

PSMA THERANOSTICS: TRANSFORMING PROSTATE CANCER CARE MOLECULAR IMAGING AND THERAPEUTICS RESEARCH PROGRAM Program Director: Frankis Almaguel, MD/PhD Post-doctoral Fellow: Alfonso Durán, MD/PhD

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What is Molecular Imaging?

VS

Molecular imaging can detect alterations in cellular metabolism function. The advantage of this approach is that most perturbations in cellular metabolism proceeds structural change, therefore allowing for the early detection of an aberrant process, such as cancer. Furthermore, since cancer within tissue types and individuals may vary, molecular imaging permits precision care.



Computerized Tomography

Molecular



⁶⁸Ga-PSMA PET/CT

Molecular Imaging Driving Precision Medicine

Paradigm Shift:

- Cancers will be classified by molecular phenotypes •Organ site \rightarrow secondary classification Molecular phenotypes will be determined by **molecular imaging** using cancer type specific biomarkers
- Treatment will be targeted specifically against the tumor
- Eliminating trial and error patterns in medicine



Targeted Molecular Imaging and Therapy



PSMA, A Novel Prostate Cancer Biomarker

antibodies

PSMA-inhibitors

'E11 antibodies

Nature Reviews | Urology

Maurer, T. et al. (2016)

Cell membrane







PSMA expression in tumors is negatively correlated with survival outcomes

Extracellular

Intracellular

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PSMA PET/CT Emerging as a Practice-changing Modality for Managing Prostate Cancer

Imaging ⁶⁸GA, ¹⁸F, lsotope Therapy ¹⁷⁷Lu, ²²⁵Ac



Highly expressed in Prostate Cancer with greater expression: Metastatic disease

- Castration-resistant cancer cells Poorly differentiated
- High grade tumors



Weak PSMA staining in a patient with Gleason score 3 + 3

PSMA and Prostate Cancer Prognosis



Strong PSMA staining

in a patient with

Gleason score 4 + 4



ADAPTED FROM HUPE, M. ET AL. (2018)



58 y/o with adenocarcinoma of the prostate, grade group 5 (Gleason patterns 4 + 5 = 9)

PSMA PET for treatment planning PSMA Guided Proton Beam Therapy (PBT)

Pre-Tx PSA 16.4 Post-Tx PSA 0.02

64 y/o adenocarcinoma of the prostate, mCRPC (Gleason 8),

PSMA PET for treatment planning revealed extensive metastatic disease.

PSMA Radioligand Therapy x 3

 $Pre-PSMA-RLT \rightarrow PSA 800$ Post-PSMA-RLT \rightarrow PSA 0.01

67 y/o with adenocarcinoma of the prostate (Gleason 4 + 4 = 8)

PSMA PET for initial diagnosis and treatment planning revealed extensive metastatic disease (Stage IV at diagnosis).

PSMA Radioligand Therapy x 1

 $Pre-PSMA-RLT \rightarrow PSA \ 200$ Post-PSMA-RLT \rightarrow PSA 0.01



Localized Prostate Cancer Treated with **PSMA Guided Proton Therapy**

⁶⁸Ga-PSMA PET/CT



Post PBT



Metastatic Castration Resistant Prostate Cancer Pre and Post PSMA-RLT



Pre PSMA-RLT



Post PSMA-RLT

Complete Response After PSMA-RLT



Pre PSMA-RLT

Post PSMA-RLT