Precision Imaging of Response to Therapy in Co-Clinical FDG-PET Imaging of Triple Negative Breast Cancer (TNBC) Patient-Derived Tumor Xenografts (PDX)

Madhusudan A. Savaikar[1], Timothy Whitehead[1], Sudipta Roy[1], Lori Strong[1], Nicole Fettig[1], Tina Prmeau[2], Jingqin Luo[3], Shunqiang Li[2], Richard L. Wahl[1], Kooresh I. Shoghi[1,4]

[1]Department of Radiology, Washington University School of Medicine, St. Louis, MO, USA

[2]Department of Medicine, Division of Oncology, Washington University School of Medicine, St. Louis, USA

[3]Department of Surgery, Washington University School of Medicine, St. Louis, USA

[4]Department of Biomedical Engineering, Washington University in St. Louis, St. Louis, MO, USA

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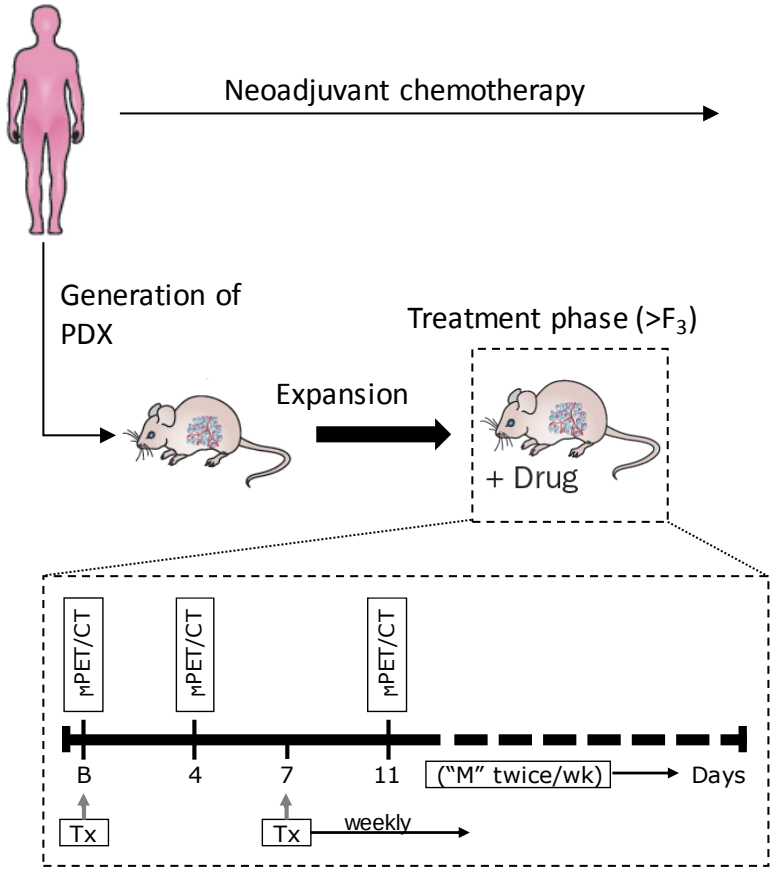
Background

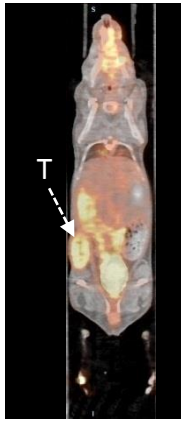
- More realistic preclinical cancer models are thought to be provided by transplantable, patient-derived tumor xenografts (PDX).
- Co-clinical trials, in which a clinical arm and a preclinical arm are coupled using PDX or another co-clinical model to develop therapeutic insights, are an emerging field of investigation
- There is a wide interest within the imaging community and NCI to develop a consensus on imaging metrics of response to Therapy.

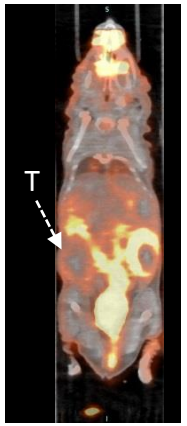
Objective

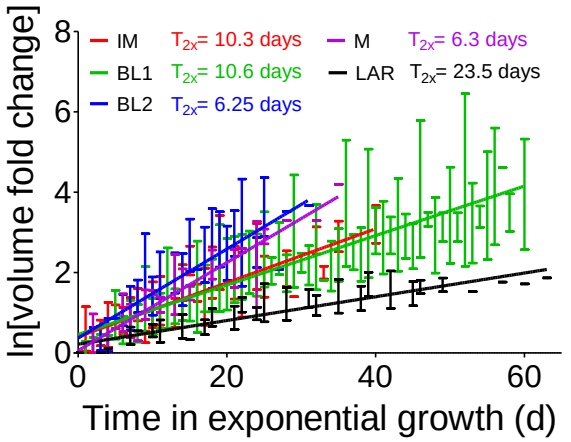
- Develop and optimize image metrics of FDG-PET to assess response to combination docetaxel/carboplatin therapy in a co-clinical trial involving triple negative breast cancer (TNBC) patient-derived transplantable xenografts (PDX).
  - Characterize growth kinetics and heterogeneity of TNBC PDX subtypes.
  - Test-retest studies on consecutive days (Day 1 vs Day 2) to assess the reproducibility of FDG-PET SUV image metrics.
  - Therapeutic study with imaging to assess the utility of FDG-PET to predict response to therapy.

Co-clinical Study Design and Characterization of TNBC PDX

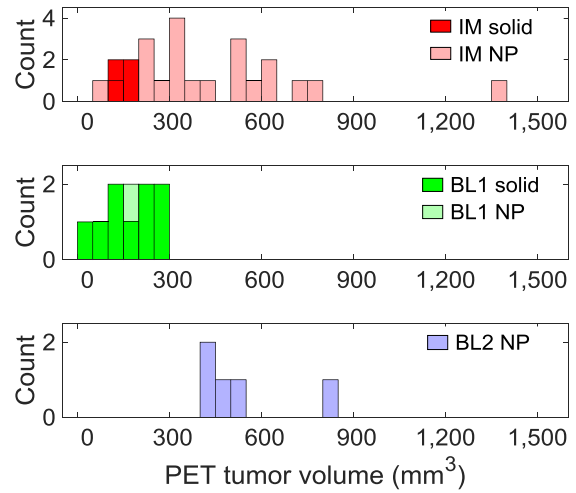


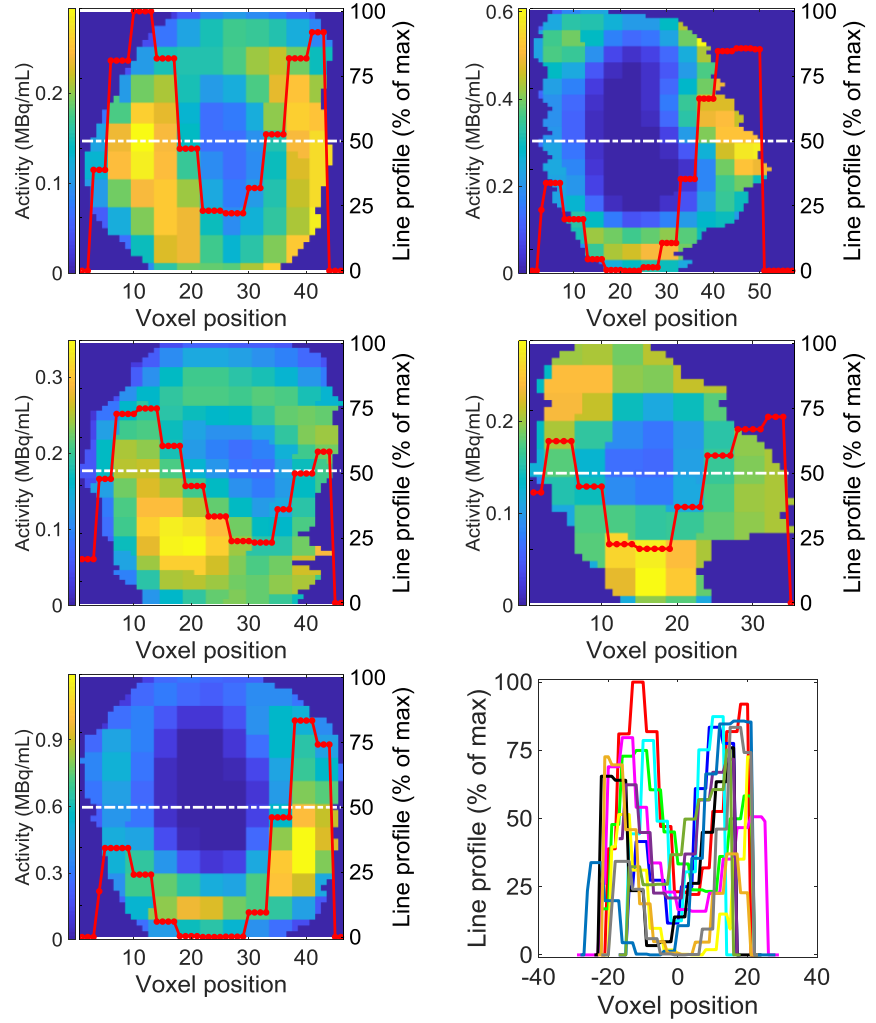






Tumor growth profile





Study design | CT-PET images | PET volume distribution | Coronal slices and PET intensity line profiles

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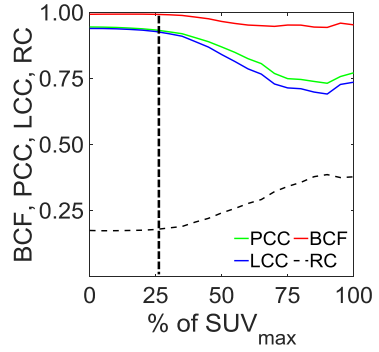
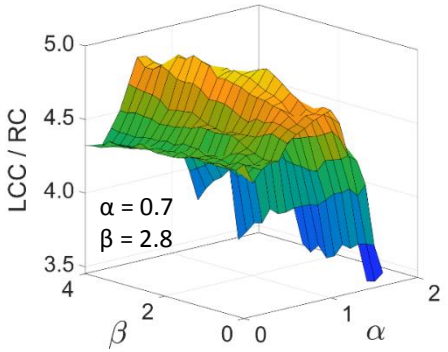
Optimization of Image Metrics for Reproducibility

Therapy Response Assessment

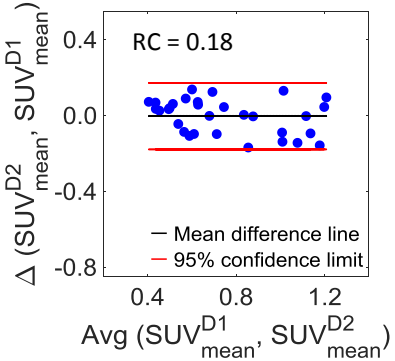
Image histogram reproducibility analysis



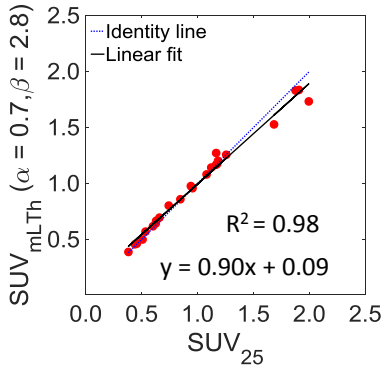
Objective function LCC/RC maximization



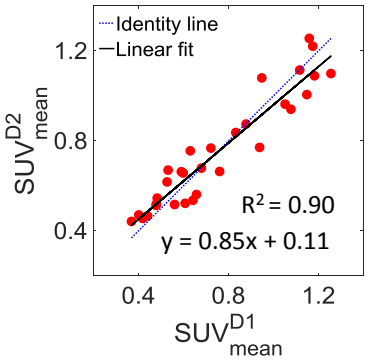
Bland-Altman plot (SUV_{mean})



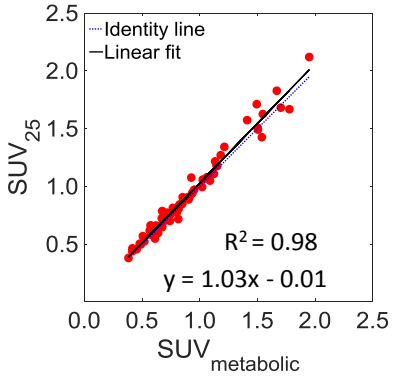
Concordance plot



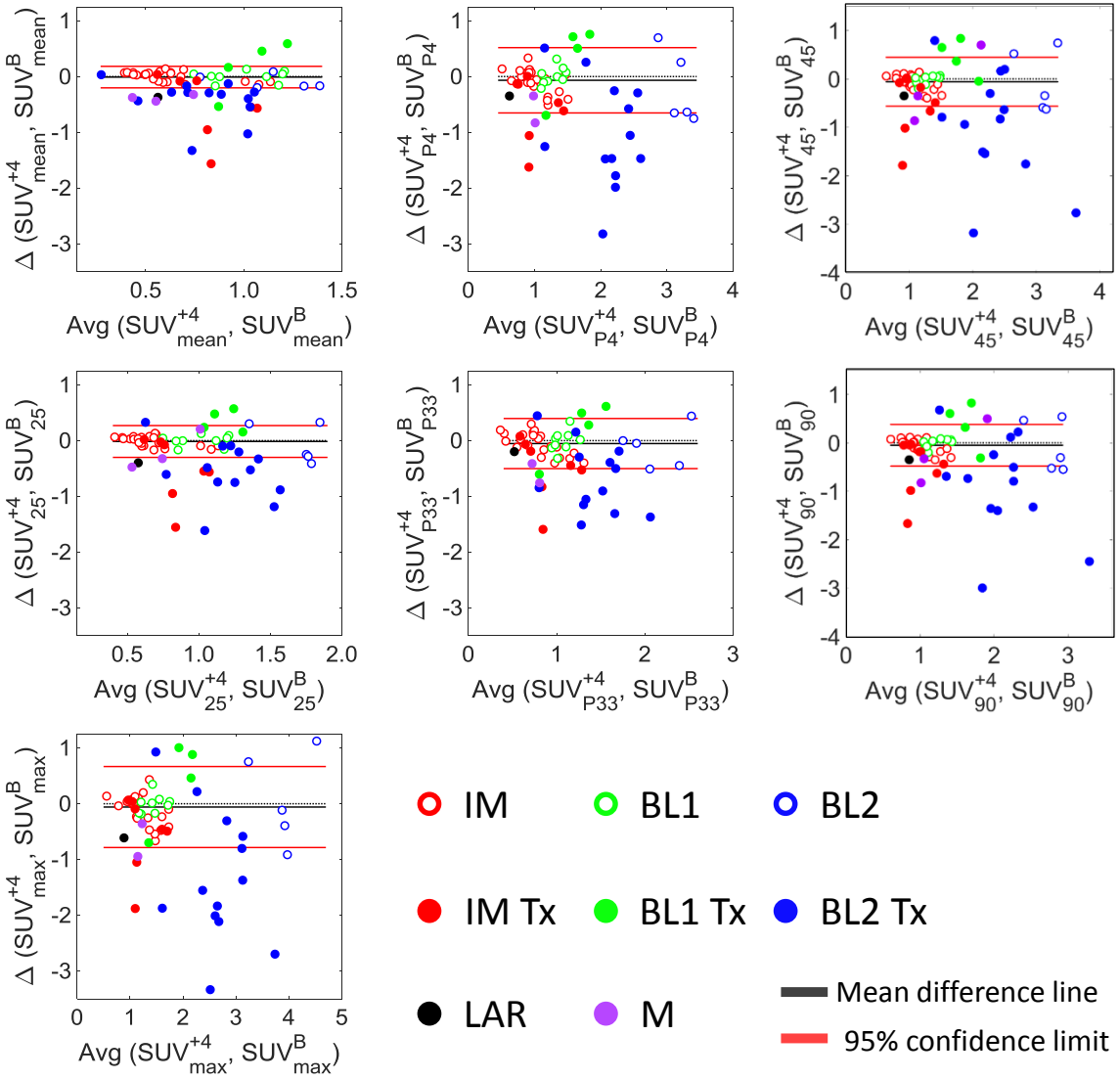
Concordance plot



Concordance plot



BA plots of image metrics



Whole tumor

Preclinical PERCIST optimization

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Imaging Metrics Performance in Predicting Response to Therapy

SUV metric	RC	F score	Uncertain fraction (%)	QRAS
ΔSUV_{max}	0.73	0.73	45	0.45
ΔSUV_{25}	**0.28**	**0.72**	**31**	**0.12**
ΔSUV_{25} (SS)	0.33	0.74	34	0.15
ΔSUV_{P4}	0.59	0.77	48	0.37
ΔSUV_{P14}	0.47	0.74	34	0.22
ΔSUV_{P33}	0.45	0.69	41	0.27
Max14	0.60	0.78	45	0.35
Max45	0.50	0.82	48	0.30
Max90	0.43	0.78	45	0.25

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Conclusions

- The work addressed a central effort within the imaging community on the reproducibility and utility of imaging metrics to assess response to therapy especially in co-clinical models.
- SUV_{25} ^{18}F-FDG PET measures are highly reproducible.
- QRAS scores favor SUV_{25}, followed by $SUVP_{14}$, as the optimal metrics for response to therapy.
- SUV_{25} strongly correlated with optimized pre-clinical PERCIST measures of tumor uptake and SUV of metabolic tumor.
- Further studies are warranted to fully characterize the utility of SUV_{25}.

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