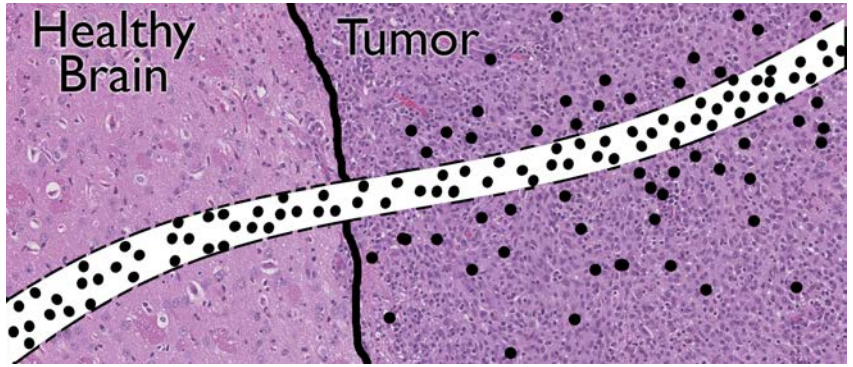
Quantitative imaging for personalized mathematical models in oncology

David A. Hormuth II, Angela M. Jarrett, Chengyue Wu, Thomas E. Yankeelov

Our central hypothesis

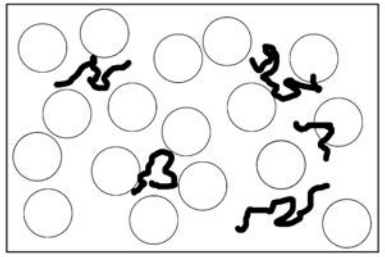
Readily-available imaging techniques can provide the data to initialize/constrain predictive models of tumor growth and treatment response for clinical application.

Dynamic Contrast Enhanced MRI

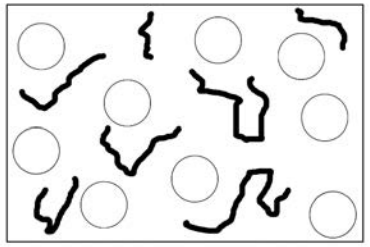


Plasma volume fraction, perfusion, extracellular extravascular volume fraction

Diffusion weighted MRI



Low cell density, Restricted water diffusion



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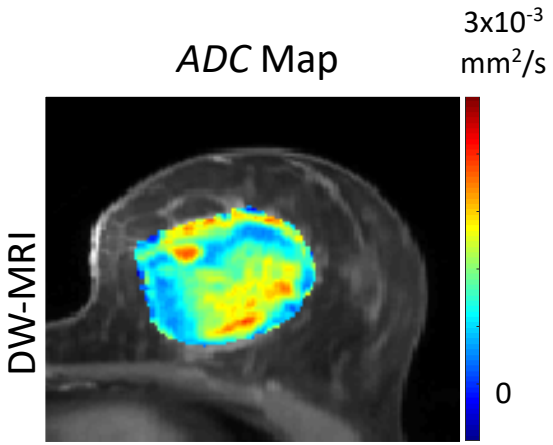
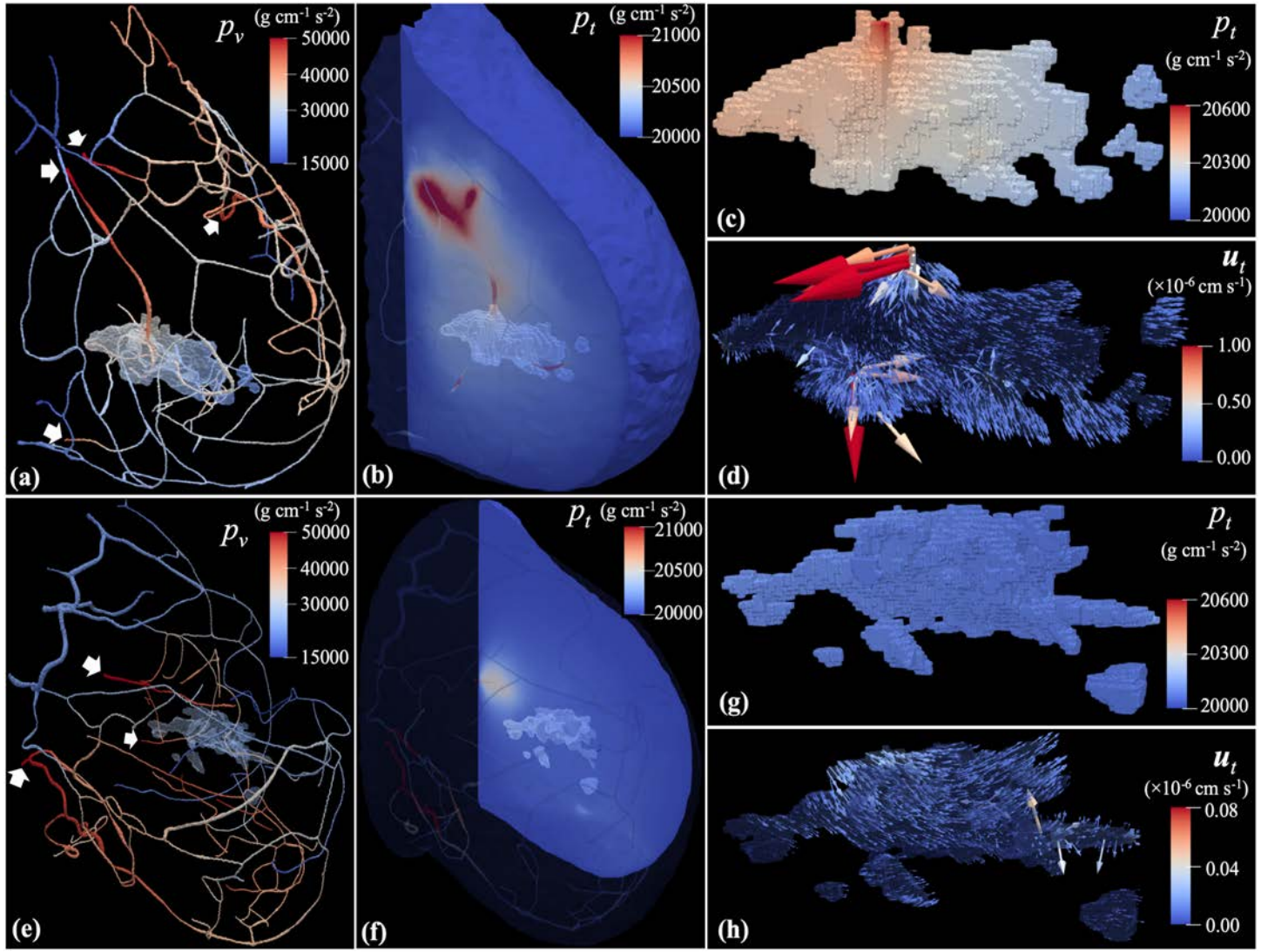


Patient-Specific Model of Breast Cancer Hemodynamics

Chengyue Wu, David A. Hormuth II, Federico Pineda, Gregory S. Karczmar, Robert D. Moser, Thomas E. Yankeelov

- Dynamic contrast-enhanced (DCE-) MRI and Diffusion-weighted (DW-) MRI are collected for breast cancer diagnosis.
- DCE-MRI provides the geometries and pharmacokinetic properties of vasculature, while DW-MRI provides estimates of tissue hydraulic conductivity
- A 1D-3D coupled computational fluid dynamic model is established and personalized using patients' imaging data to simulated tumor-associated blood supply and interstitial transport. The computation quantifies hemodynamic characteristics, including blood pressure (p_v), vascular extraction rate (q_e), interstitial pressure (p_t) and interstitial flow velocity (u_t) .
- Our results in a 16-case clinical cohort indicate that malignant lesions tend to have larger magnitude of interstitial flow velocity, and greater heterogeneity in blood pressure and vascular extraction rate. These preliminary analyses suggest a fundamentally new way to employ contrast agent pharmacokinetics for the evaluation of breast cancer.



Predicting response to fractionated radiation therapy

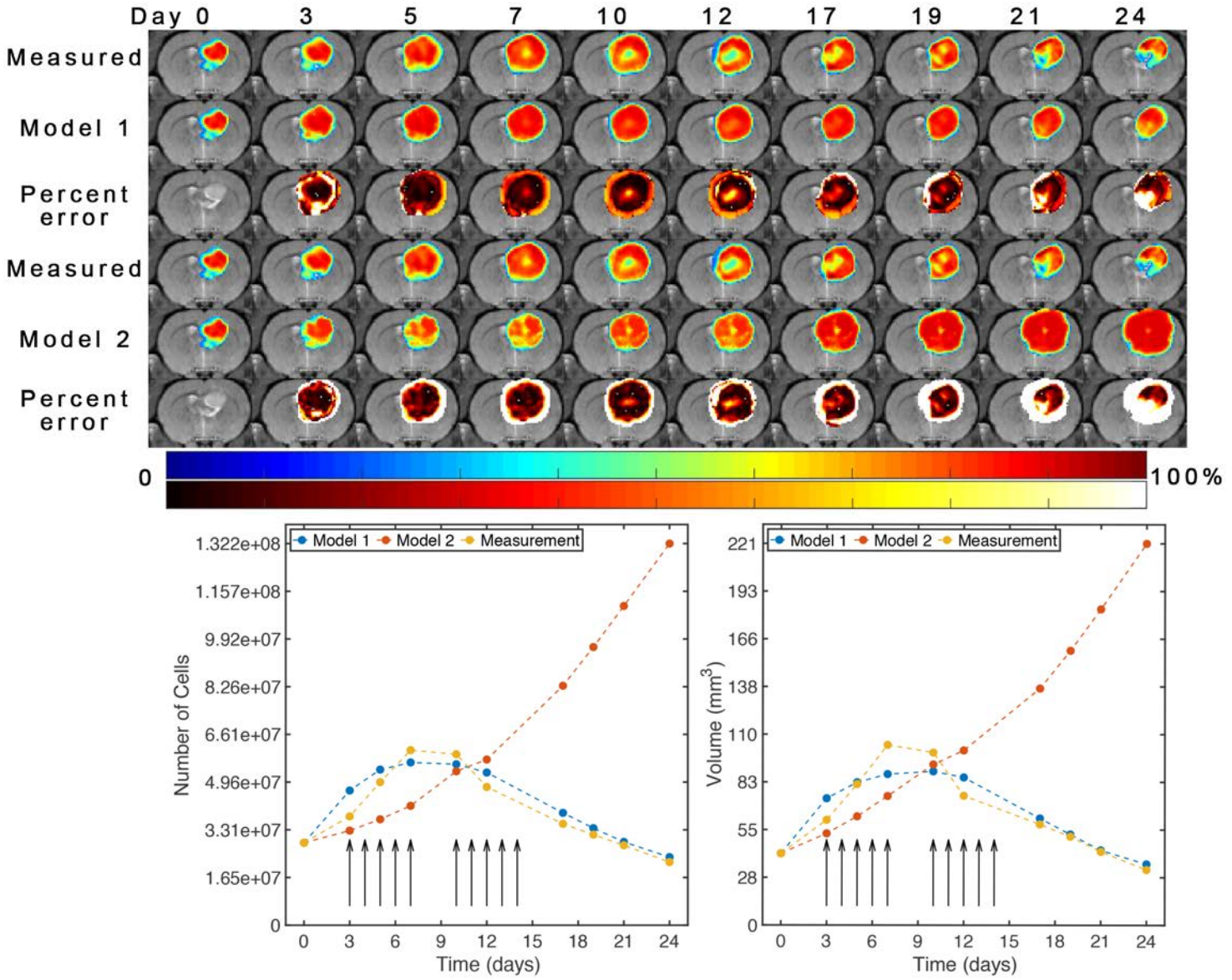
David Hormuth, Angela Jarrett, Thomas Yankeelov

Diffusion-weighted MRI and Dynamic contrast-enhanced MRI are collected at 10 points before, during, and after radiation therapy

DW-MRI provides estimates of cellularity, while DCE-MRI provides estimates of blood volume fraction

A coupled, 3D model of tumor growth and angiogenesis is initialized and calibrated from the DW- and DCE-MRI measurements for each animal. The calibrated parameters are then used to predict future tumor growth

Our model (model 1) out performs the standard linear quadratic model (model 2) in describing and predicting future response



Predicting response to chemotherapy

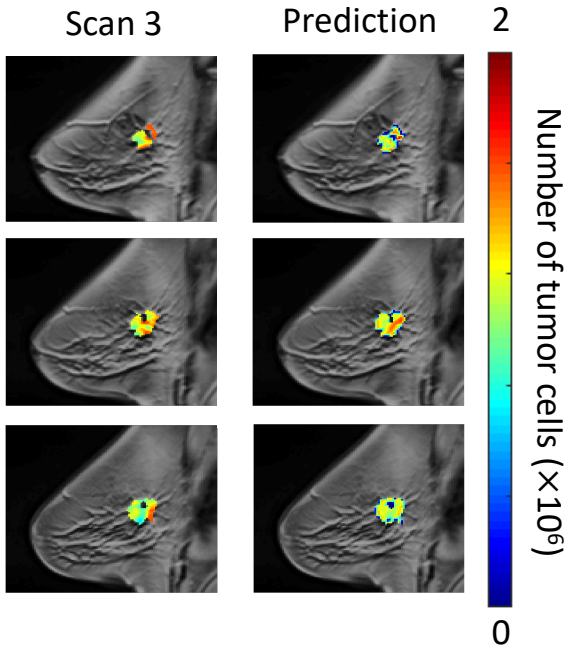
Angela M. Jarrett, David. A. Hormuth, II, Chengyue Wu, Jack Virostko, Anna G. Sorace, Julie C. DiCarlo, Debra Patt, Boone Goodgame, Sarah Avery, Thomas E. Yankeelov

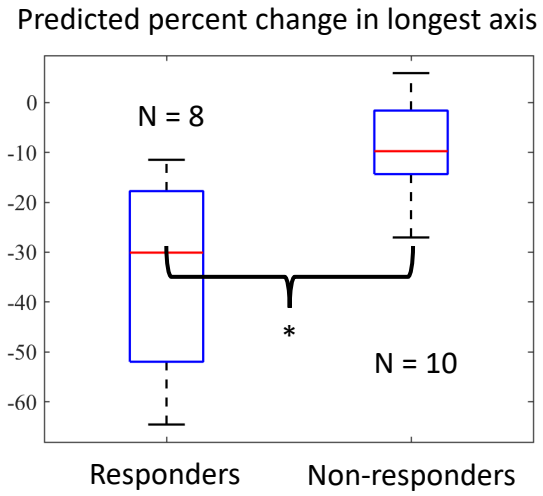
DW-MRI and DCE-MRI are collected during neoadjuvant (NAT) chemotherapy for breast cancer patients.

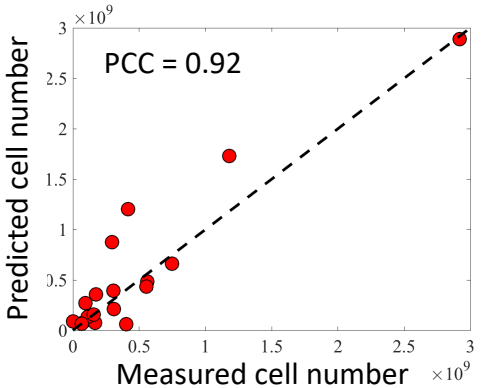
DW-MRI provides estimates of cellularity, while DCE-MRI provides a means to approximate drug distribution in the tumor tissue.

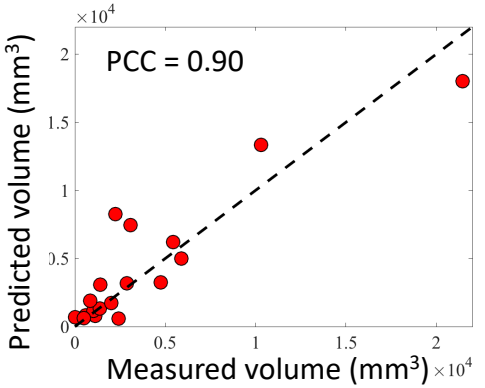
A 3D model of tumor growth is calibrated with the DW- and DCE-MRI measurements from early in the course of each patient's NAT regimen, and the calibrated parameters are used in the model to predict tumor growth at the completion of therapy for each individual patient.

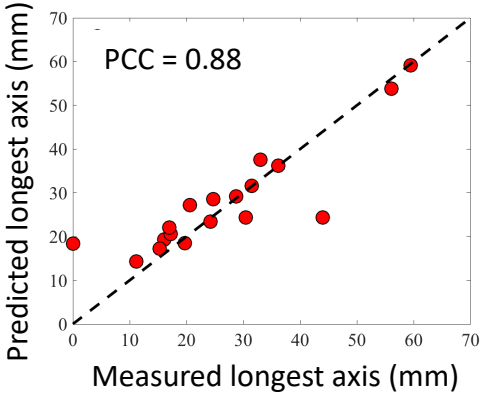
The model's predictions are found to be strongly correlated with actual tumor response (PCC ≥0.88, N = 18, $p<0.01$) and able to distinguish between responding and non-responding patients as defined by the response evaluation criteria for solid tumors (RECIST) for percent change in longest axis from diagnosis to therapy completion (*$p < 0.001$).











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These three different modeling applications demonstrate the versatility of quantitative imaging measurements in the field of mathematical oncology.

Importantly, by using clinically relevant imaging data, these approaches could be extended to improve treatment planning or design optimal therapy regimens based on an individual's own data.

To learn more about these projects please check out these recent publications by Chengyue, David, and Angela *et al.*

[1] Wu C, et al. 2020; IEEE Trans Med Imaging. 1 (In press).
[2] Hormuth DA,et al. 2020; Radiat Oncol. 15; 1.
[3] Jarrett A, et al. 2018; Phys Med Biol. 63; 10 .

Acknowledgements: NCI-U24CA226110, NCI-R01CA186193, NCI-U01CA174706, CPRIT RR160005, AAPM Research Seed Grant. TEY is a CPRIT Scholar.