R01 CA204189 Development of Anatomical Patient Models to Facilitate MR-only Treatment Planning

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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

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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!!

Application Number: 1 R01 CA204189-01

Principal Investigator

GLIDE-HURST, CARRI KAYE PHD

Applicant Organization: HENRY FORD HEALTH SYSTEM

Review Group: ZRG1 SBIB-D (57)
Center for Scientific Review Special Emphasis Panel
PAR Panel: Academic Industrial Partnership

Meeting Date: 10/15/2015 RFA/PA: PAR15-075
Council: JAN 2016 PCC: 5PDI
Requested Start: 04/01/2016

Dual IC(s): EB

Project Title: Development of Anatomical Patient Models to Facilitate MR-only Treatment Planning

SRG Action: Impact Score: 44 Percentile: 37 #

Next Steps: https://grants.nih.gov/grants/next_steps.htm

Human Subjects: 30-Human subjects involved - Certified, no SRG concerns

Animal Subjects: 10-No live vertebrate animals involved for competing appl.

Gender: 1A-Both genders, scientifically acceptable

Minority: 1A-Minorities and non-minorities, scientifically acceptable

Children: 3A-No children included, scientifically acceptable

Clinical Research - not NIH-defined Phase III Trial

The score came with a caveat…

If you choose to submit a resubmission application for the next review cycle under this policy for new investigators, 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!!!!

Application Number: 1 R01 CA204189-01A1

Principal Investigator

GLIDE-HURST, CARRI KAYE

Applicant Organization: HENRY FORD HEALTH SYSTEM

Review Group: ZRG1 SBIB-D (57)
Center for Scientific Review Special Emphasis Panel
PAR Panel: Academic Industrial Partnership

Meeting Date: 02/18/2016 RFA/PA: PAR15-075
Council: MAY 2016 PCC: 5PDI
Requested Start: 07/01/2016

Dual IC(s): EB

Project Title: Development of Anatomical Patient Models to Facilitate MR-only Treatment Planning

SRG Action: Impact Score:20 Percentile:5 #

DELIVERABLES

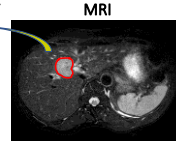
	HFHS TEAM: GLIDE-HURST	PHILIPS TEAM: RENISCH
Aim 1: Geometric and patient-specific distortion assessments and corrections	• GNL assessment and correction • Volunteer study: patient-specific distortion • Develop end-to-end (E2E) phantom to benchmark patient-specific distortions • Develop SlicerMRinRT toolkit • SlicerMRinRT end user evaluation 1	• Sequence optimization • Volunteer study: patient-specific distortion • On-line reconstruction of patient-specific distortion corrections • Enable temporal model reconstructions • Industry guidance: structured user requirements
Aim 2: Synthetic CT generation and auto-segmentation	• Integrate Philips pelvic bone masks • Develop female pelvis synCT solution • Translate pelvis synCT pipelines to 1.5/3.0T • SynCT/OMAR benchmarking: E2E phantom • Translate brain synCT pipeline to 1.5/3.0T • SlicerMRinRT end user evaluation 2	• MR-CAT generation for pelvis cases • SPICE delineation benchmarking • Facilitate 3rd party evaluation: WashU • Final translational recommendations • Integration of validated final tools on-console
Aim 3: Workflow evaluation, virtual clinical trial, final integration	• End-to-end testing • Virtual clinical trial: brain/pelvis/OMAR • Physician delineations • IGRT, margin calculation • Plan evaluation: dosimetry /radiobiology • Physician-physicist guidelines	• 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

Clinical Motivation/Significance

STANDARD OF CARE: CT

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

MRI



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

MR-only Treatment Planning

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.)

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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)

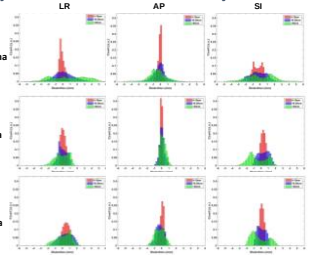
Object/Patient Induced:

-Susceptibility, Chemical Shift

-May change as patient conditions change

3D Dist[illegible] Phantom

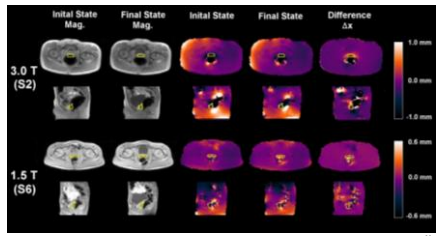
Key Scientific Outcomes: System-level Distortions



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

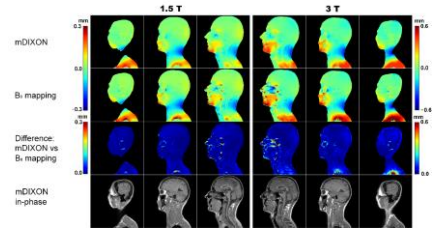
Price et al. MedPhys, 2017

Key Scientific Outcomes: Patient Specific Distortions



Glide-Hurst et al, Radiation Oncology, 2018

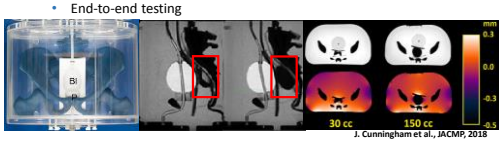
Key Translational Outcome: Simplifying Patient Specific Distortions



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



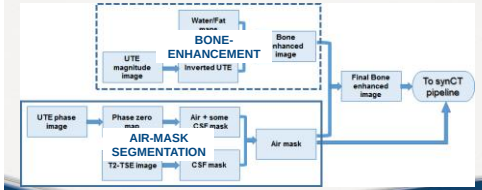
J. Cunningham et al., JACMP, 2018

MRI Distortion Take-Homes

- 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)

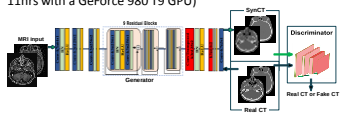
Previous Complex SynCT Pipeline for Brain



Zheng, W et al., Red Journal, 2015

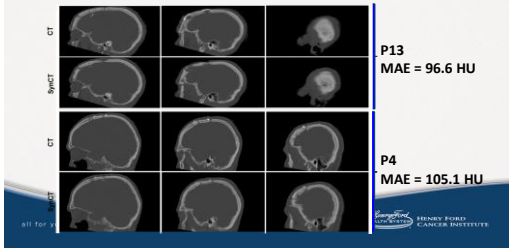
Key Scientific Outcome: Deep Learning SynCT Solution Generative Adversarial Networks (GAN)

- 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)

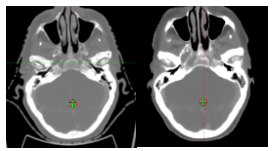


Emami H, et al. Generating synthetic CTs from magnetic resonance images using GAN. Med Phys (2018).

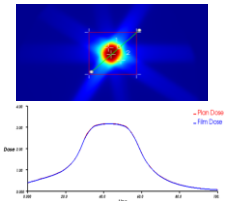
Results: GAN SynCT



SRS Cerebellum : 6XFFF Dynamic Arc, 18 Gy



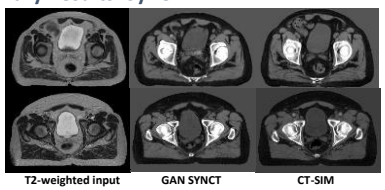
CT-SIM GAN-CT



Data Credit: Ning Liu, MS, HFCI

Gamma	3%1mm	2%2mm	2%1mm	1%1mm
% Pass	100.0	100.0	99.7	97.2

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

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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

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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!

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