Digital Twins in Radiation Oncology

Heiko Enderling, PhD, FSMB
Department of Radiation Oncology
Institute for Data Science in Oncology

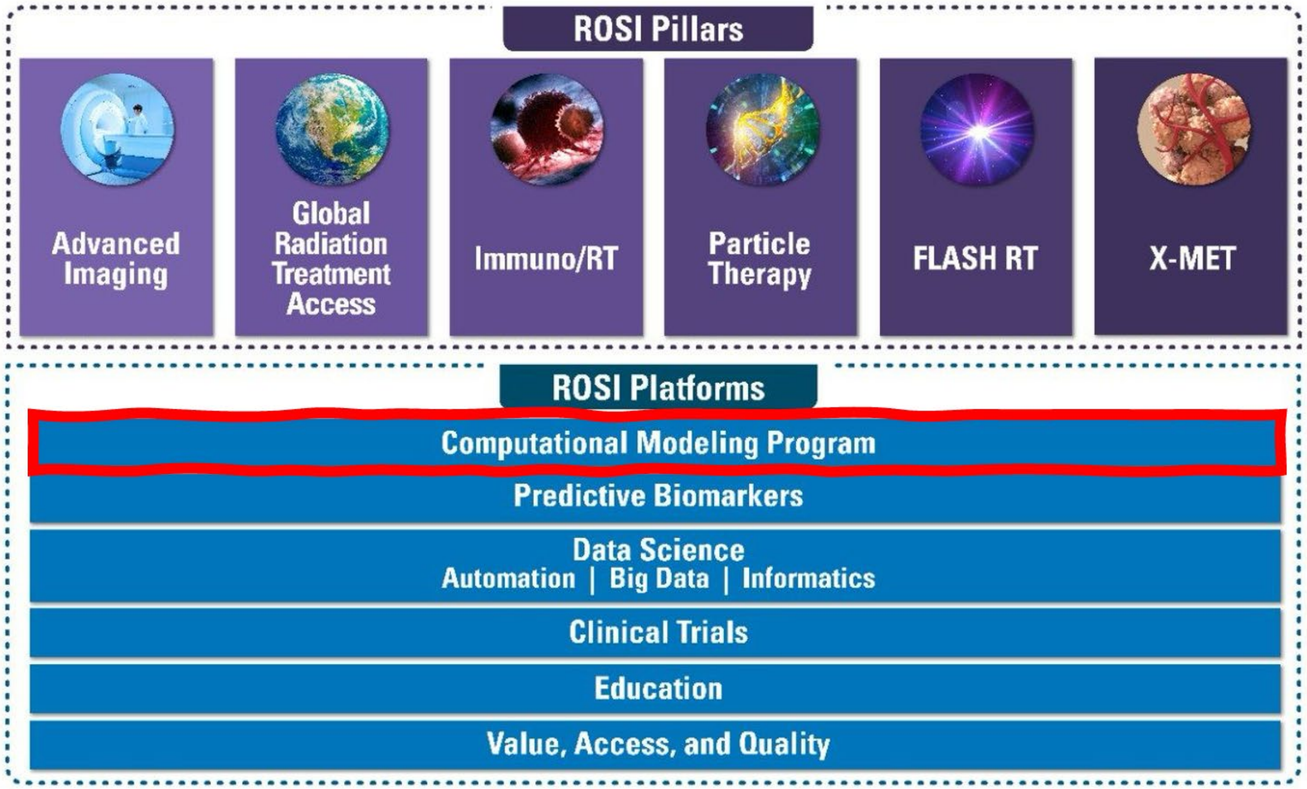
henderling@mdanderson.org

PRISM
PERSONALIZED RADIOTHERAPY WITH INTEGRATED SCIENTIFIC MODELING

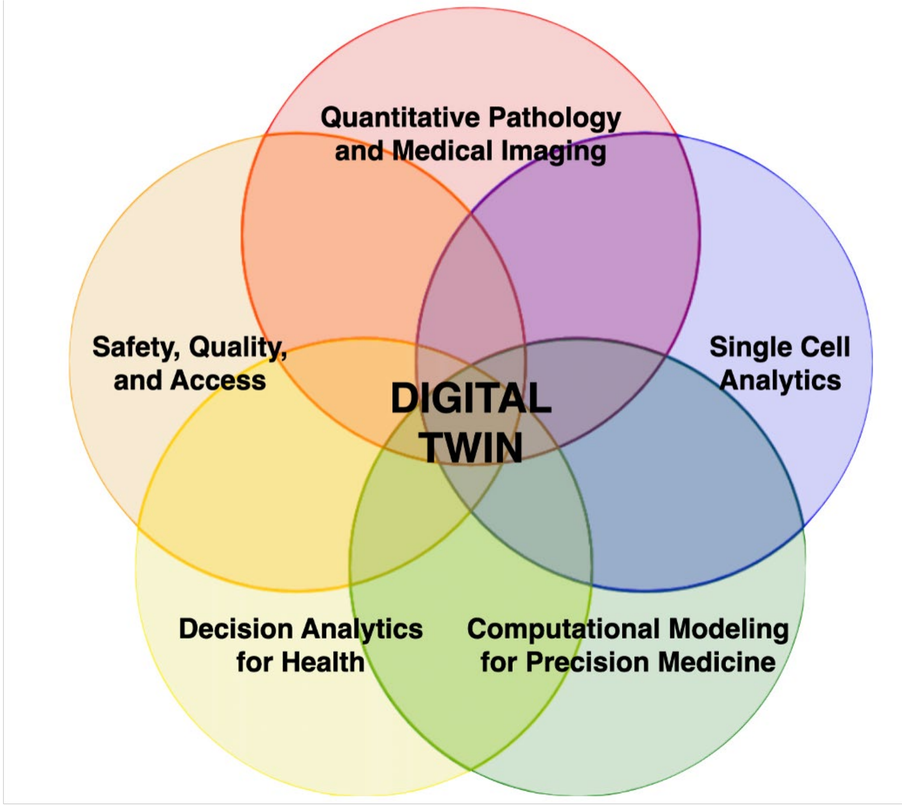
THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Computational Modeling at MDACC

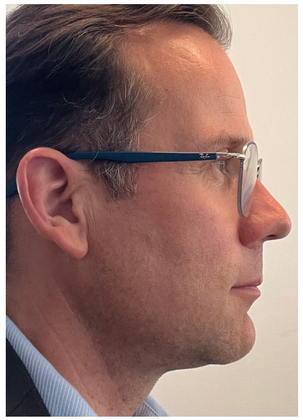
Radiation Oncology Strategic Initiatives (ROSI)

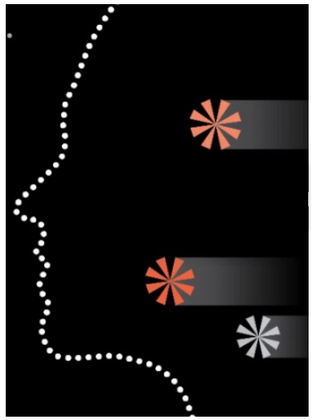


Institute for Data Science in Oncology (IDSO)



Digital Twin





Dr. Caroline Chung

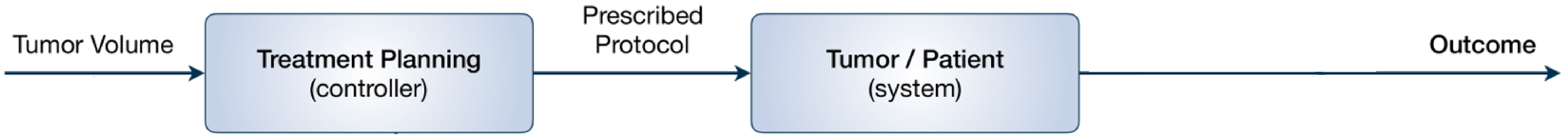
> *A digital twin is a set of virtual information constructs that mimics the structure, context, and behavior of a natural, engineered, or social system (or system-of-systems), is dynamically updated with data from its physical twin, has a predictive capability, and informs decisions that realize value. The bidirectional interaction between the virtual and the physical is central to the digital twin.*

https://nap.nationalacademies.org/catalog/26922/opportunities-and-challenges-for-digital-twins-in-biomedical-research-proceedings

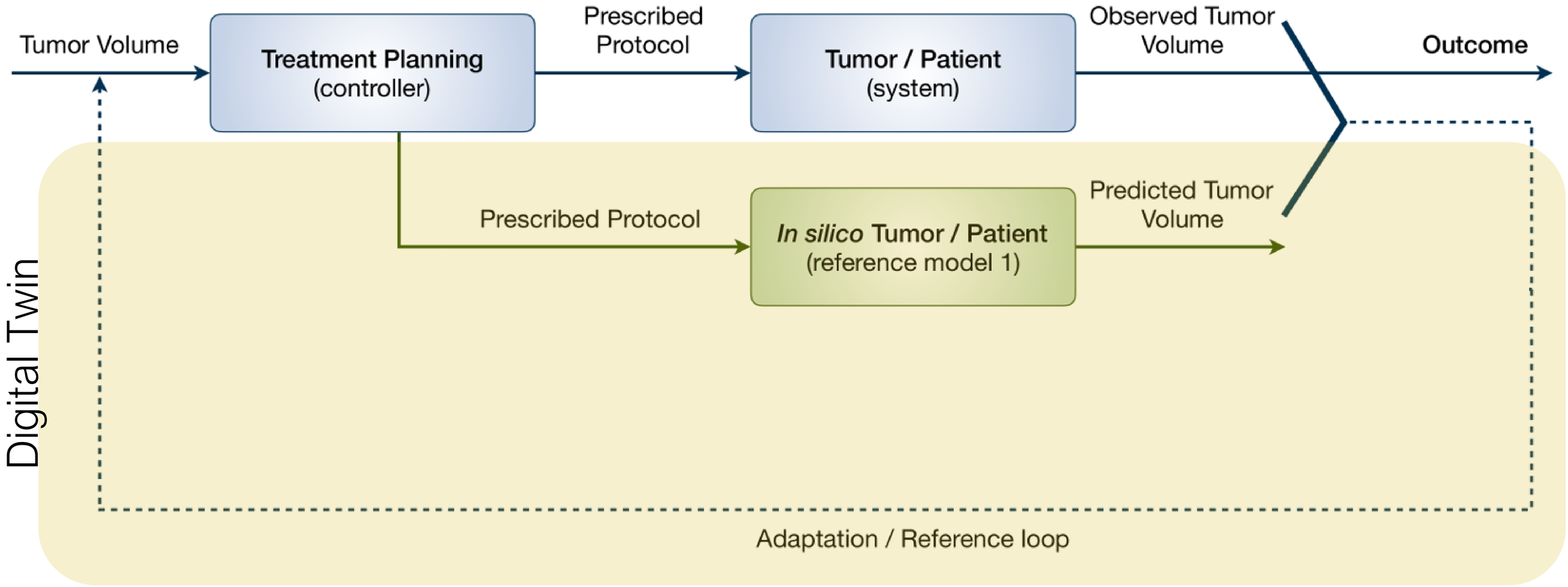
NATIONAL ACADEMIES Sciences Engineering Medicine

Committee's definition builds on a definition from an AIAA and AIA Position Paper (2020)

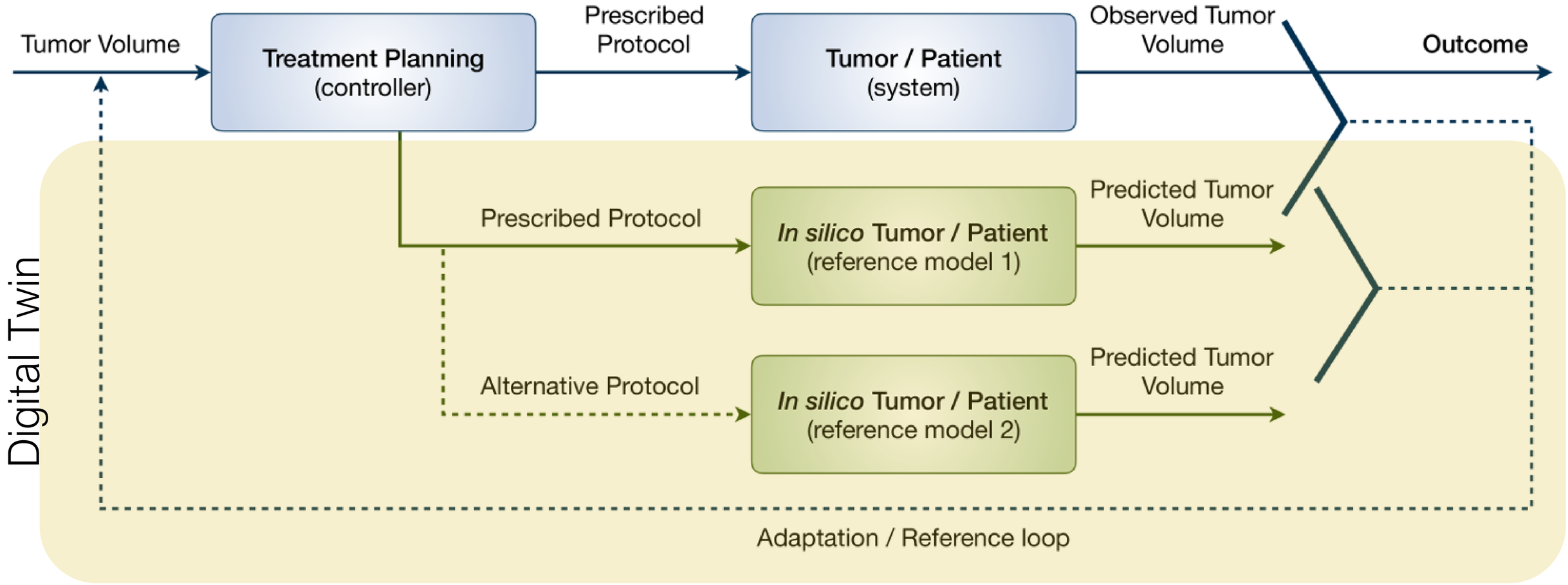
Courtesy of Dr. Caroline Chung



Enderling et al., Trends In Cancer, 2019



Enderling et al., Trends In Cancer, 2019



Enderling et al., Trends In Cancer, 2019

Dr. Jimmy Caudell
Moffitt Cancer Center

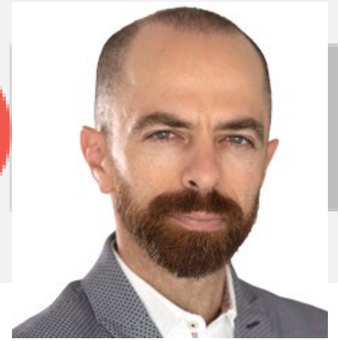
Can we use a digital twin

- to simulate head and neck cancer radiotherapy ?
- to predict patient-specific radiation responses ?
- to personalize radiotherapy dose and dose fractionation ?

PRiSM
PERSONALIZED RADIOTHERAPY WITH INTEGRATED SCIENTIFIC MODELING

Research at MD Anderson

Proliferation Saturation Index, PSI

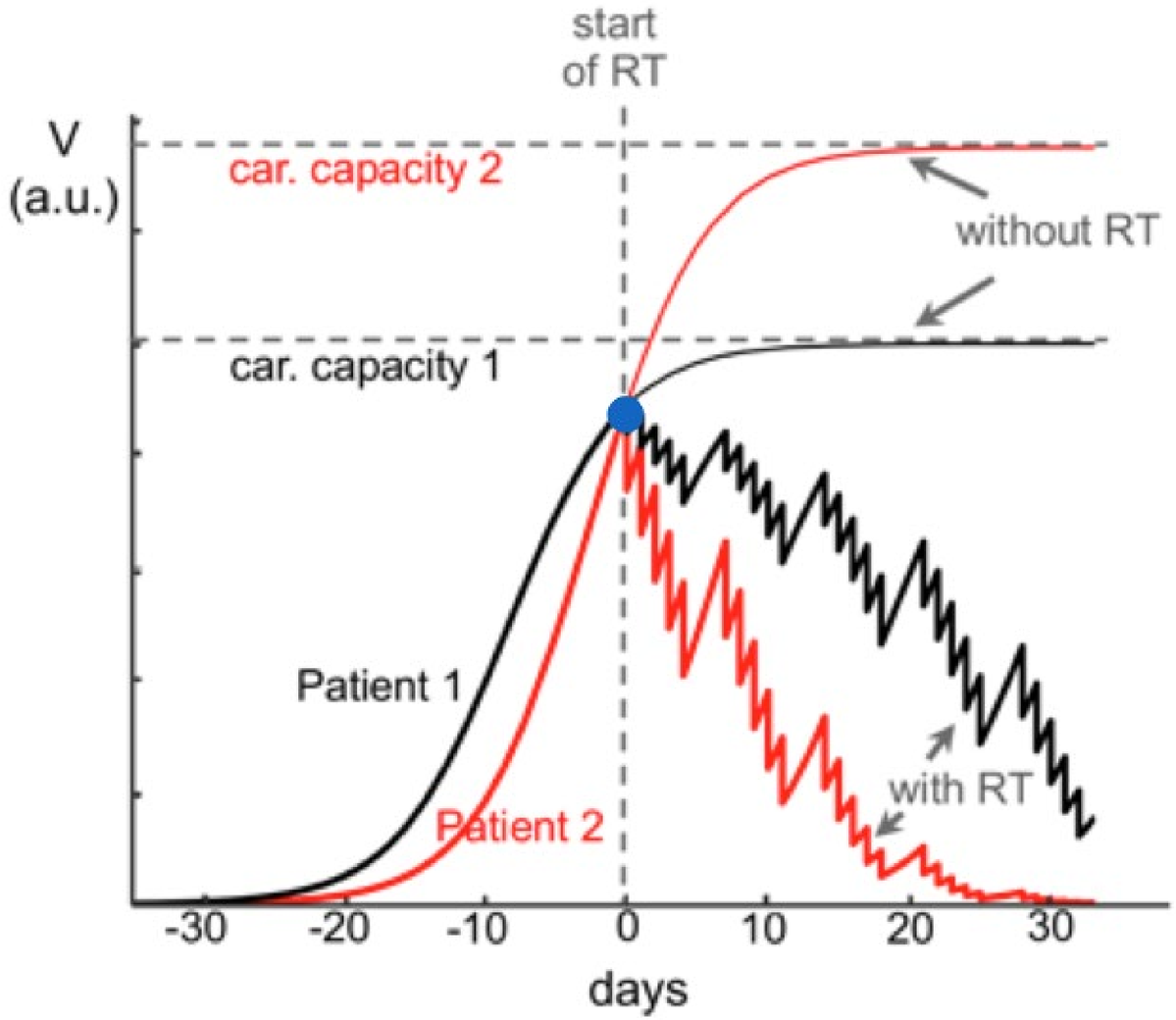


Dr. Sotiris Prokopiou

$$\frac{dV}{dt} = \lambda V\left(1 - \frac{V}{K}\right)$$

$$\textbf{PSI} = \frac{V_0}{K}$$

$$V^{post} = V - a\,V\left(1 - \frac{V}{K}\right)$$



Prokopiou et al., *Radiat. Oncol.*, 2015

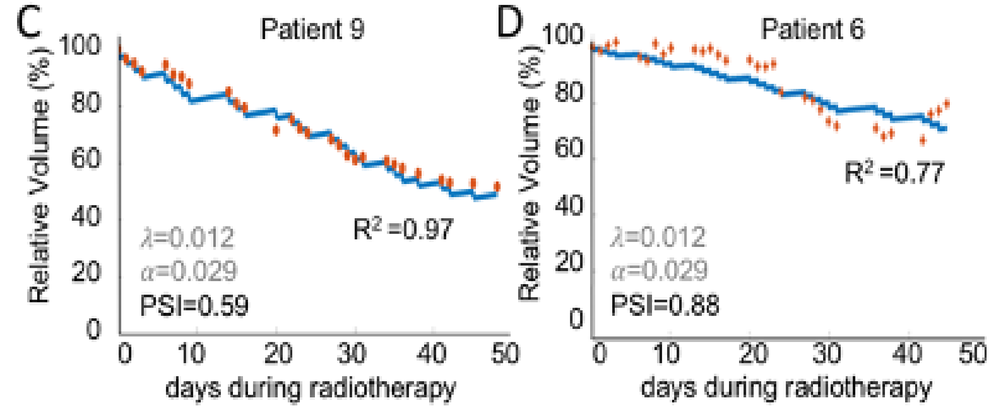
Research at MD Anderson

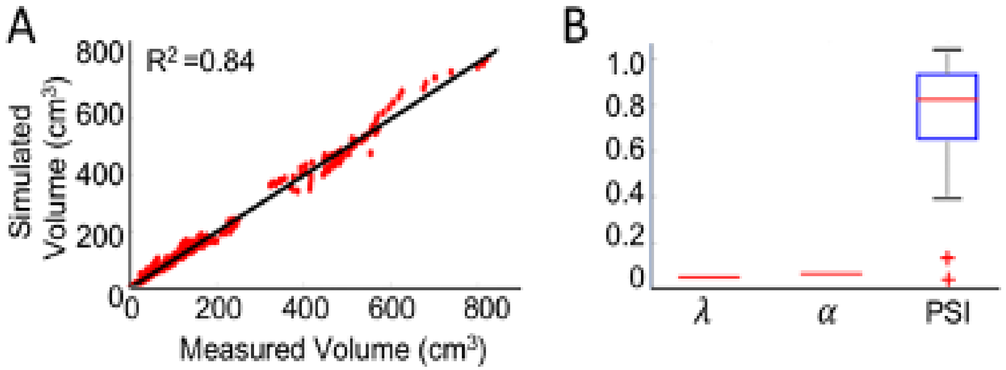
Proliferation Saturation Index, PSI

Dr. Enakshi Sunassee

Dr. Thomas Lewin

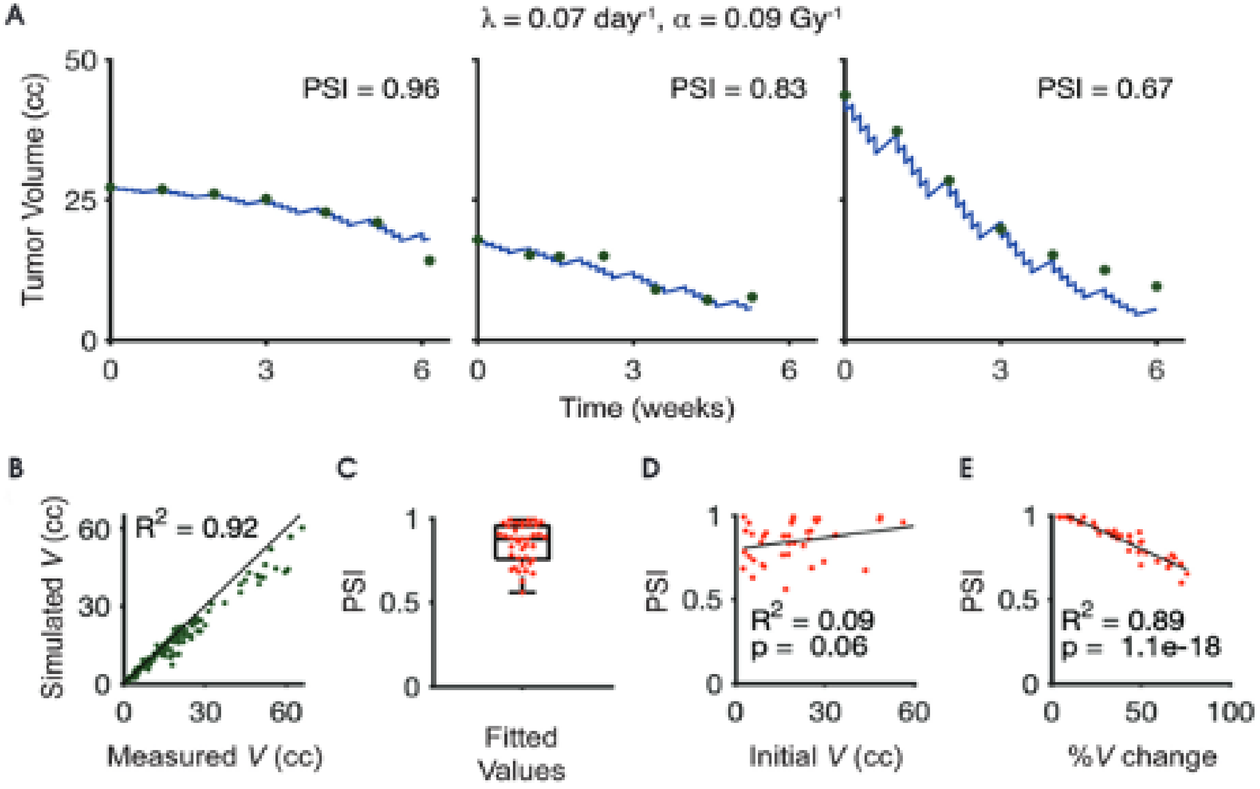
Non-small cell lung cancer





Prokopiou et al., *Radiat. Oncol.*, 2015
Sunassee et al, *Int. J. Radiat. Biol.*, 2019

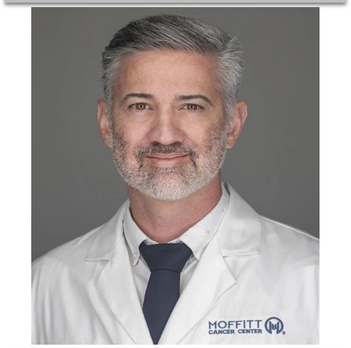
Head and neck cancer



Poleszczuk et al., *Bull. Math. Biol.*, 2018
Zahid et al., *Appl. Rad. Oncol.*, 2021
Kutuva et al., *Front. Oncol.*, 2023
Mohsin et al., *J. Theor. Biol.*, 2024

PSI correlates with volumetric response

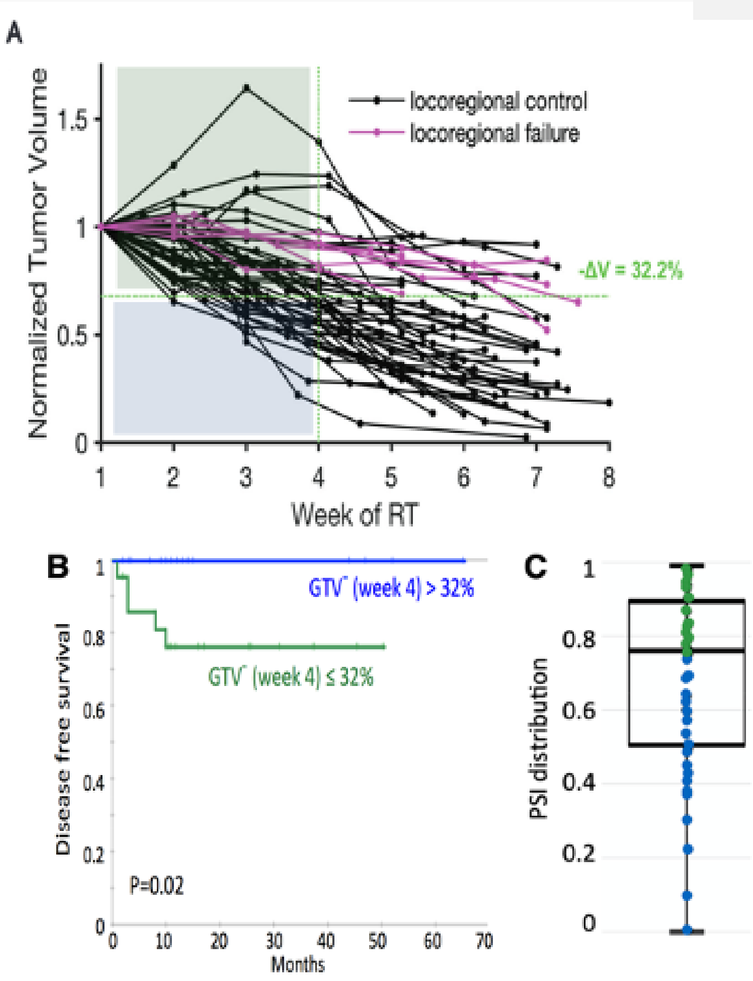
Dr. Mohammad Zahid



Dr. Jimmy Caudell
Moffitt Cancer Center

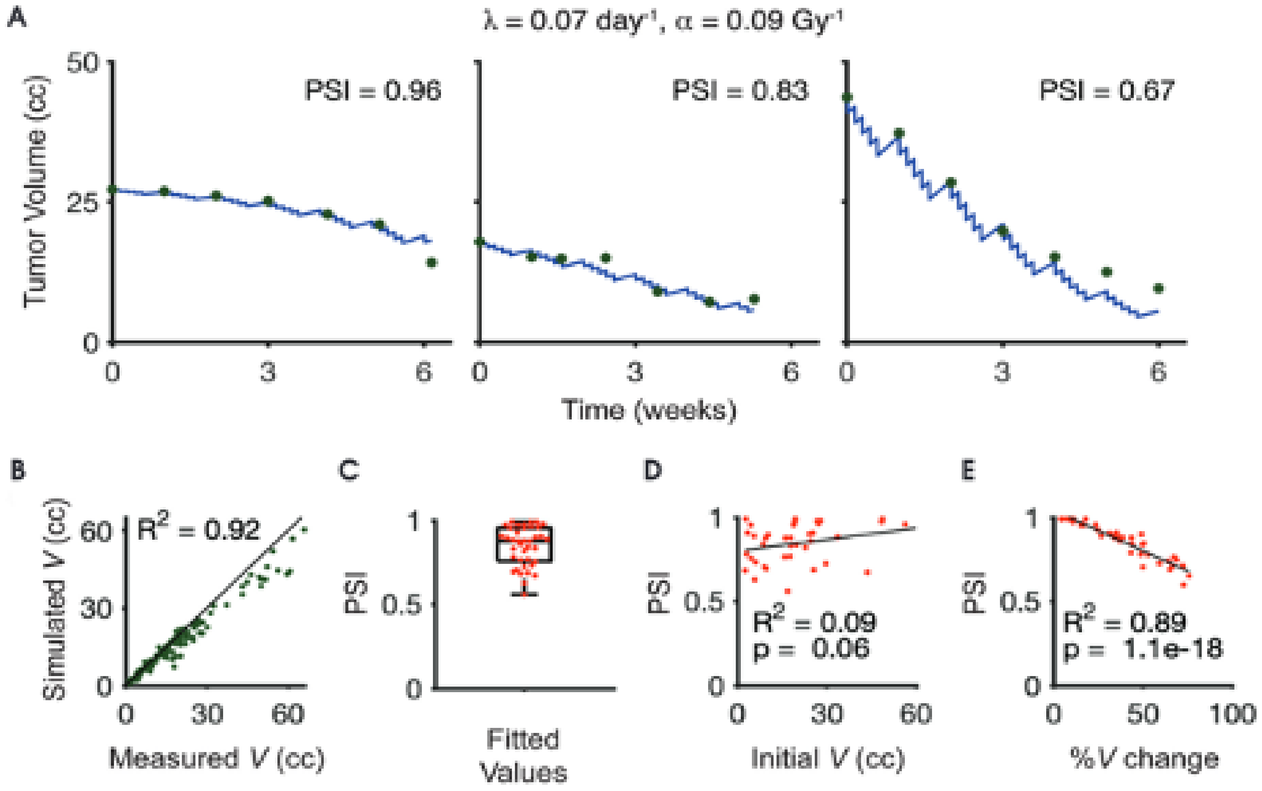
Dr. C. Dave Fuller

Dr. Thomas Lewin



Zahid et al., *Red Journal*, 2021
Zahid et al., *Appl. Rad. Oncol.*, 2021
Zahid et al., *J. Pers. Med.*, 2021

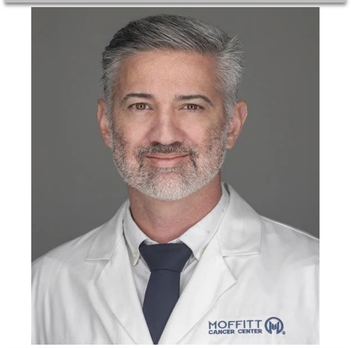
Head and neck cancer



Poleszczuk et al., *Bull. Math. Biol.*, 2018
Zahid et al., *Appl. Rad. Oncol.*, 2021
Kutuva et al., *Front. Oncol.*, 2023
Mohsin et al., *J. Theor. Biol.*, 2024

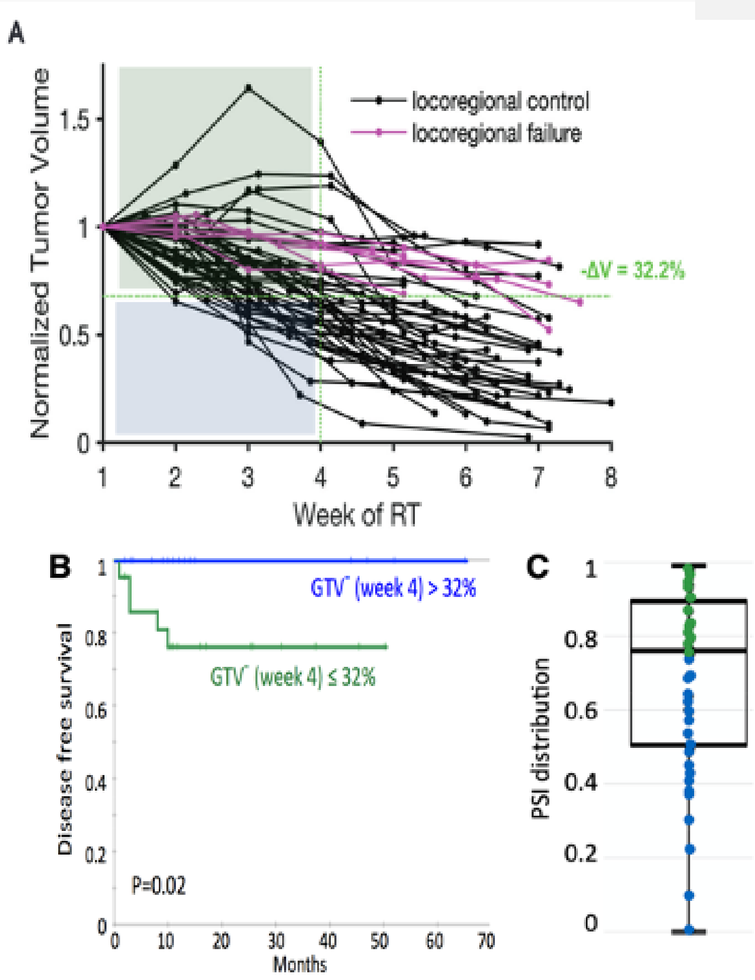
PSI determines response to radiation fractionation

Dr. Mohammad Zahid



Dr. Jimmy Caudell
Moffitt Cancer Center

Dr. C. Dave Fuller

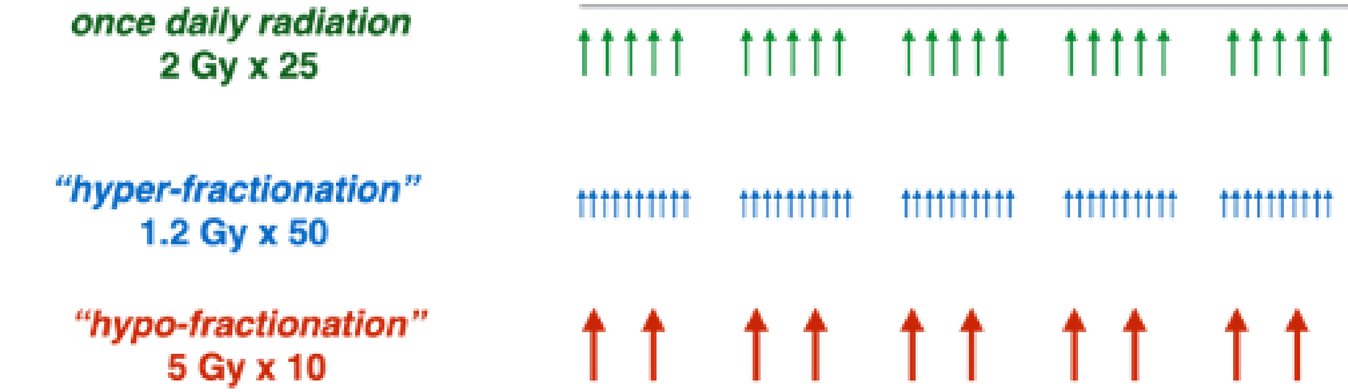


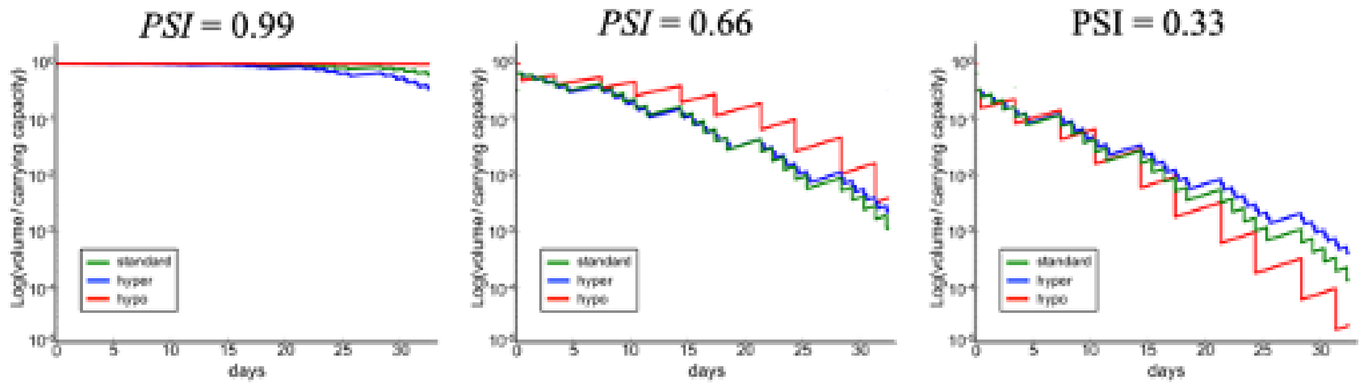
Zahid et al., *Red Journal*, 2021
Zahid et al., *Appl. Rad. Oncol.*, 2021
Zahid et al., *J. Pers. Med.*, 2021

once daily radiation
2 Gy x 25

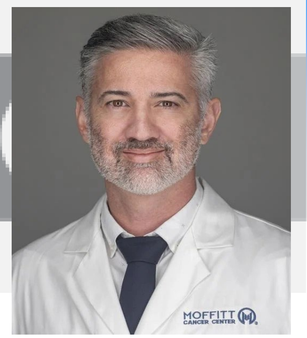
"hyper-fractionation"
1.2 Gy x 50

"hypo-fractionation"
5 Gy x 10





Worldwide first mathematics-guided prospective radiation fractionation clinical trial



Dr. Jimmy Caudell
Moffitt Cancer Center

Patient population

HPV+ OPC
T1-2, N0, M1

Math-model guided stratification

PSI < 0.75: 2 Gy q.d.

total dose: 66 Gy

PSI ≥ 0.75: 1.2 Gy b.i.d.
(> 6 hours apart)

total dose: 60 Gy

Primary Endpoint

Tumor volume reduction at week 4
by cone beam CT or MRI

ESTRO 2023 | 12-16 May 2023 Vienna, Austria

Prospective Trial of Personalized Fractionation in Low-risk HPV Positive Oropharyngeal Cancerroph

Jimmy Caudell, *USA*

Presentation Number: OC-0106

Abstract

Abstract Title: Prospective Trial of Personalized Fractionation in Low-risk HPV Positive Oropharyngeal Cancerroph

Authors: Jimmy Caudell[1], Michelle Echevarria[1], George Yang[1], Youngchul Kim[2], Kedar Kirtane[3], Julie Kish[4], Jameel Muzaffar[3], Christine Chung[3], Heiko Enderling[5]

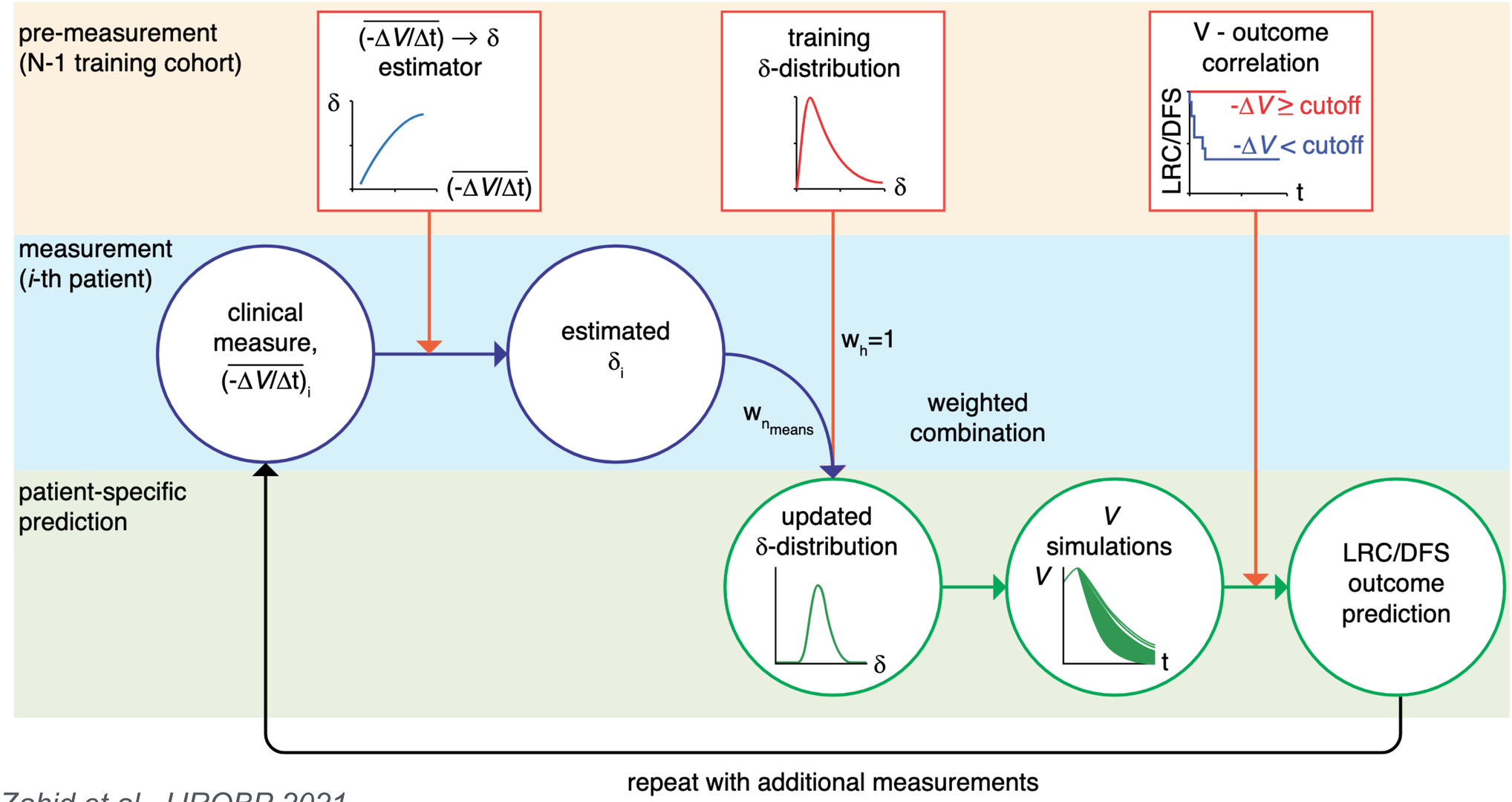
Conclusion

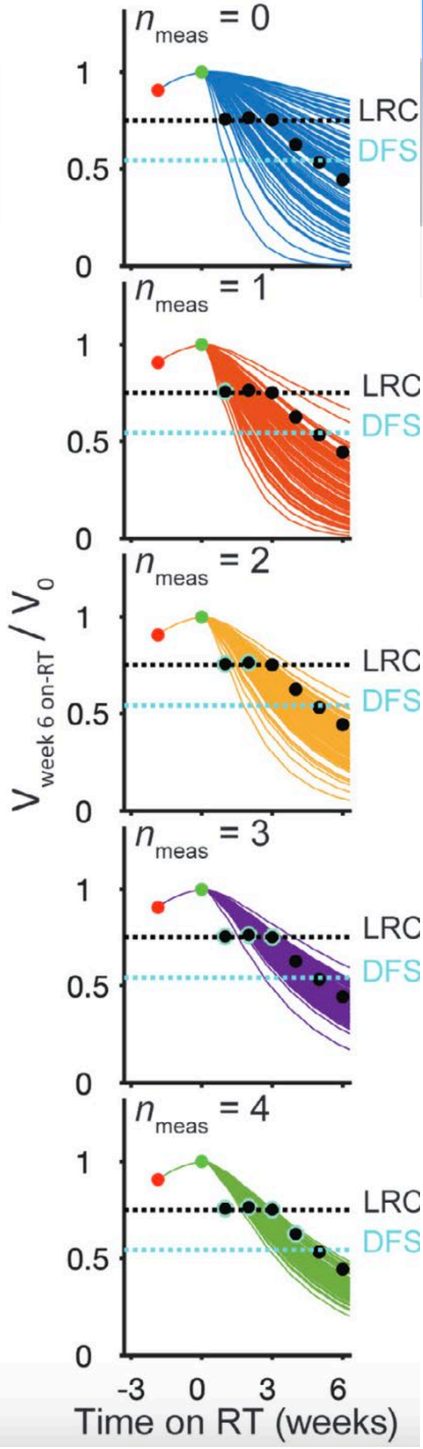
Selection of personalized radiotherapy fractionation using the PSI model appears to be a promising approach, with a 12% improvement in the percentage of patients achieving a mid-treatment imaging response.

NIH U.S. National Library of Medicine
ClinicalTrials.gov

NCT03656133. Use of a Proliferation Saturation Index to Determine Personalized Radiotherapy for HPV+ Oropharyngeal Cancers (OPC).

Dynamic prediction of patient-specific radiation response / outcome

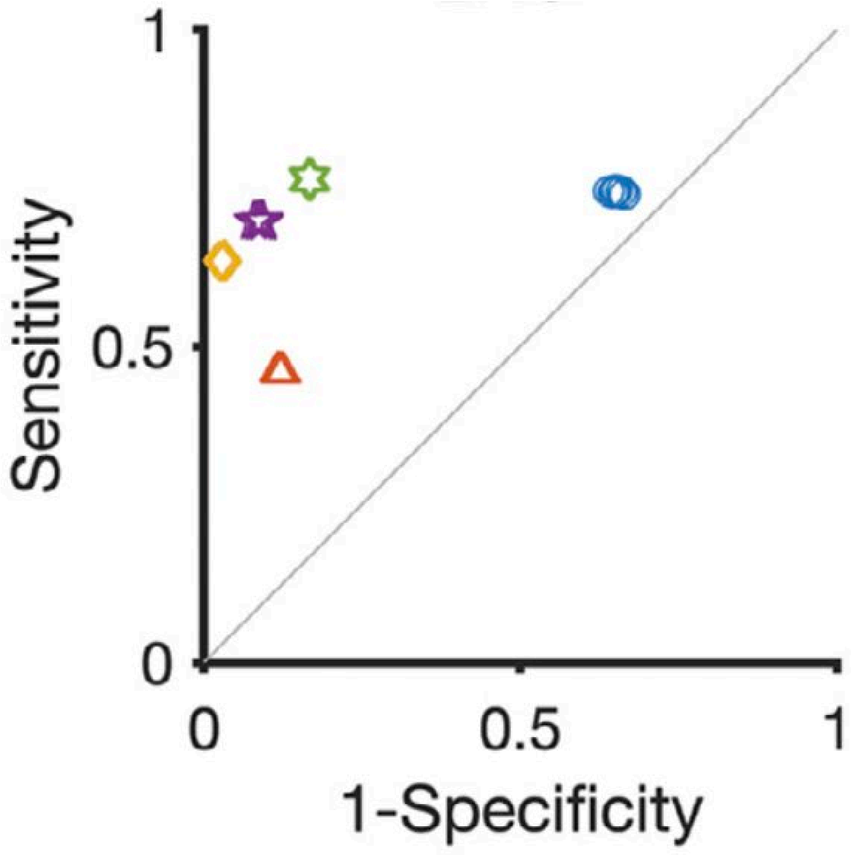




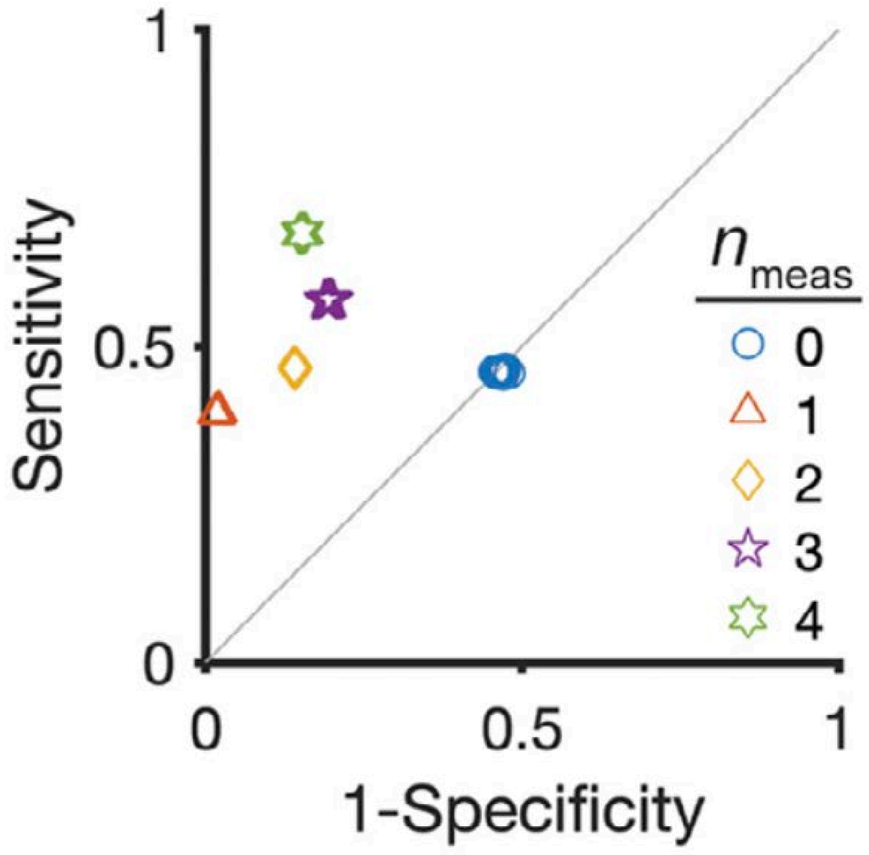
Zahid et al., IJROBP 2021

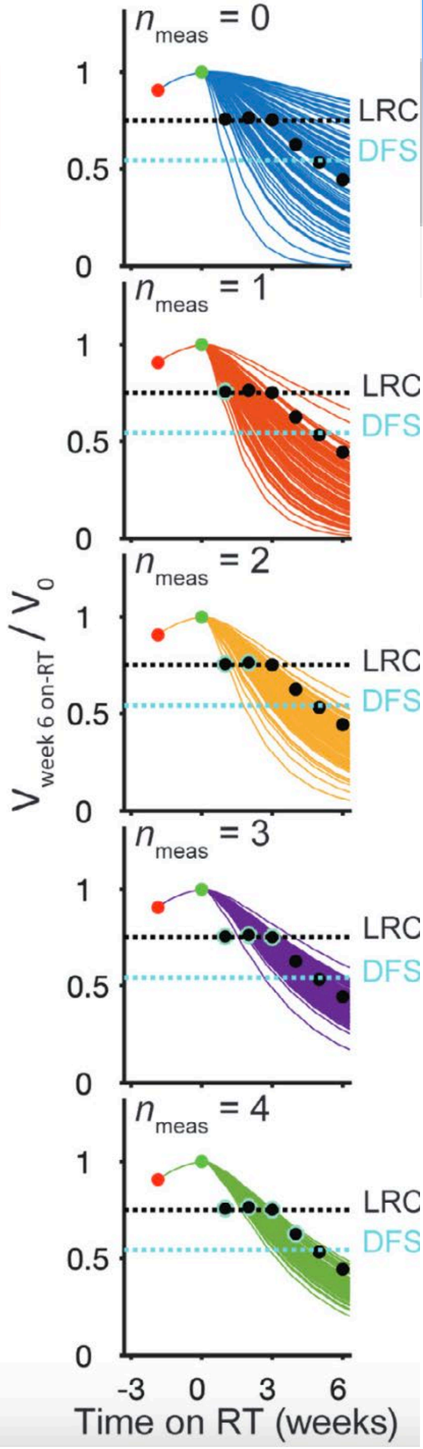
Dynamic prediction of patient-specific radiation response / outcome

Locoregional control



Disease-free survival





Zahid et al., IJROBP 2021

Dynamics adapted radiation dose (DARD)

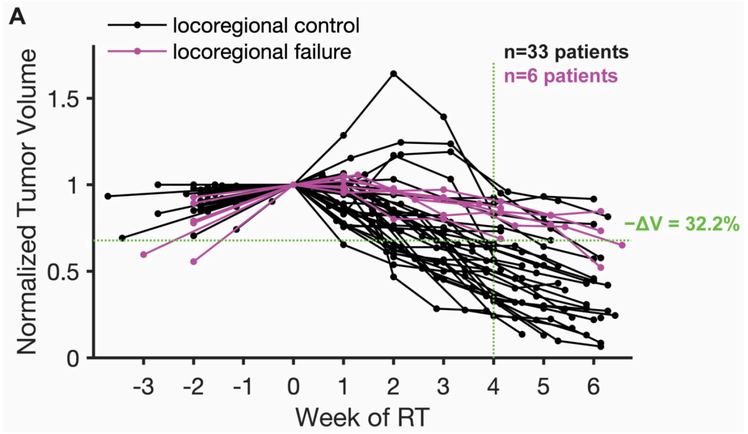
Journal of *Personalized Medicine*

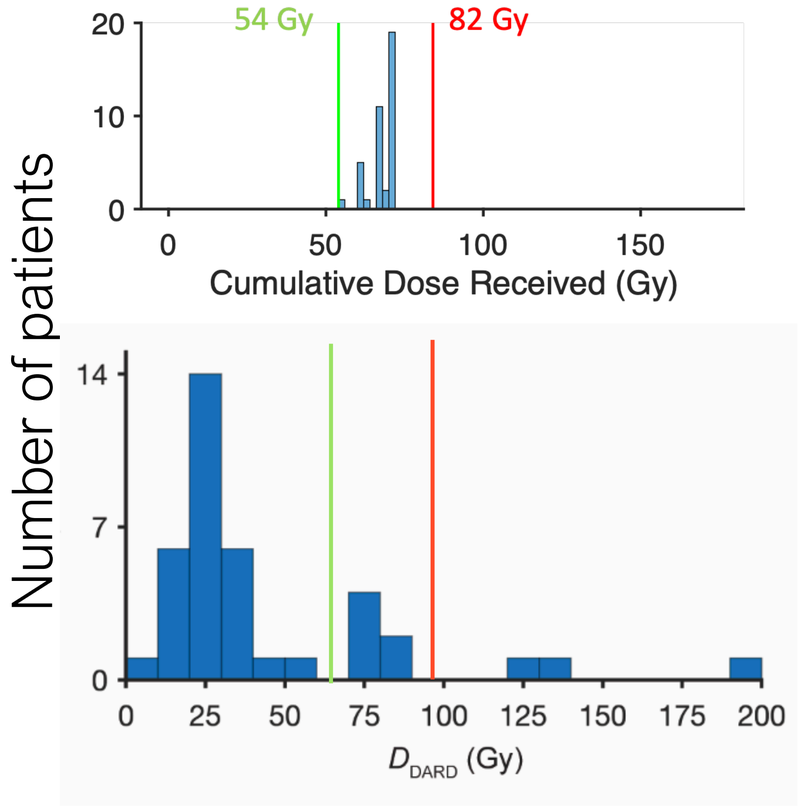
MDPI

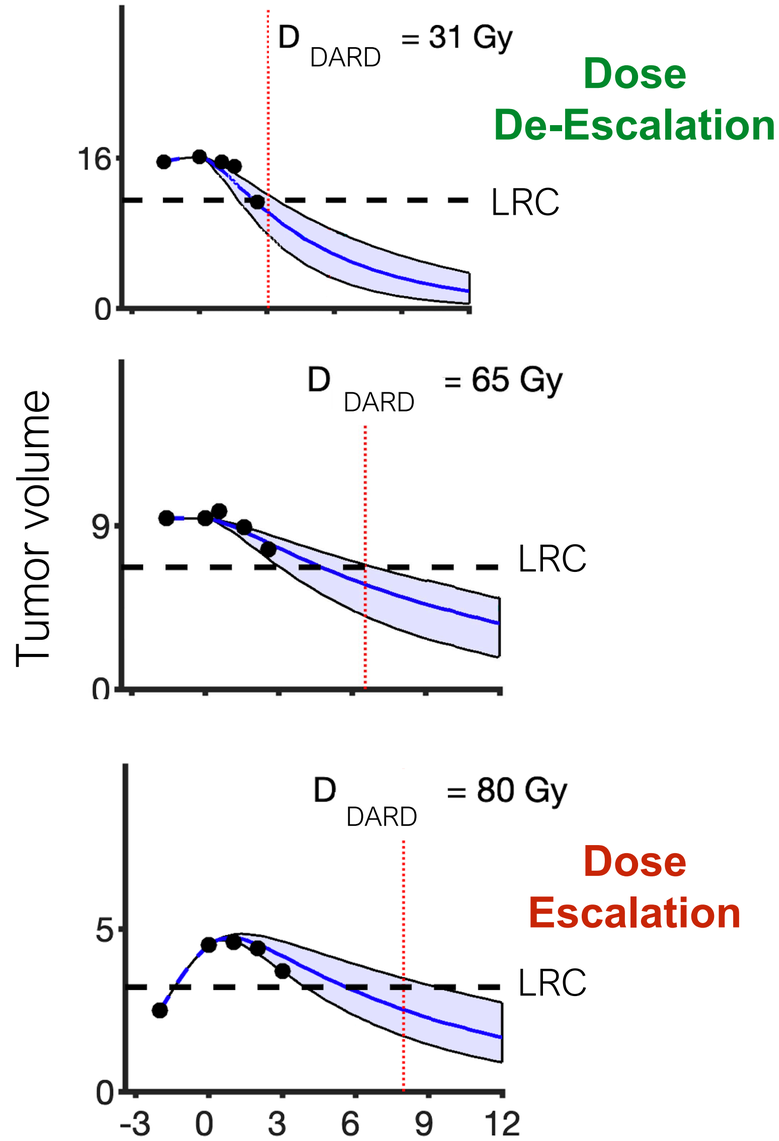
Article

Dynamics-Adapted Radiotherapy Dose (DARD) for Head and Neck Cancer Radiotherapy Dose Personalization

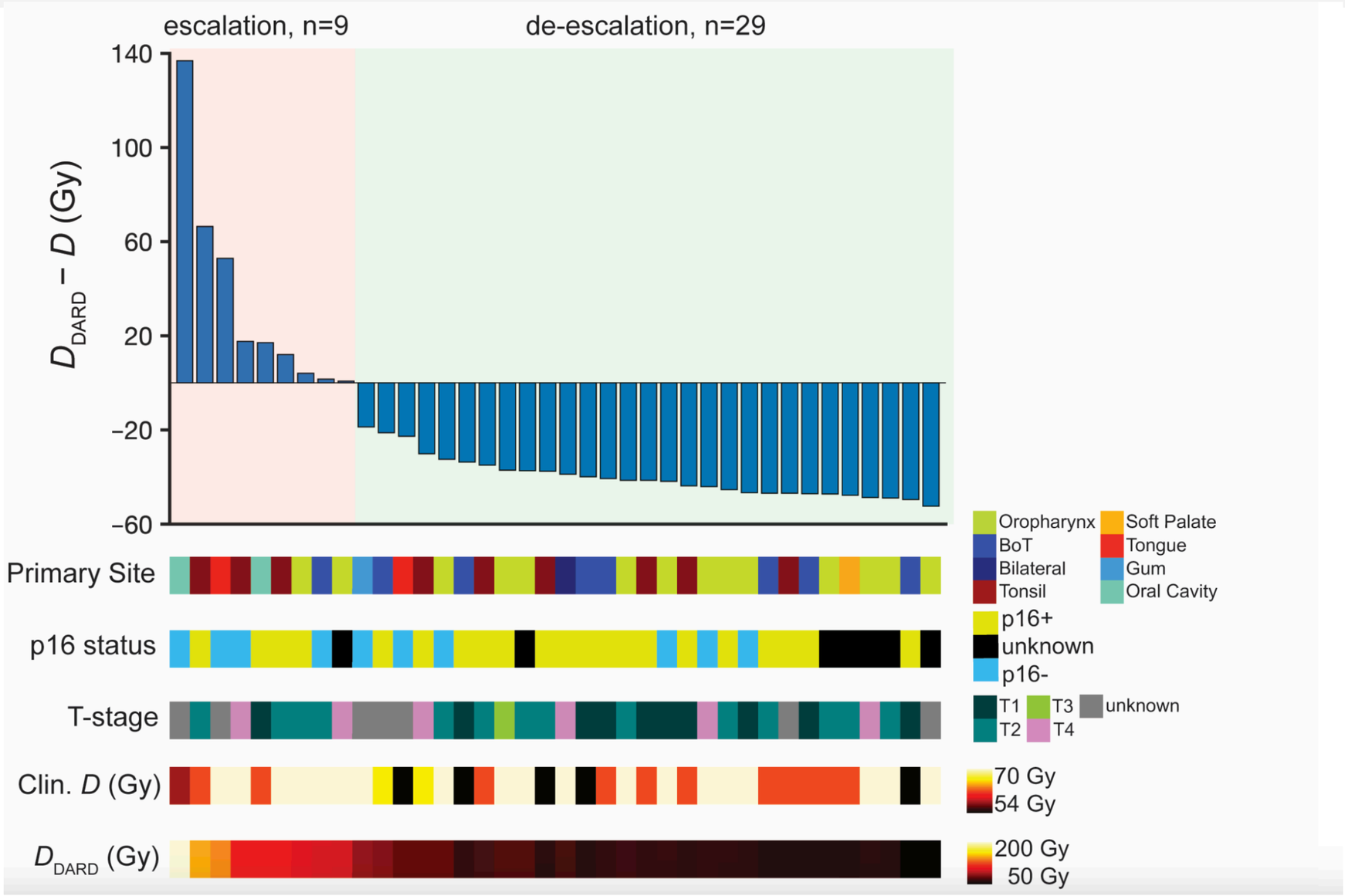
Mohammad U. Zahid [1], Abdallah S. R. Mohamed [2], Jimmy J. Caudell [3], Louis B. Harrison [3], Clifton D. Fuller [2], Eduardo G. Moros [3] and Heiko Enderling [1,3,*]

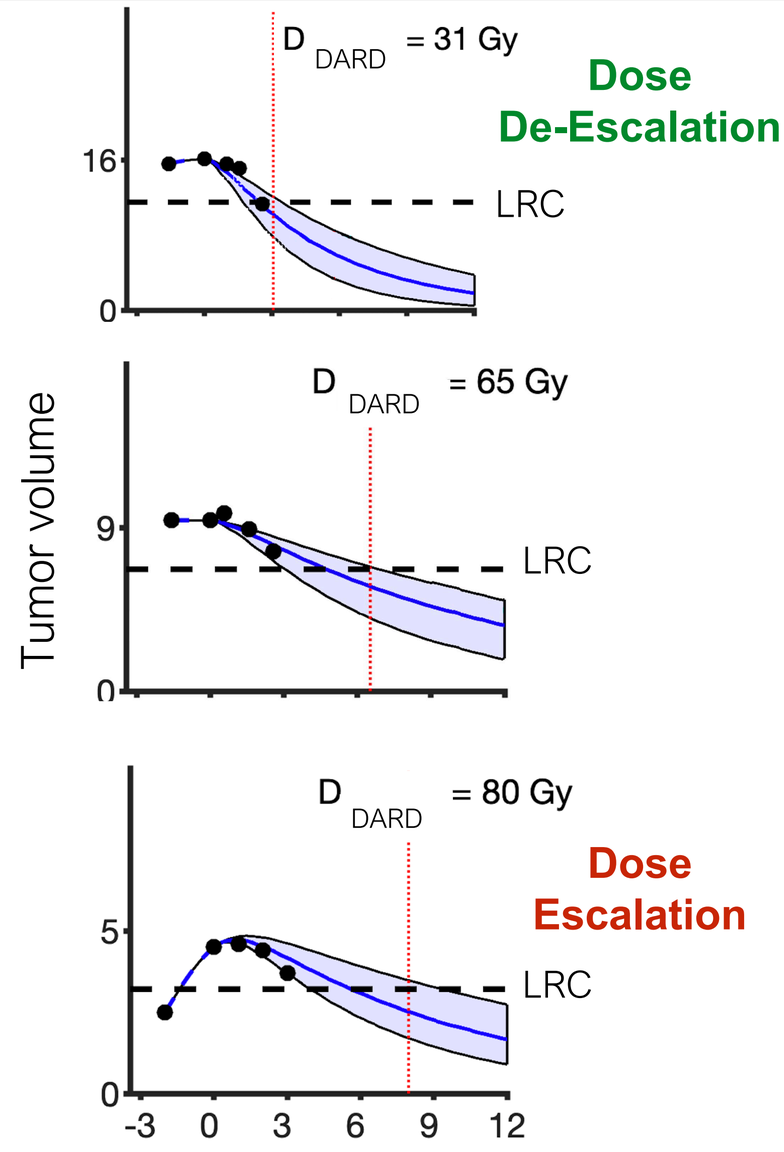






Dynamics adapted radiation dose (DARD)

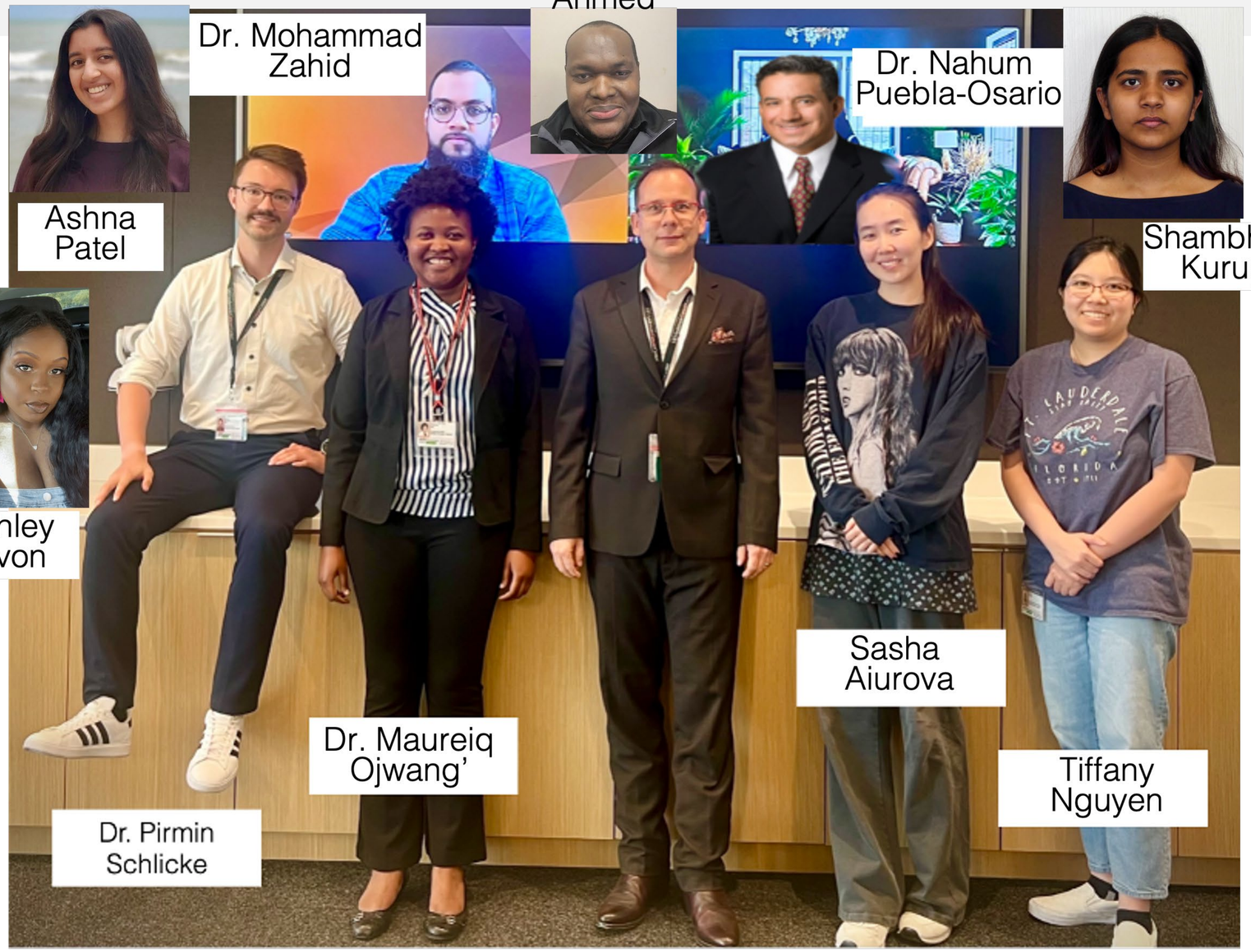




Summary

- Predictive mathematical and computational models are being translated into clinical decision making
- Engines of ***Digital Twins*** to personalize oncology
- Prospective clinical trials about to open at MDACC

Acknowledgements



PRiSM

PERSONALIZED RADIOTHERAPY WITH INTEGRATED SCIENTIFIC MODELING

NIH NATIONAL CANCER INSTITUTE

U01 CA244100
U01 CA280849

JAYNE KOSKINAS TED GIOVANIS Foundation for Health and Policy