Quantitative Imaging for Treatment Response Assessment

Amita Dave, Neelam Tyagi, Sang Ho Lee, Miria Crispin-Ortuzar, Jeho Jeong, John Humm, Milan Grkovski, Joe Deasy et al.

Thanks to

• Harini Veeraraghavan, PhD
• Jung Hun Oh, PhD
• Aditya Apte, PhD
• Maria Thor, PhD
• Mireia Crispin-Ortuzar, PhD
• Andreas Rimner, MD
• Matthew Hellman, MD
• Charles Rudin, MD

• John Humm, PhD
• Margie Hunt, MS
• Amita Dave, PhD
• Neelam Tyagi, PhD
• Nancy Lee, MD
• Heiko Shoeder, MD
• Sang Ho Lee, PhD
• Milan Grkovski, PhD
• And many more...

(Funding from NIH, Varian, and Philips)

Predicting response to RT or chemo can be based on:

• Volumetrics
• Radiomics
• Imaging relevant to drug bioavailability
• Imaging relevant to tumor microenvironment (e.g., hypoxia)
• Models of TCP that include imaging variables
• ...using PET, MRI, CT.
To dose or not to dose...

If hypoxia is resolved on F-MISO scan in two weeks...de-escalate to 30 Gy!

Dose De-escalation in HPV+ Oropharyngeal Cancer (IV)

Significant Acute Toxicity Reduction

At 30Gy, no anticipation of late complications such as xerostomia, dysphagia, and osteoradionecrosis

Characterizing and monitoring response in head and neck cancers: IVIM-DW MRI (II)

(Slide courtesy of Amita Dave)
Combined PET and CT radiomics features predict maximum FMISO uptake in head and neck cancer (Crispin-Ortuzar et al.)

- FDG PET + contrast-enhanced CT to predict maximum FMISO TBR
- 79 training, 42 hold-out validation
- LASSO + 10x10-fold CV
- Selected predictors:
  - P90 FDG SUV
  - Long-run high grey level emphasis in raw-FDG subregion
- Validation AUC = 0.83

Cellular State Simulations to Predict Response to Radiation Therapy

Jeho Jeong, Mireia Crispin-Ortuzar, Andrew Fontanella, and Joe Deasy
Simulation model: the basics

- We introduce a 'constant-resource' tumor response model (Jeong et al. PMB (2013) 58:4897)

- Chemical supply is assumed constant over the course of RT

Assume re-compartmentalization: this leads to reoxygenation

- Assume oxygen and glucose can 'feed' a constant number of cells
- Then re-distribution constantly occurs that assumes P is the preferred state, then I, then H.
- This implies a 'reoxygenation' process

Lung tumor cohort dose-response

- Three additional cohorts (including WUSTL, NKI) (N=512)

(Jeong et al., Clinical Cancer Res, In press)
Use the model at 2 Gy/day as a reference

- 2 Gy/fx (5 fx/wk)
- 4.5 Gy/fx (3 fx/wk)

Treatment duration = 45.4 days
TD_{50} = 66.8 Gy (in EQD2)

Treatment duration = 23 days
TD_{50} = 62 Gy (in EQD2)

Images courtesy John Humm
Including heterogeneity & cell migration

The model can make predictions of H&N hypoxia histogram evolution during RT

Works well for about 60% of tumors studied thus far.

Lung cancer response: Apparent Diffusion Coefficient (ADC)

- Pre-treatment
- After first fraction (8 Gy)
- After last fraction (40 Gy)
- Four weeks post-treatment

Median (mm²/s *10⁻³): 1.5
- Pre-treatment
- After first fraction (8 Gy)
- After last fraction (40 Gy)
- Four weeks post-treatment

Rectal cancer Example 1 poor responder

- Pre-induction
- Pre RT
- Early RT
- Mid RT
- Post RT

Example 2: Good responder

- Pre-induction
- Pre RT
- Early RT
- Mid RT
- Post RT

Tyagi et al, works in progress
ADC as a marker of therapy response for rectal cancer

Semi-quantitative Parametric Analysis in DCE-MRI: Preliminary Application to Mesothelioma & Non-small Cell Lung Cancer

Neelam Tyagi, Sang Ho Lee, Andreas Rimner, et al.

Semi-quantitative Parameters

(Slide courtesy Neelam Tyagi and Sang Ho Lee)
Why semi-quantitative parameters?

- Because Gd flows and is not trapped in cells...
- ...therefore kinetic models that do not include intervoxel diffusion are unlikely to be realistic.
- Empirical parameters such as TTHP are likely to be robust with respect to imaging parameters
- ....and relevant to drug delivery as well as radiobiological microenvironmental conditions
- Hypothesis: histograms of TTHP might be predictive of drug or radiotherapy response

PET-CT Fusion

(slides courtesy of Tyagi et al.)
Example case: Semiquantitative parameters derived from DCE-MRI

Pre-treatment

After first fraction (8 Gy)

After last fraction (40 Gy)

Four weeks post-treatment

Time to half peak (tthp) Mean (min)

0.22

0.54

0.06

0.142

0.175

0.103

(Neelam Tyagi, Sang Ho Lee, Andreas Rimner, Margie Hunt et al.)
Looking ahead [1/2]

- Need to organize and test relatively simple image biomarkers from
  - dynamic contrast measurements (e.g., TTHP)
  - ADC and related parameters
  - Caveat: diffusion parameter behavior during RT is site specific
- Such parameters are probably relevant to both RT and cytotoxic drug response
- Could become a standard part of Phase I drug response analyses
- Could form a personalized ground for adaptation, as well as disease phenotype classification

Looking ahead [2/2]

- Many opportunities to not only better understand individual tumor physiology vs. response, but also many opportunities to monitor and adapt to variable response.
- The relatively empirical use of hypoxia imaging during RT to choose dose is already proving useful in H&N.
- There is the potential to use multi-modality imaging with tumor response modeling to predict tumor response and to identify radiobiological outliers