

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

Carri Glide-Hurst, PhD, DABR, FAAPM

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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!!

Principal Investigator
GLIDE-HURST, CARRI KAYE PhD
Application Number: 1 R01 CA204189-01

Applicant Organization: HENRY FORD HEALTH SYSTEM

Review Group: ZRG1 SBIB-D (S7)
Center for Scientific Review Special Emphasis Panel
FAIR Panel: Academic Industrial Partnership

Meeting Date: 10/15/2015 RFA/PA: PAR15-075
Council: MAY 2015 PCC: SPDI
Requested Start: 04/01/2016

Dual IC(s): EB

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

SRG Action: **Impact Score: 44 Percentile: 37 #**

Next Steps: www.fda.gov/oc/ohrt/ohrt_steps.htm

Human Subjects: 30-Human subjects involved - Certified, no SRG concerns
Animal Subjects: 10-No live vertebrate animals involved for competing app.
Gender: 1-A.Both genders, scientifically acceptable
Minority: 2-A.Minorities and non-minorities, scientifically acceptable
Children: 2-A.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!!!!

Principal Investigator
GLIDE-HURST, CARRI KAYE
Application Number: 1 R01 CA204189-01A1

Applicant Organization: HENRY FORD HEALTH SYSTEM

Review Group: ZRG1 SBIB-D (S7)
Center for Scientific Review Special Emphasis Panel
FAIR Panel: Academic Industrial Partnership

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

Dual IC(s): EB

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

SRG Action: Planning
Impact Score:20 **Percentile:5 #**

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DELIVERABLES

Aim 1: Geometric and patient-specific distortion assessments and corrections

Aim 2: Synthetic CT generation and auto-segmentation

Aim 3: Workflow evaluation, virtual clinical trial, final integration

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 toolkits
- SlicerMRinRT end user evaluation 1

- Integrate Philips pelvic bone masks
- Develop female pelvic synCT solution
- Translate pelvic synCT pipelines to 1.5/3.0T
- SynCT/OMAR benchmarking: ISE phantom
- Translate brain synCT pipeline to 1.5/3.0T
- SlicerMRinRT end user evaluation 2

- End-to-end testing
- Virtual clinical trial: brain/pelvic/OMAR
- Physician delineations
- IGRT, margin calculation
- Plan evaluation: dosimetry/radiobiology
- Physician-physicist guidelines

PHILIPS TEAM: RENISCH

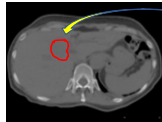
- Sequence optimization
- Volunteer study: patient-specific distortion
- On-line reconstruction of patient-specific distortion corrections
- Enable temporal model reconstructions
- Industry guidance: structured user requirements

- MR-CAT generation for pelvic cases
- SPICE delineation benchmarking
- Facilitate 3rd party evaluation: WashU
- Final translational recommendations
- Integration of validated final tools on-console

- MR-CAT pelvic modifications:
 - Bone mask output for MFHS synCT
 - Revised bladder/bone values
 - Female pelvis
- Optimize OMAR.XD at 1T, 1.5T, 3.0T
- Auto-segmentation models in SPICE

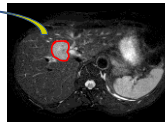
Clinical Motivation/Significance

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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HOVON 6703D
RADIATION ONCOLOGY
MAYO CLINIC
ROSENBERG CANCER INSTITUTE

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

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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

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3D Distortion Quantification Phantom

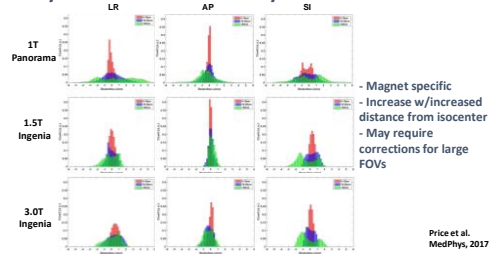
Siemens Symphony

Siemens Aera, Skyra, Verio, & Philips Ingenia

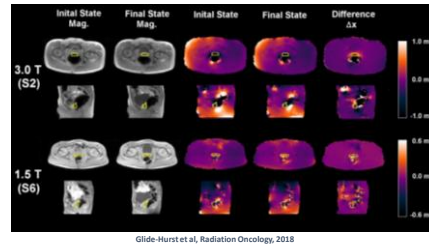
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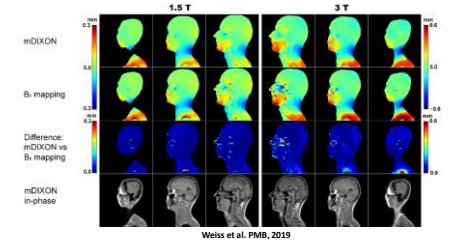
Key Scientific Outcomes: System-level Distortions



Key Scientific Outcomes: Patient Specific Distortions

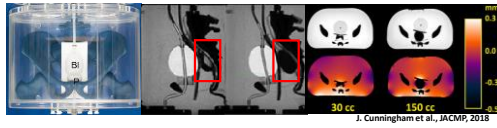


Key Translational Outcome: Simplifying Patient Specific Distortions



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



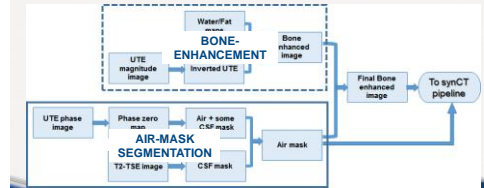
MRI Distortion Take-Homes

- 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)

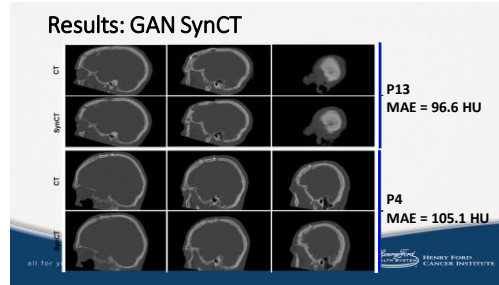
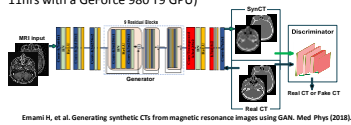


Previous Complex SynCT Pipeline for Brain

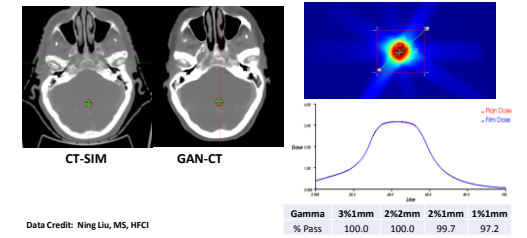


Key Scientific Outcome: Deep Learning SynCT Solution Generative Adversarial Networks (GAN)

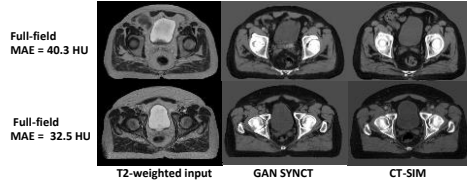
- Generator: Residual network with 3 convolutional layers, 9 residual blocks and 2 transposed convolutional layers to generate synCTs
- Discriminator: Central neural network with 5 convolutional layers to classify input images as real or synthetic
- SynCT generated from a single T1-weighted Post-Gd MR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



SRS Cerebellum : 6XFFF Dynamic Arc, 18 Gy



Preliminary Results: SynCT



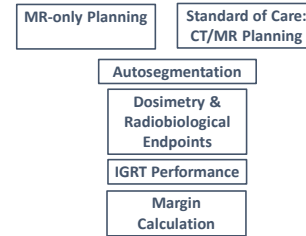
*Bladder well-preserved between MRI & synCT, bowel/rectal gas are WIP
 *Major gains over our voxel-based weighted summation pipeline requiring manual bone contouring, 4 input MRIs, MAE ~74 HU (Kim *et al*, IJROBP, 2015)

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)



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/revise/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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