THE CHALLENGE of ^{64}Cu PET/CT IMAGING in PROSTATE CANCER and the THERANOSTIC VISION

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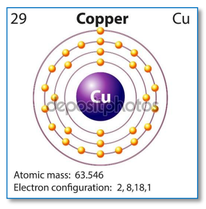
INTRODUCTION

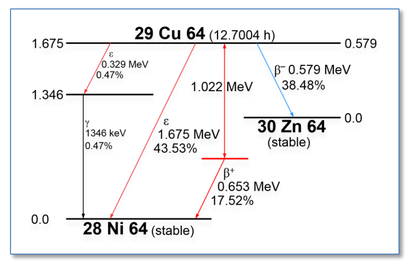
Prostate cancer (PCa), one of the most common cancers in males, is a topic of active interest in imaging research. Conventional imaging modalities (**CI**) , including bone scan, CT, ultrasound, and MR imaging, are currently used to detect primary PCa and metastatic disease for staging and risk stratification. However, CI have been poor in disease localization in the setting of patient with biochemical recurrence **(BCR)** following primary treatment. Molecular and functional imaging with positron emission tomography (**PET**) has shown promise of being a superior imaging modality both in early identification of disease recurrence and in therapy monitoring. In addition PET /CT is increasingly used to guide radiotherapy (**RT**) management and target delineation. Hence, in the last two decades multiple newer radiotracers have been developed to realize a precise molecular disease characterization even at early clinical states of the PCa disease.

COPPER

Copper (64CuCl2) is a new appealing **PET radiotracer** with high affinity for biological tissue and physical characteristic adequate to both imaging and therapy thus representing a good candidate as ***THERANOSTIC AGENT***.

The copper transporter Ctr1 has been clearly demonstrated to be highly overexpressed in cancerous cells compared to normal prostate epithelial cells





The challenge

VALIDATE DIAGNOSTIC PERFORMANCE OF 64CuCl in PCa & DEFINE the BEST PROTOCOL

EVALUATE SAFETY, AND PAHARMACOKINETIC

VALIDATE DOSIMETRY

TEST the POTENTIAL THERAPY USE & THERANOSTIC VALUE

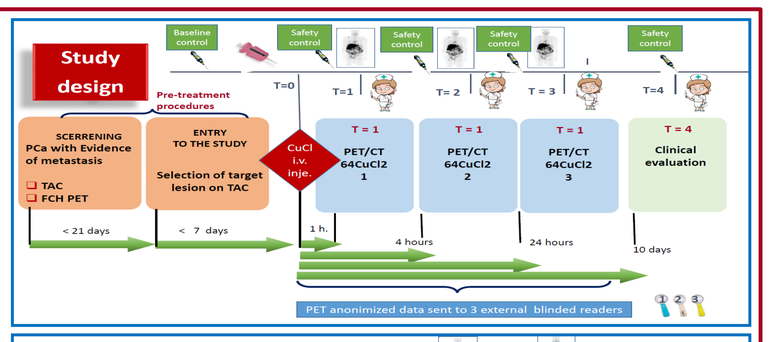
RESEARCH PROJECT

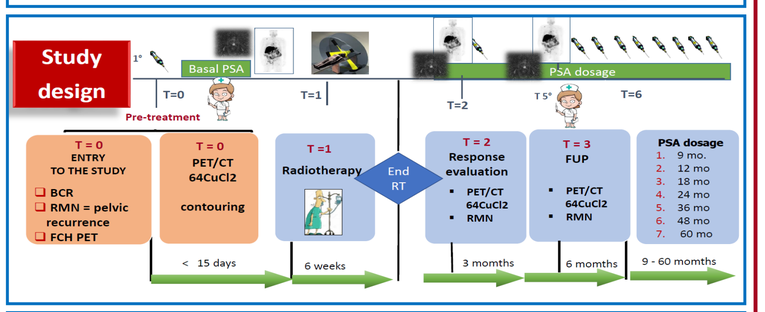
On the basis of these evidences IRE Nuclear Medicine has implemented a **MULTISTEP RESEARCH PROJECT** aimed first to validate the diagnostic role of ^{64}Cu PET in PCa with the perspective to investigate also the potential use as theranostic agent.

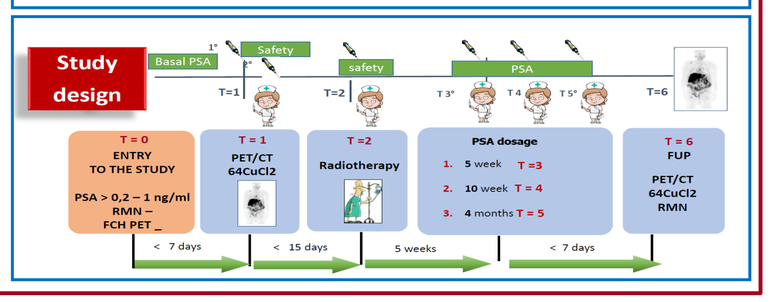
1 **phase II study** on a sample of 50 patients with known **metastatic PCA** aimed to evaluate **diagnostic performance and safety** of Cu-PET and target /non target **dosimetry.** — CLOSED

2 a **pilot study** on a sample of 50 PCa patients with **early recurrence** comparing the **diagnostic performance** of **MR and 64Cu-PET** and their **accuracy in target delineation** **to guide RT** — ONGOING

3 **multicentric phase III study**, aimed to validate on a large number of PCa patients (n = 138) the **^{64}Cu-PET diagnostic value** in **patients candidate to salvage radiotherapy** with biochemical recurrence but negative conventional imaging (RMN and F-choline PET) — RECENTLY STARTED







RESULTS STUDY 1

DIAGNOSTIC PERFORMANCE :

High sensitivity : all target lesions were correctly identified

Better performance ***than standard F-Choline (FCH) PET***

Higher Sensitivity (100% vs 80%)

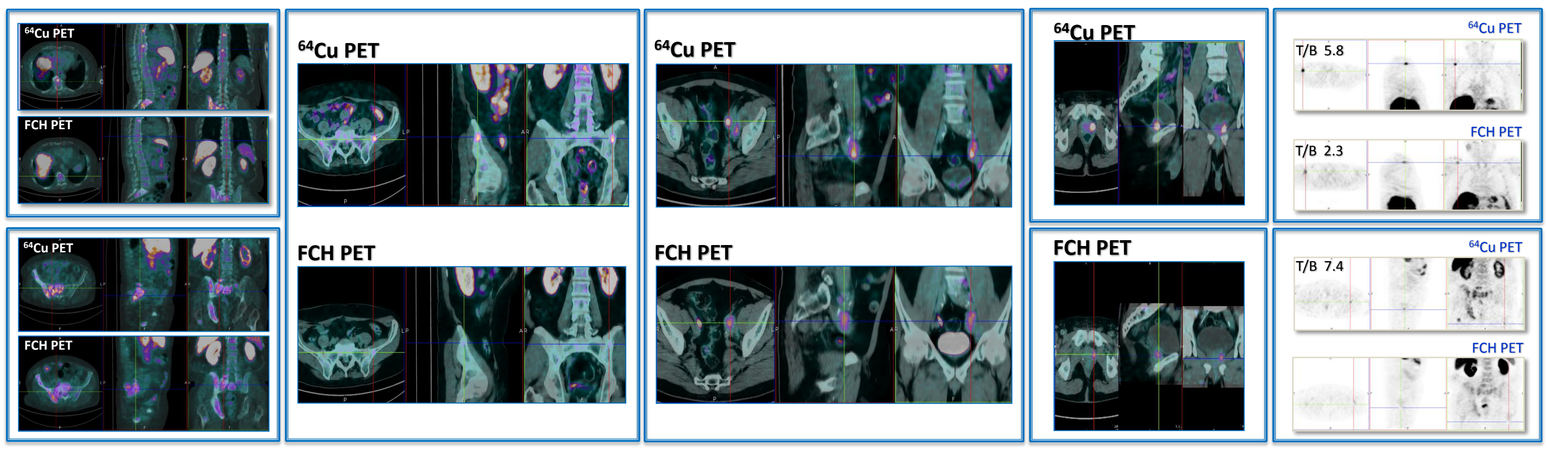
Higher Tumor/Background (3-5 :1)

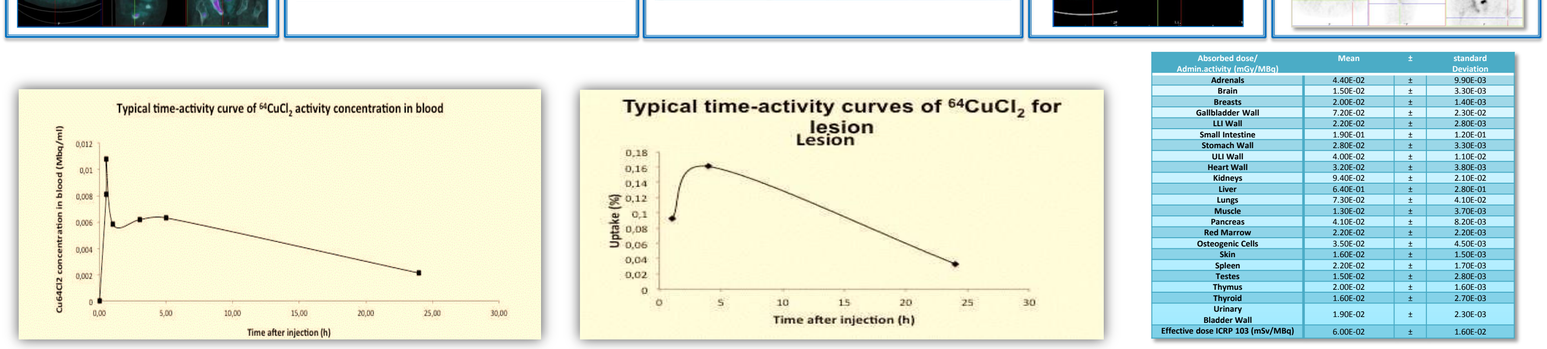
High intra and inter-observer **reproducibility** (100% , 90%)

SAFETY

No adverse effects and good tolerability were observed

Dosimetry and biodistribution **are favourable** to diagnostic use, while additional studies are ongoing for therapeutics application

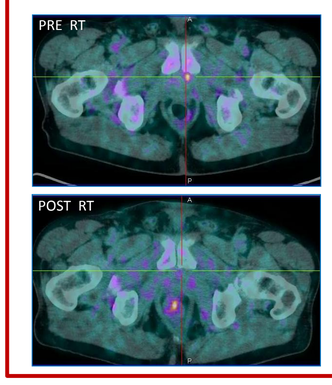


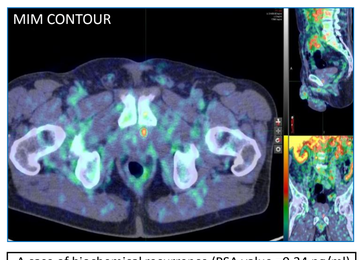


PRELIMINARY RESULTS STUDY 2

On first 28 patients enrolled CuCl PET showed effective in:

- **Contouring very small lesions (> 3 mm) in prostatic bed to guide RT**
- **Monitoring RT response**





A case of biochemical recurrence (PSA value =0,34 ng/ml) in PCa (Gleason 7: 3+4, pT3pN0)

- Baseline 64 Cu PET evidenced a focal uptake on left side of prostatic bed corresponding to a 5 mm nodule
- 64 Cu PET repeated 3 months after the end of RT evidenced a complete response

IMPACT OF THE RESEARCH

The impact is relevant taking into consideration the prevalence of PCa and the need of early diagnosis to increase effectiveness of available treatments. Also, new treatment perspective are welcome especially in metastatic patients.

In particular, the following results are expected from our studies:

- **to improve image based diagnosis in early phase of PCa at very low PSA values (< 1 ng/ml)**
- **to evaluate the potential role of 64 Cu as theranostic agent in PCa patients by the analysis of bio-kinetic, bio-distribution and previsional dosimetry**

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