



# Establishing the link between prostate cancer microstructure and MRI

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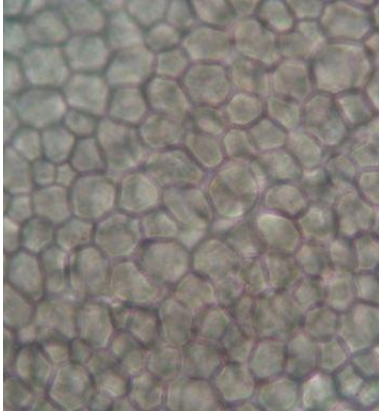


# Magnetic resonance imaging

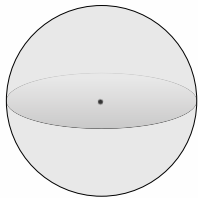
- Signal form hydrogen
  - Mainly from water
- Depicts morphology and function
- Non-invasive and safe
- Advanced methods promise a 'virtual in vivo biopsy'



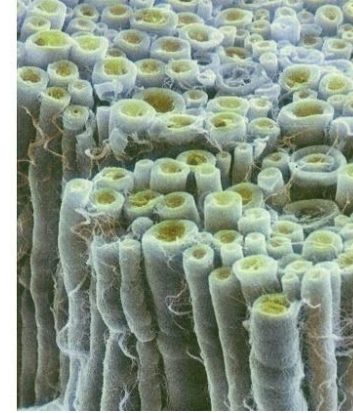
# Microstructure from diffusion MRI



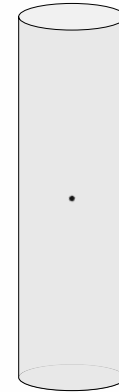
Spherical cells



Free Diffusion



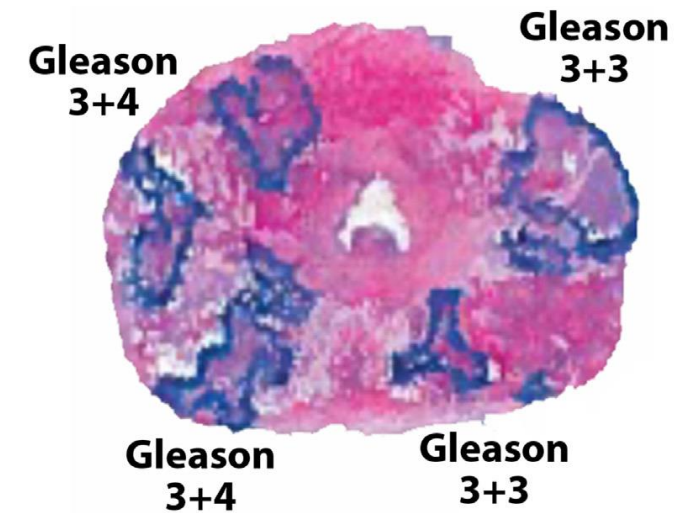
Elongated axons



During 100 ms, water molecules move approximately 20  $\mu\text{m}$  (same scale as cells is coincidental)

# Why prostate cancer?

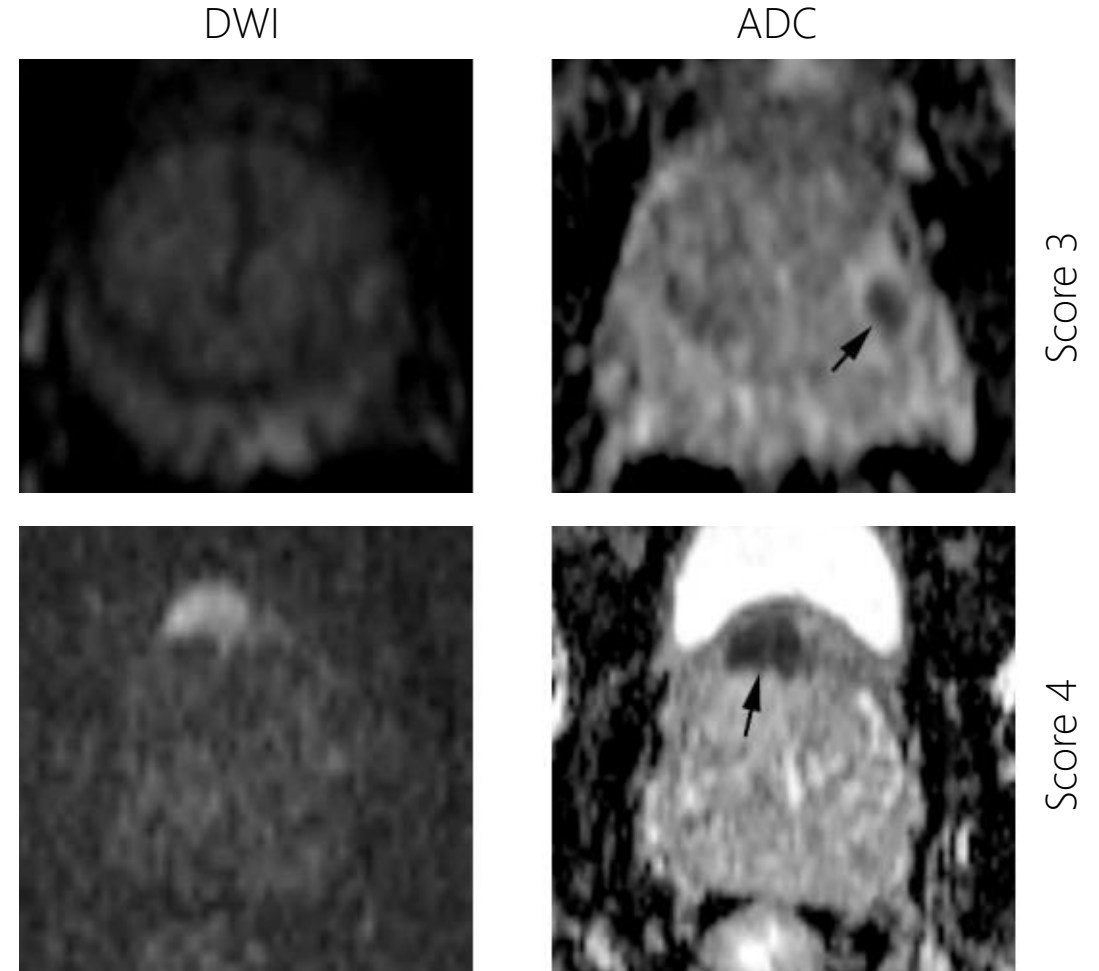
- Prostate cancer is common and deadly
- Current challenges
  - Early detection and prognosis (wait or act?)
  - Heterogeneity between and within patients
  - Biopsy and radiotherapy guidance
  - Treatment monitoring
- Diagnostics by routine MRI are lacking
  - Old method and theory
  - Moderate detection rate
  - Poor specificity



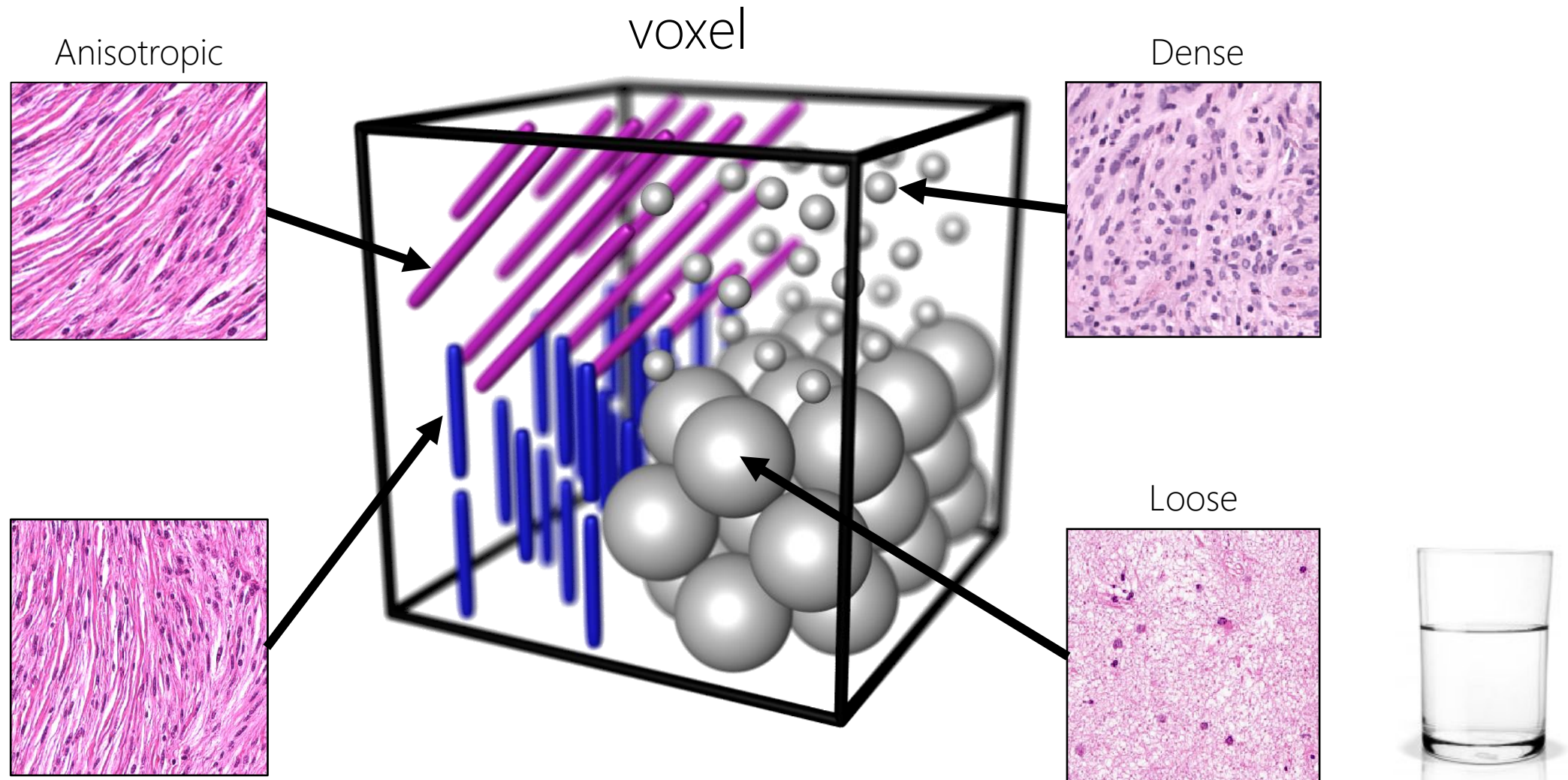
Chatterjee et al. 2020 Acad Radiol 2020:1–9

# Current clinical MRI routine for diagnosis

- Clinical evaluation employs "multiparameteric" MRI
  - Morphology
  - Perfusion by "dynamic contrast enhancement"
  - Tissue density by "diffusion-weighted imaging"
- Clinical significance determined by qualitative evaluation
  - With some dubious criteria
- Ignores tissue heterogeneity!

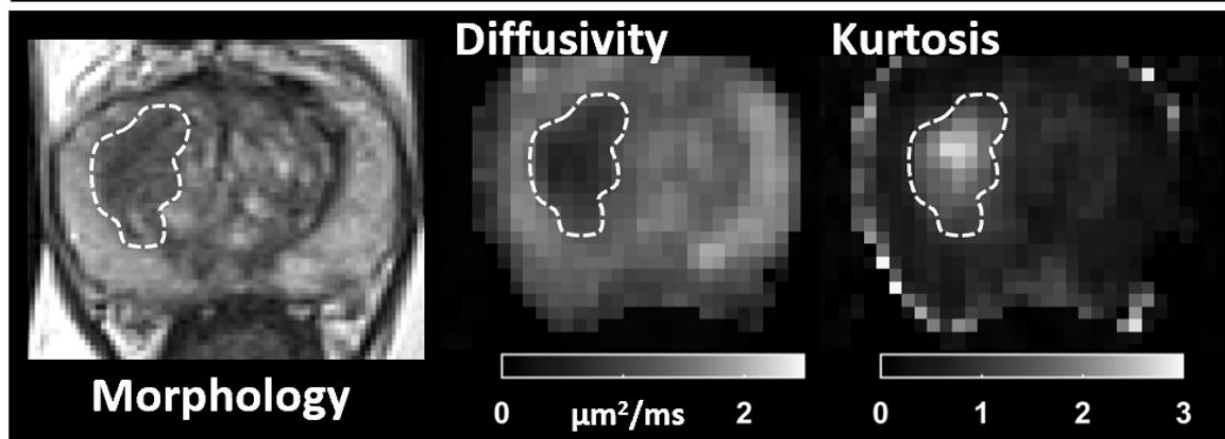


# Heterogeneity requires multidimensional MRI

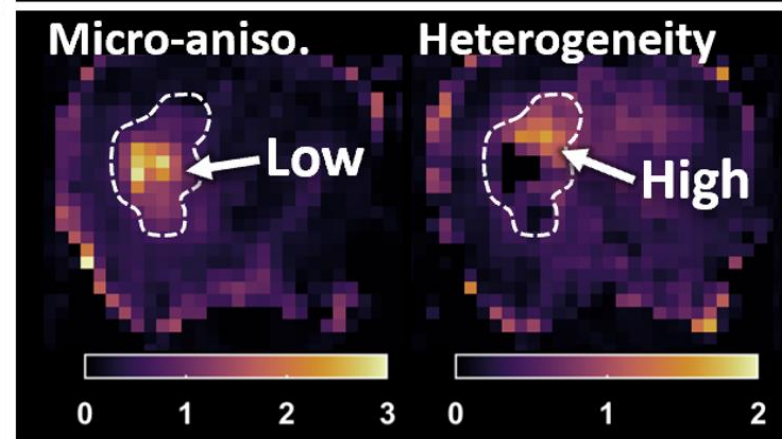


Preliminary data in patient shows that heterogeneity matters!

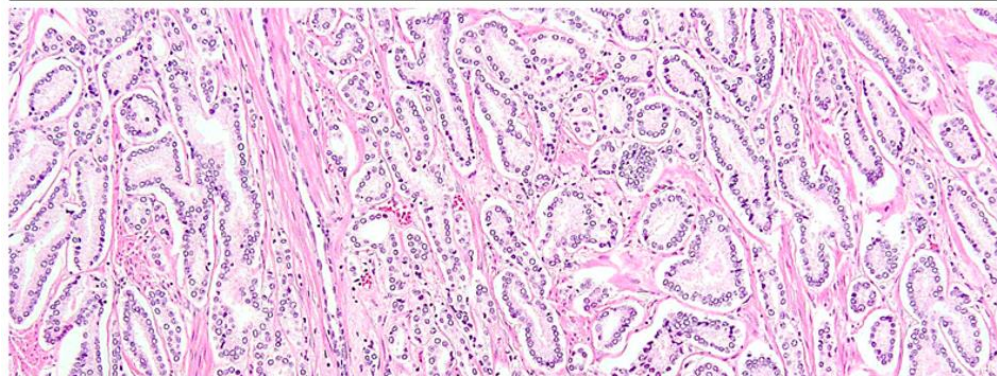
**Conventional MRI**



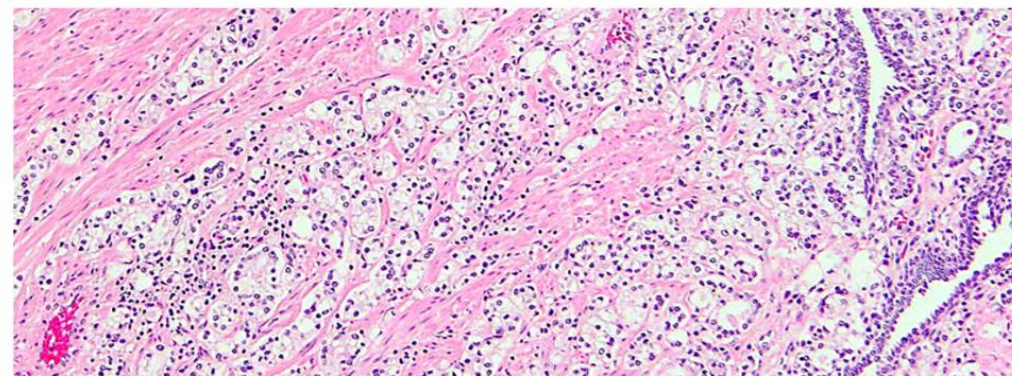
**Multidimensional MRI**



**Low-grade (Gleason 3) with well-formed glands**



**High-grade (Gleason 4) with poorly formed glands**



# Project outline

CORE team  
Filip + Malwina + Fardin + PostDoc

2022

2023

2024

2025

2026

2027



Aim I

Microstructure parameters from multidimensional MRI  
CORE team



Clinical diagnostic performance in patients  
CORE + Johan Bengtsson

*Diagnostic  
Radiology*



Dose painting in clinical external radiotherapy  
CORE + Lars E Olsson, PostDoc, PhD cand

*Radiation  
Oncology*



Aim II

Longitudinal MRI study of radiotherapy in mice  
CORE + Joanna Strand, Crister Ceberg, PhD cand

*Systematic  
Radiotherapy*



Aim III

Whole tumor microstructure by  $\mu$ CT and link to MRI  
CORE + Martin Bech and Jens Sjölund

*X-Ray Phase  
Contrast*





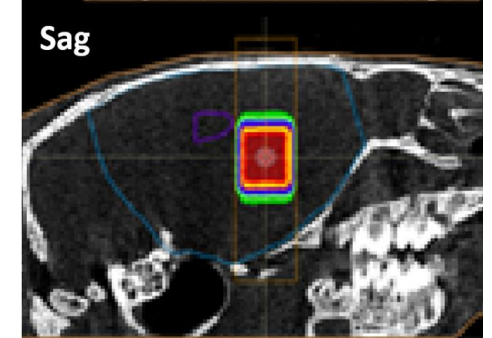
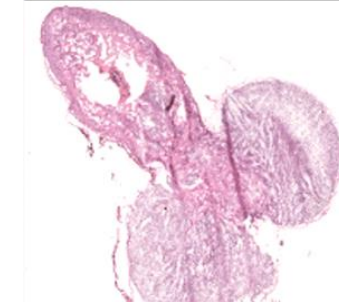
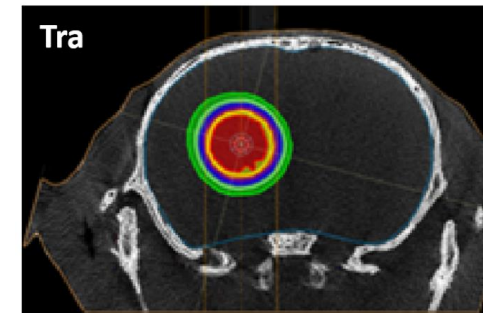
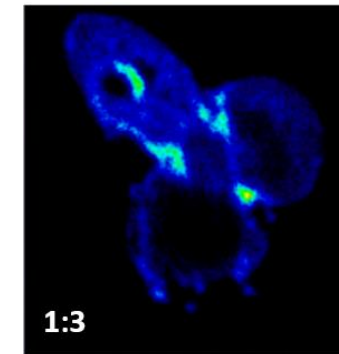
## Aim V

Monitoring radionuclide and external radiotherapy in mice  
CORE + Joanna Strand and Crister Ceberg



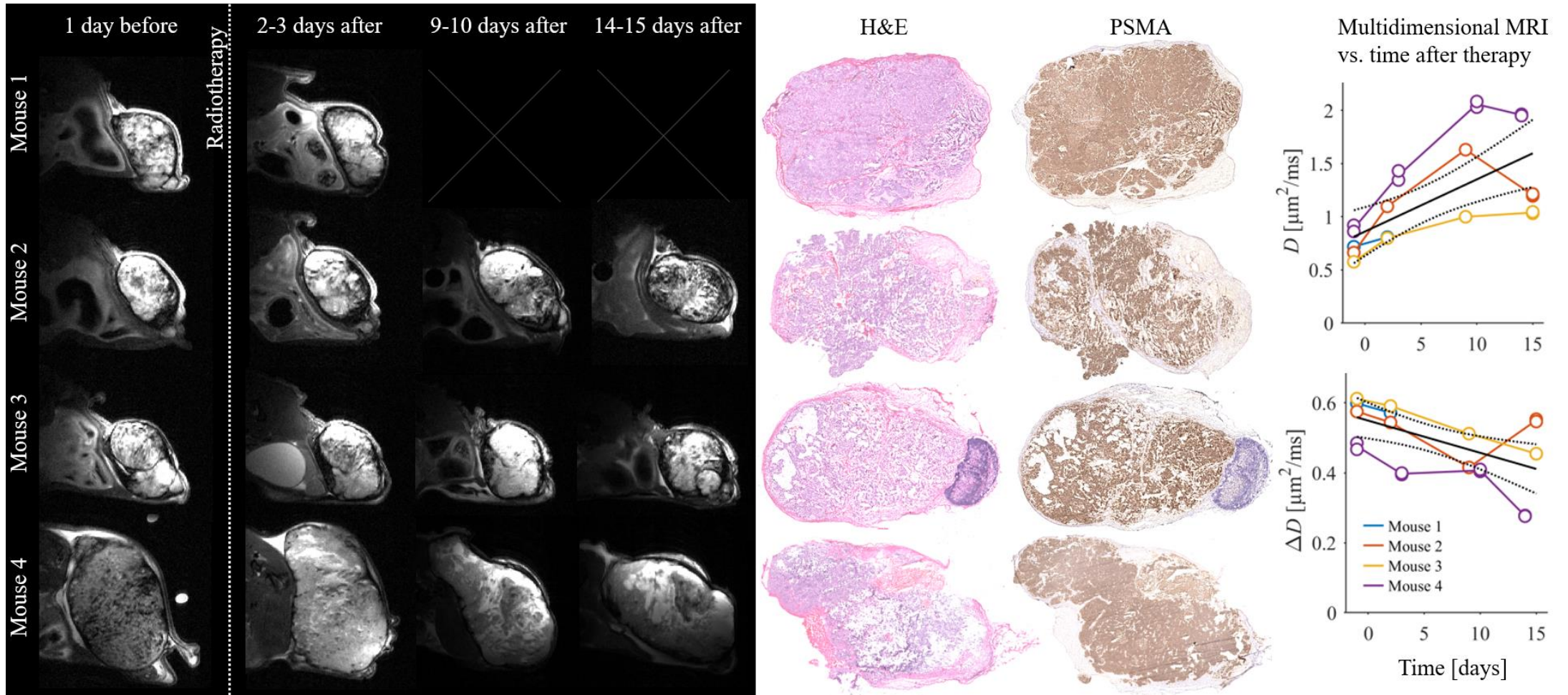
- Study in collaboration with Systematic Radiotherapy
  - Sven-Erik Strand and Joanna Strand et al.
  - Support from Michael Gottschalk and Matthew Budde
- Study of mice ( $n \approx 40$ ) with human prostate cancer
  - Multiple radionuclide treatments
  - External radiotherapy at XenX unit
  - Longitudinal multidimensional MRI
  - Histopathology, autoradiography and outcome
- Goals
  - Predict therapeutic effect and link MRI to absorbed dose and histopathology
- Future additions
  - Perfusion, metabolism, oxygenation and more

Internal and external radiotherapy



Images courtesy Joanna Strand and Crister Ceberg

# Pilot study of human prostate cancer in mice

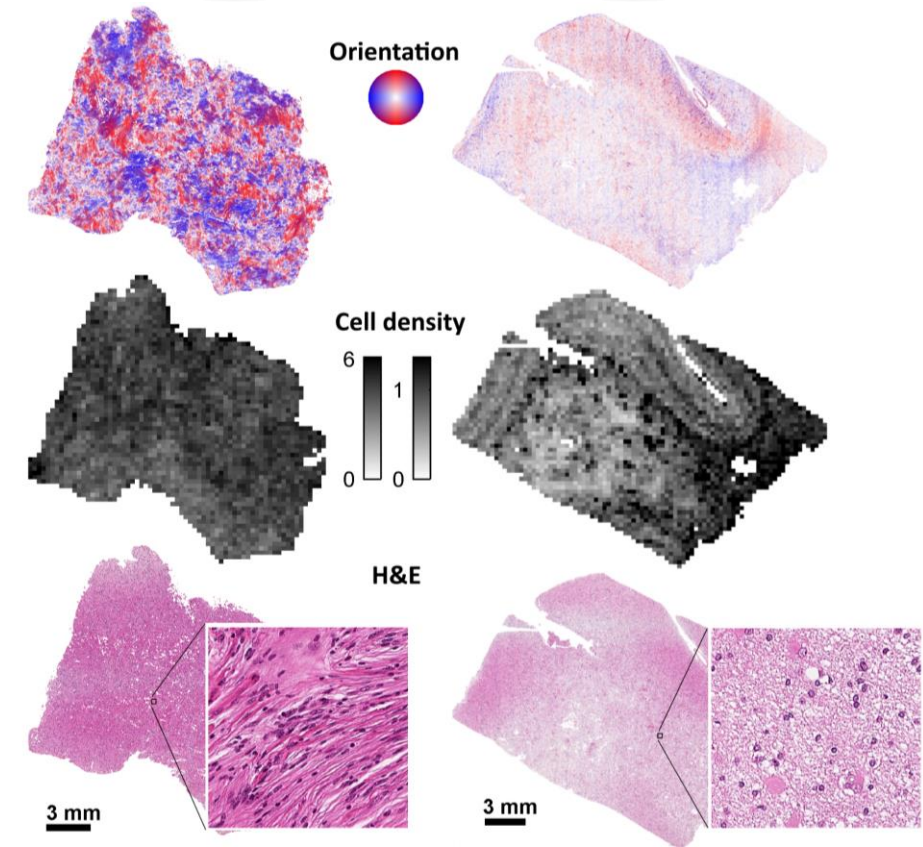




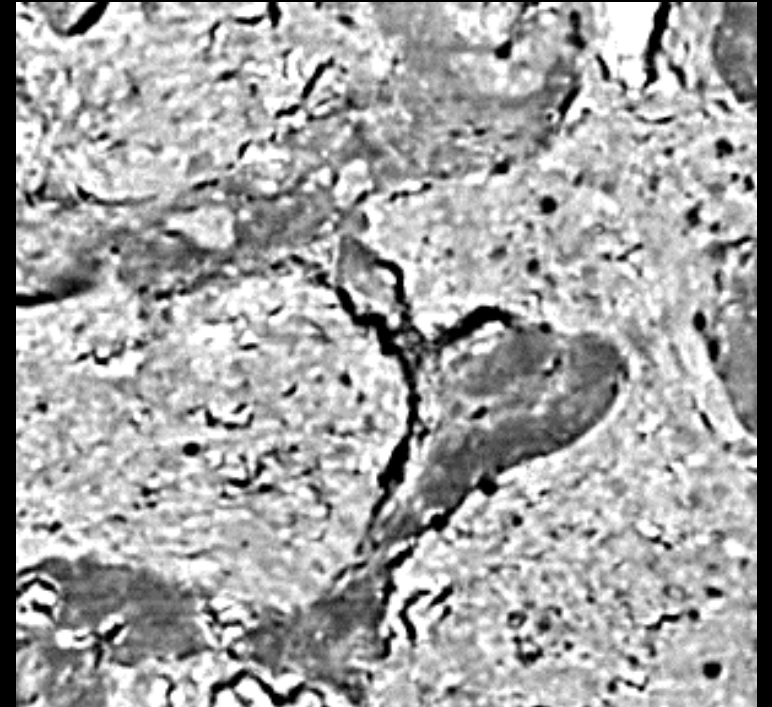
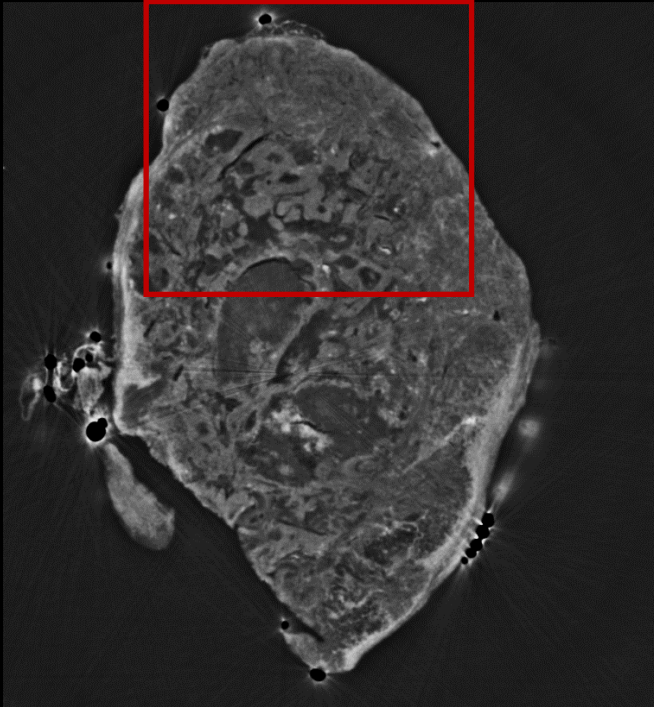
### Aim III

Whole tumor microstructure by  $\mu$ CT and link to MRI  
CORE + Martin Bech and Jens Sjölund (Uppsala)

- Explain the origin of MRI contrast
  - "Classical" quantitative histology vs MRI
  - Effect of internal and external radiotherapy
  - Investigate predictors for treatment efficacy
- Whole sample computed tomography (micro-CT)
  - Collaboration with Martin Bech (LU)
  - Synchrotron x-ray phase contrast depicts **3D microstructure at micron resolution**
  - Pilot data from TOMCAT, Switzerland
- Machine learning to create "forward model"
  - Collaboration with Jens Sjölund (UU)
  - Machine learning to capture essential features
  - Big data infrastructure
  - **Guide design of optimally sensitive/specific MRI biomarkers**



# 3D micro-CT phase-contrast in prostate cancer after radiotherapy



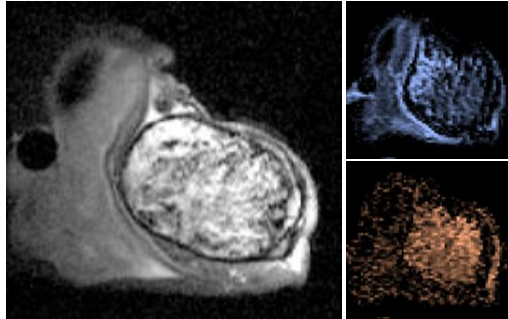
X-ray Phase Contrast Imaging–Computed Tomography at TOMCAT (Swiss Light Source)  
1.6  $\mu\text{m}$  isotropic resolution

Tissue is heterogeneous on all length scales  
50 to 150 Gb of data per sample

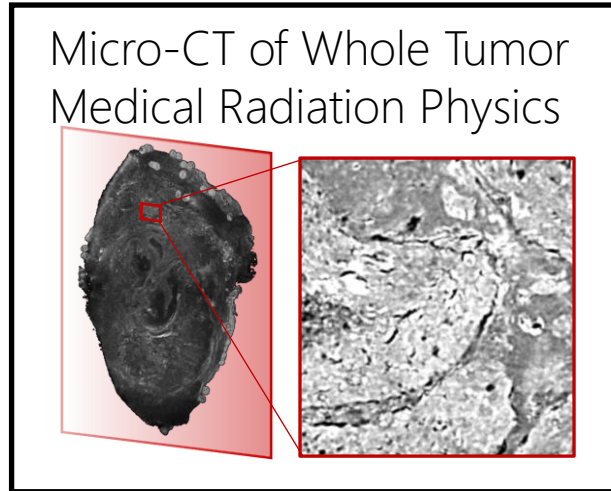
# Prostate Cancer Imaging Group

Medical Radiation Physics, IKVL, Lund University

Microstructure MRI at  
Lund Biomed Imaging Center

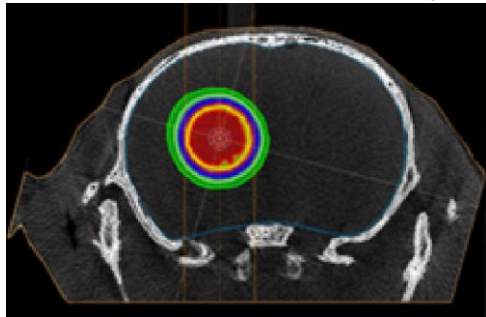


Micro-CT of Whole Tumor  
Medical Radiation Physics

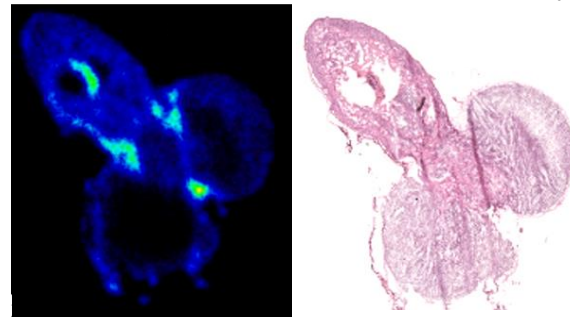


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Medical Radiation Physics



Radionuclide Therapy at  
Systematic Radiation Therapy



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