Disclosures

- Research funding provided by:
  - NIH R01CA204189
  - Philips Healthcare
  - HFHS A-Grant
- Research Collaborations with Modus Medical Devices, ViewRay, Inc.
- Honorarium/Travel/Research Agreements with ViewRay, Inc.

Funding Overview

- PAR-15-075, Academic-Industrial Partnerships for Translation of Technologies for Cancer Diagnosis and Treatment (R01)
- 5-year grant, July starts year 4 of 5
- Academic (and overall PI): Carri Glide-Hurst, PhD + team (scientists, clinicians, statistician)
- Industry (Philips Healthcare Hamburg, Germany, PI): Steffen Renisch, PhD + team (scientists)
- Modus Medical subcontract for end-to-end phantom development & build
Submitted, June 2015 → Nov, 2015, I got a score!!

The score came with a caveat...

If you choose to submit a resubmission application for the next review cycle under this policy for new investigation, your amended application must be received at NIH no later than Thursday, December 10, 2015.

<1 month!! To recover from a 37th percentile!!

WOOOOO HOOOO!!!!
Aim 1: Geometric and patient-specific distortion assessments and corrections

- PHILIPS TEAM: RENISCH
  - Sequence optimization
  - volunteer study: patient-specific distortion
  - On-line reconstruction of patient-specific distortion corrections
  - Enable temporal model reconstructions
  - Industry guidance: structured user requirements

- HFHS TEAM: GLIDE-HURST
  - GNL assessment and correction
  - Volunteer study: patient-specific distortion
  - Develop end-to-end (E2E) phantom to benchmark patient-specific distortions
  - Develop SlicerMRinRT toolkit
  - SlicerMRinRT end user evaluation 1
  - Integrate Philips pelvic bone masks
  - Developed female pelvic (SynCT) solution
  - Translated pelvis SynCT pipelines to 1.5/3.0T
  - SynCT/OMAR benchmarking: E2E phantom
  - Translated brain SynCT pipeline to 1.5/3.0T
  - SlicerMRinRT end user evaluation 2
  - MR-CAT pelvis modifications: Bone mask output for HFHS SynCT
  - Revised bladder/bone values
  - Female pelvis
  - Optimize OMAR-XD at 1T, 1.5T, 3.0T
  - Auto-segmentation models in SPICE
  - End-to-end testing
  - Virtual clinical trial: brain/pelvis/OMAR
  - Physician delineations
  - IGRT, margin calculation
  - Plan evaluation: dosimetry/radiobiology
  - Physician physicist guidelines
  - MR-CAT generation for pelvis cases
  - SPICE delineation benchmarking
  - Facilitate 3rd party evaluation: WashU
  - Final translational recommendations
  - Integration of validated final tools on console

Clinical Motivation/Significance

### STANDARD OF CARE: CT

- Limited soft tissue contrast
- Excellent spatial fidelity
- Electron density information
- Bone/air signal (DRRs)
- Ionizing radiation

### MR

- Unparalleled tissue contrast
- Distortions at large FOV
- No direct relationship to ED
- Limited bone/air signal
- Non-ionizing radiation
- Needs to be ec

Ideal Synthetic CT (SynCT)

- Derived from commonly acquired sequences (or) fast sequence
- Accurate geometry (distortions mitigated)
- Accurate electron density
- For use in treatment planning/IGRT
- Site-specific solutions (Brain, Pelvis, etc.)
Relevant Prior Experience/Preliminary Data

- Board certified Medical Physicist, ~7 years experience at submission (2-year postdoc)
- Several MR-simulation/4DMRI publications, imaging publications
- Published synthetic CT solutions in pelvis & brain requiring refinement
- Long-standing collaboration/publications with Philips Healthcare (CT + MRI) although not with the specific Philips team used in collaboration

Aim 1: MRI Distortion Quantification

**System Level:**
- Inhomogeneities in $B_0$ field
- Non-linearity of the spatial encoding gradients (GNL)

**Object/Patient Induced:**
- Susceptibility, Chemical Shift
- May change as patient conditions change

3D Distortion Phantom

Key Scientific Outcomes: System-level Distortions

- Magnet specific
- Increase w/increased distance from isocenter
- May require corrections for large FOVs

Key Scientific Outcomes: Patient Specific Distortions

Key Translational Outcome: Simplifying Patient Specific Distortions

Price et al. MedPhys, 2017

Glide - Hurst et al. Radiation Oncology, 2018

Weiss et al. PMB, 2019
Key Translational Outcome: Meet PETE!

- Designed & built a novel MR-compatible pelvic end-to-end (PETE) phantom with Modus Medical
- Used patient-informed considerations
  - Determine impact of organ volumes on system interactions
  - Benchmark MR-only planning
  - Evaluate patient-specific distortions
  - End-to-end testing

MRI Distortion Take-Home:

- Gradient non-linearity is magnet-specific, can be non-negligible away from isocenter, may require corrections
- Patient-specific distortions are small, but location may be significant if near lesions, dental fillings, etc.
- Further development of more efficient:inline distortion quantification and corrections are warranted
  Now let’s worry about the electron density (AIM 2)!
  (emphasis on brain)

Previous Complex SynCT Pipeline for Brain:

Key Scientific Outcome: Deep Learning SynCT
Solution Generative Adversarial Networks (GAN)

- Generator: Residual network with 3 convolutional layers, 9 residual blocks and 2 transposed convolutional layers to generate SynCTs
- Discriminator: Central neural network with 5 convolutional layers to classify input images as real or synthetic
- SynCT generated from a single T1-weighted Post-Gd MR dataset in 7s (training took ~11hrs with a GeForce 980 T9 GPU)

Results: GAN SynCT

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P13
MAE = 96.6 HU

P4
MAE = 105.1 HU

SRS Cerebellum: 6XFFF Dynamic Arc, 18 Gy

Data Credit: Ning Liu, MS, HFCI
Preliminary Results: SynCT

- Bladder well-preserved between MRI & synCT, bowel/rectal gas are WIP
- Major gains over our voxel-based weighted summation pipeline requiring manual bone contouring, 4 input MRIs, MAE ~74 HU (Kim et al., IJROBP, 2015)

Synthetic CT Take-Homes

- Deep learning has vastly accelerated our ability for accurate & efficient synthetic CT generation
- Dosimetry & IGRT performance appear robust
- Modified aims via progress reports to accommodate this new technology
- To be used in Virtual Clinical Trial

Year 4-5: Virtual Clinical Trial (40 Brain/80 Pelvis)

- MR-only Planning
- Standard of Care: CT/MR Planning
- Autosegmentation
- Dosimetry & Radiobiological Endpoints
- IGRT Performance
- Margin Calculation
Potential Future Research Directions

• Build on MR-guided radiation therapy applications
• Functional or adaptive radiation therapy
• Potential renewal of AIP R01

Grant Advice for AAPM Members

• Establish yourself as an expert in a focused area related to grant submission (1st/last author publications)
• Find high quality collaborators/co-investigators to engage and work with you
• Persistence is key: I have 4 R01 submissions, 3 not scored (as recent as June, 2019 review), 1 scored/revised/funded
• Make friends with those who are also writing grants. Share funded proposals, response letters, and progress reports ➔ Pay it forward

THANK YOU!