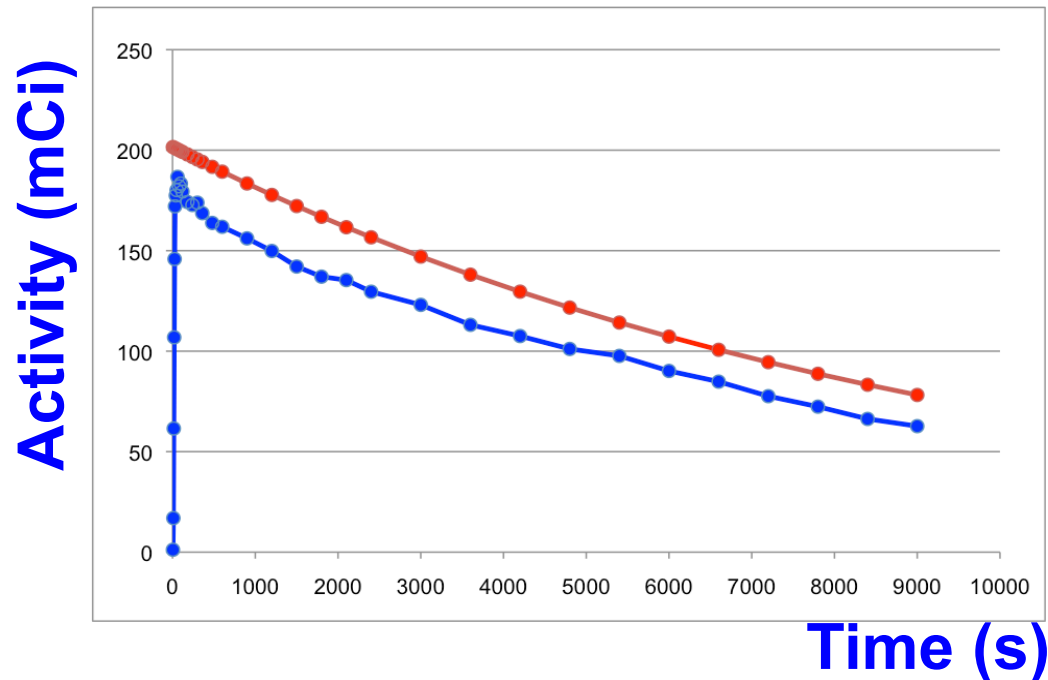
Pisa - CNR: in vivo with ^{18}F - FDG - GNP



in vivo measurements



Pisa - CNR: in vivo with ^{18}F - FDG - GNP



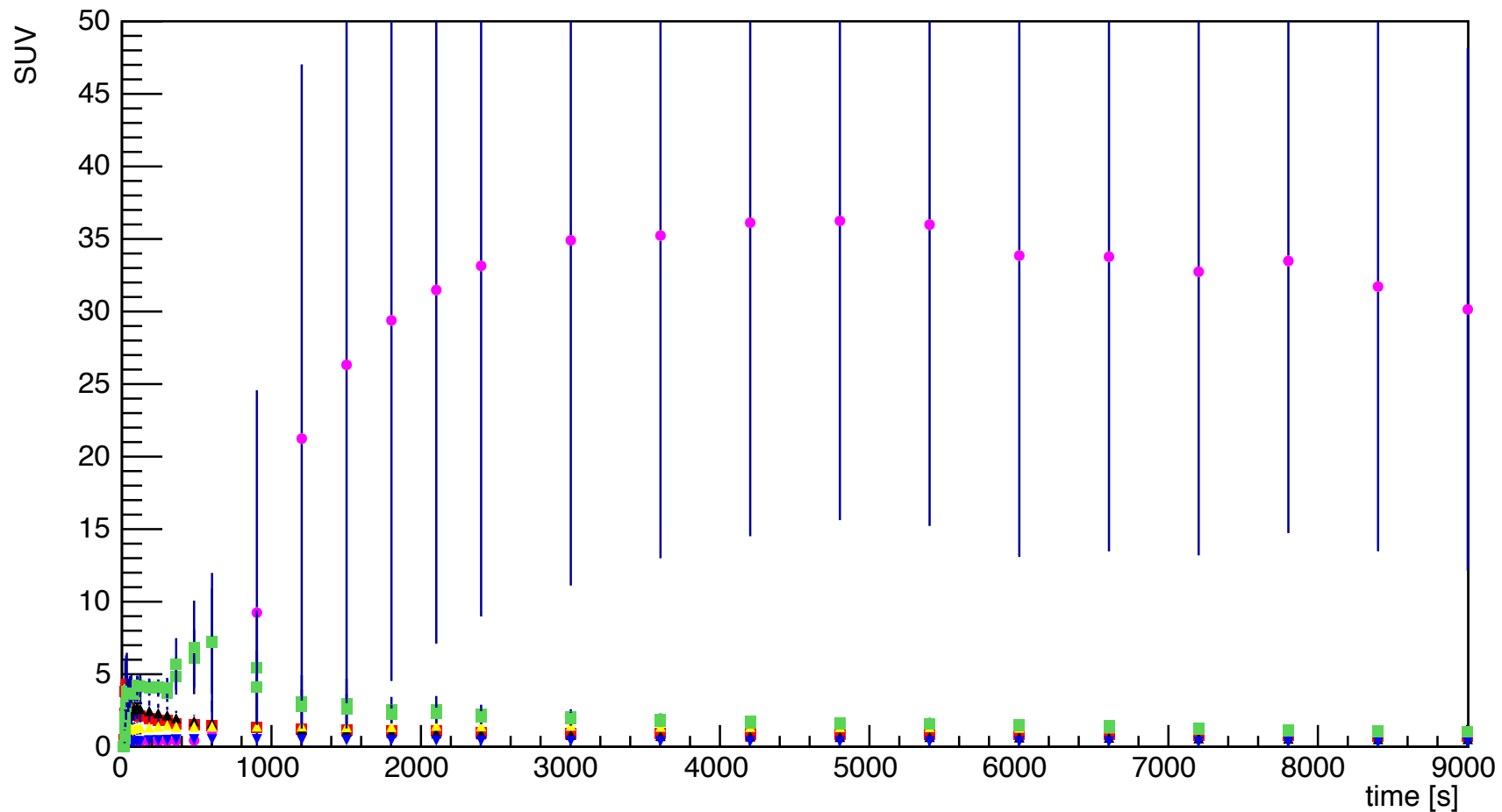
- Time span: 2.5 h
- Activity pattern as expected
- Losses caused by Field Of View acceptance

in vivo measurements



Pisa - CNR: in vivo with ^{18}F - FDG - GNP

- Uptake dynamics

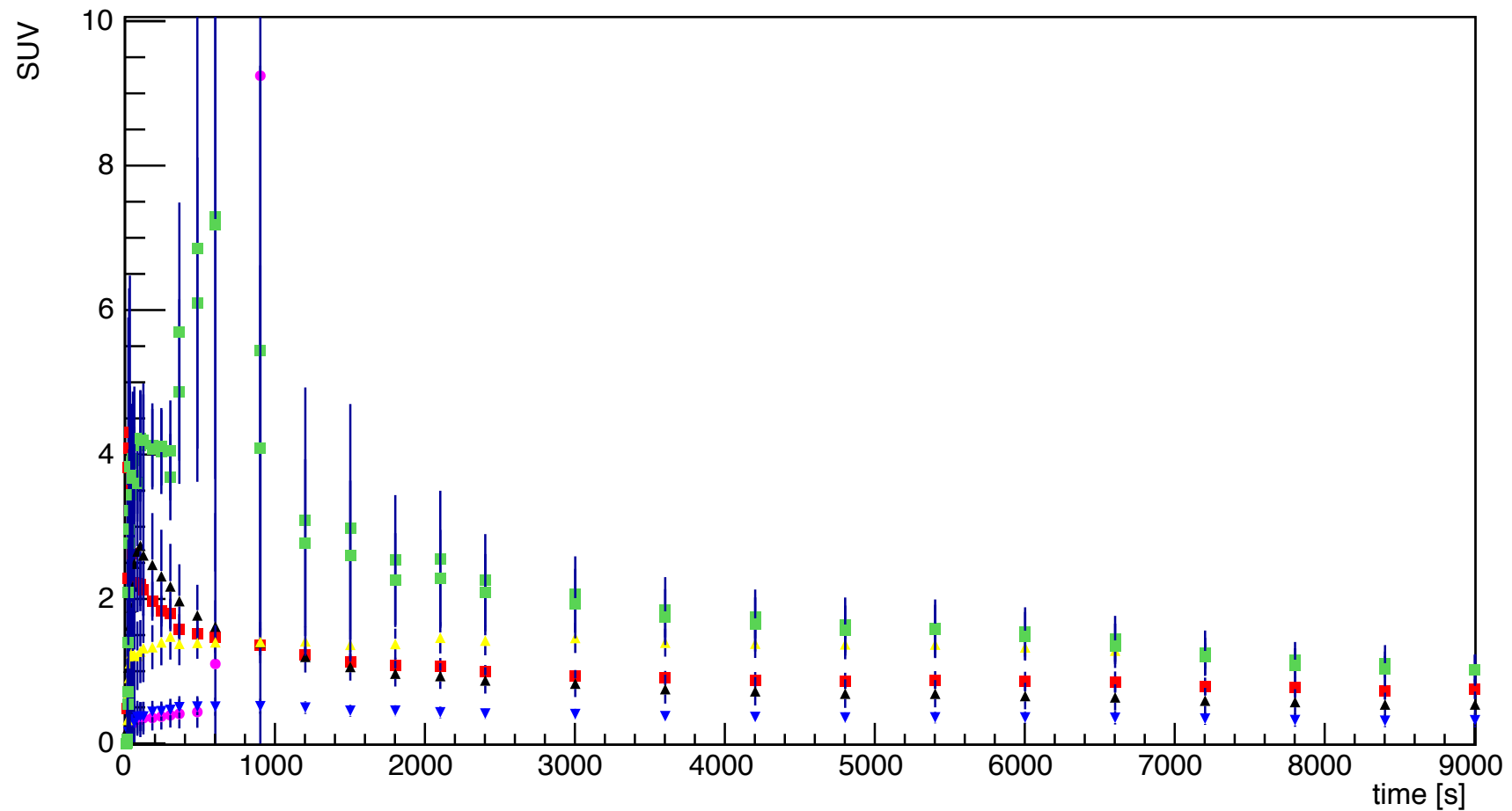


in vivo measurements



Pisa - CNR: in vivo with ^{18}F - FDG - GNP

- Uptake dynamics

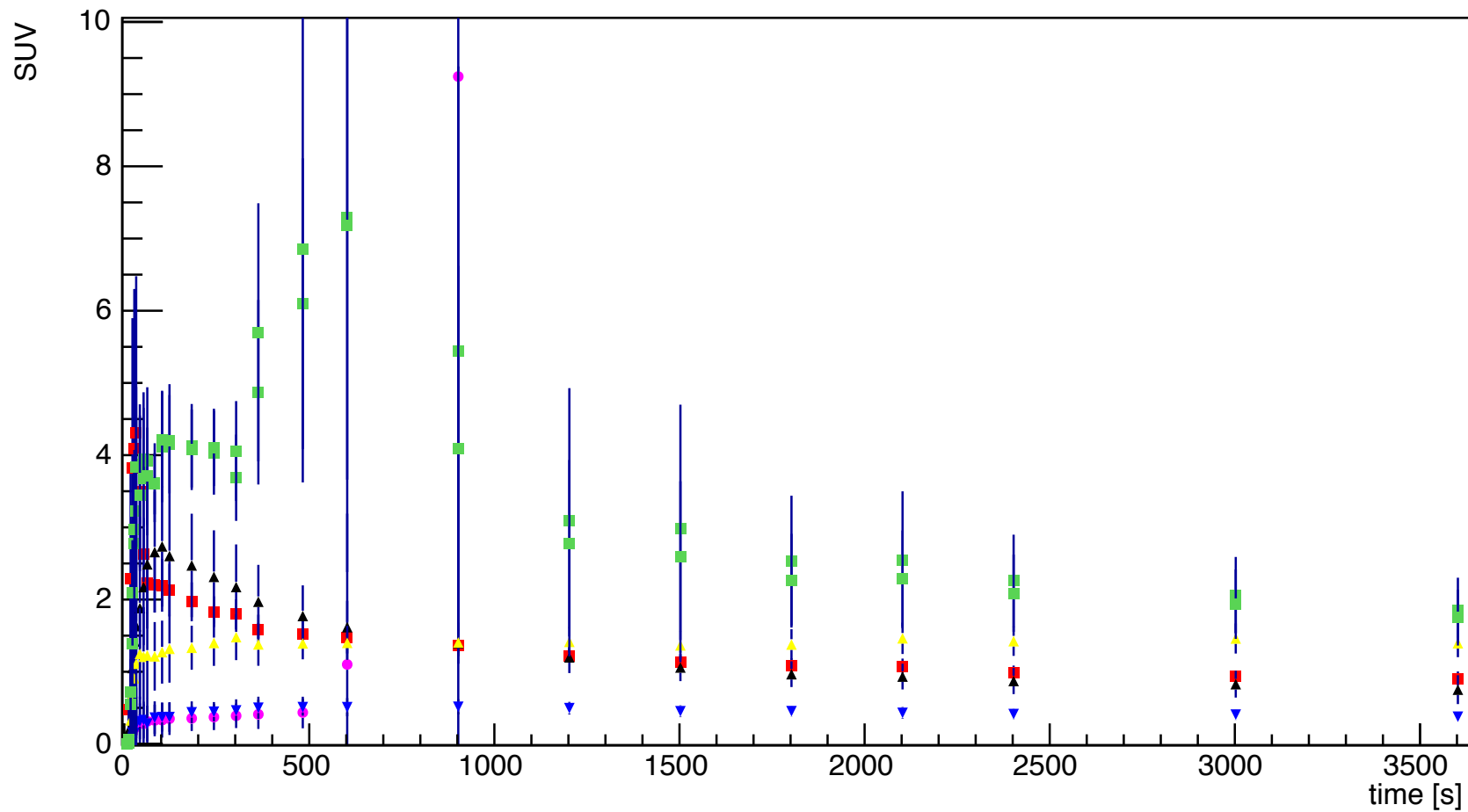


in vivo measurements



Pisa - CNR: in vivo with ^{18}F - FDG - GNP

- Uptake dynamics

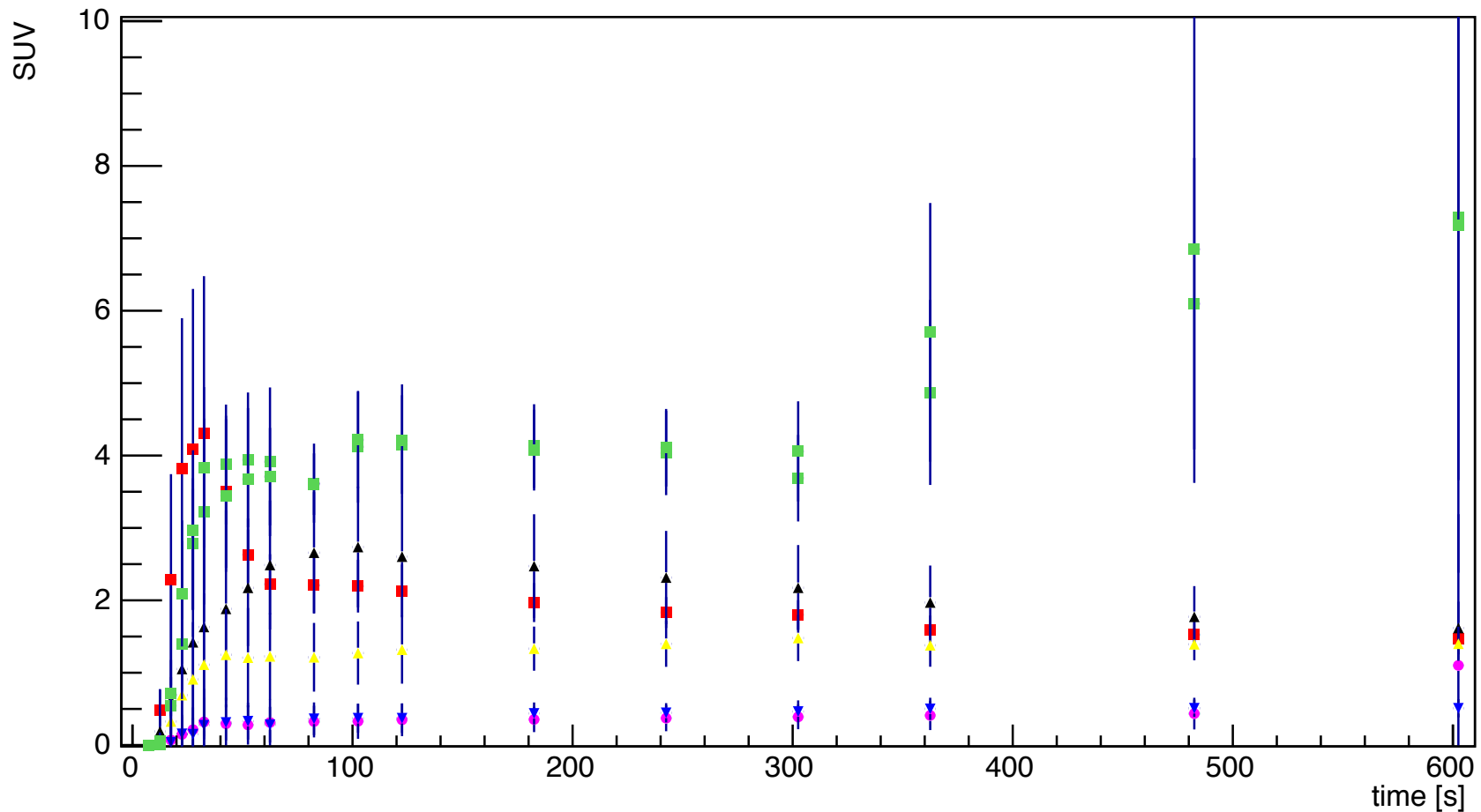


in vivo measurements



Pisa - CNR: in vivo with ^{18}F - FDG - GNP

- Uptake dynamics



in vivo measurements

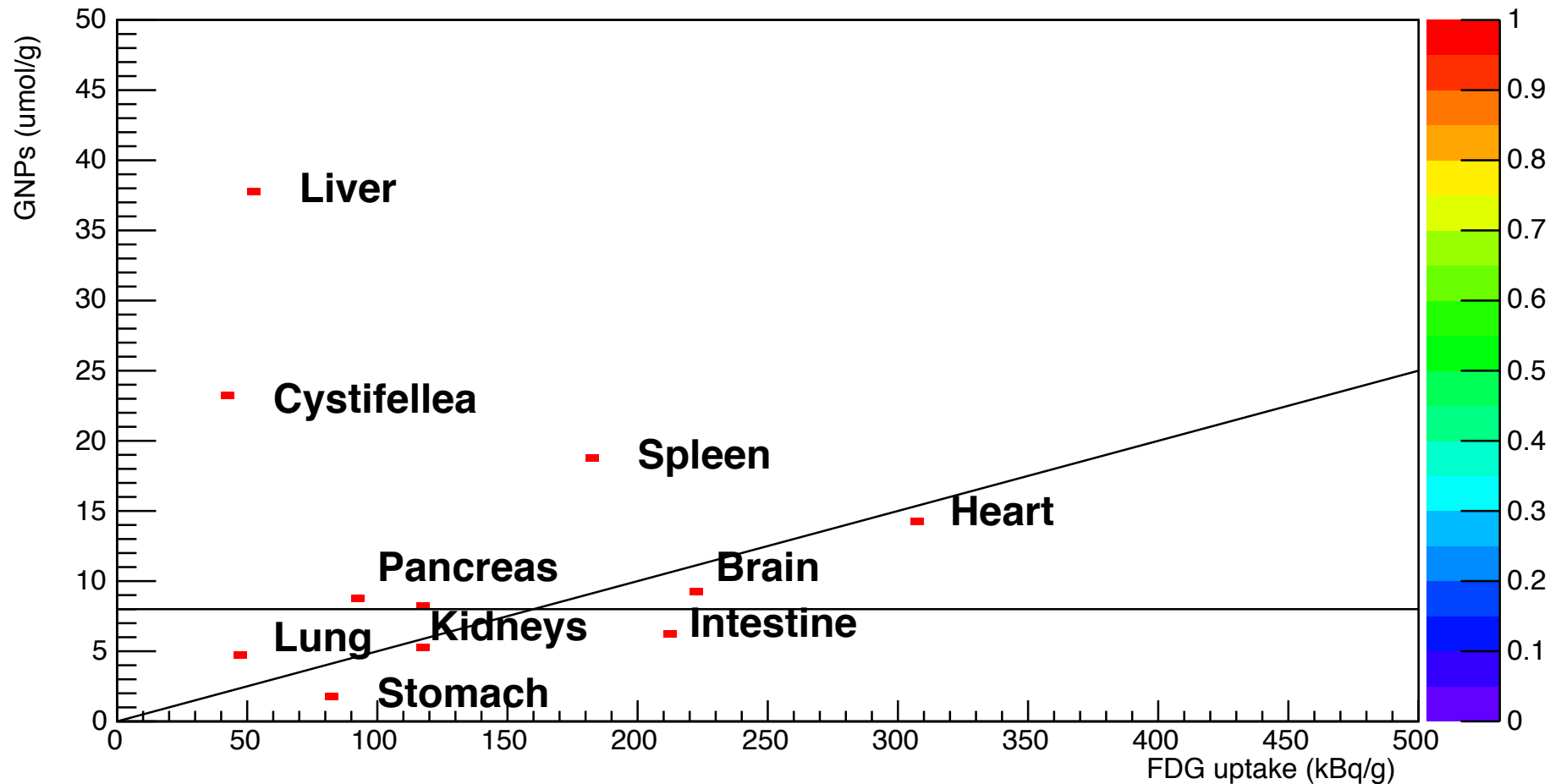


Pisa - CNR: in vivo with ^{18}F - FDG - GNP

Total organ weight (g): 6.9289

Total gold (mg): 21.936

GNP (umol/g) vs. FDG (kBq/g)



Acknowledgements



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