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# Automating Treatment Planning in Radiation Therapy

Lekan Ogunmolu

Perelman School of Medicine

University of Pennsylvania, Philadelphia, PA

February 04, 2021

# Talk Outline

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- Patient Head Motion Correction in External Beam Radiation Therapy
  - Magnetic Resonance Imaging and Linear Accelerator Systems (MRI-LINACs)
  - Intensity-Modulated RT (IMRT): Earlier PhD Work
- Beam Orientation Optimization (BOO)
  - Monte Carlo Tree Search and Neuro-Dynamic Programming for BOO
  - Column Generation as Pretraining for MCTS for BOO
- Robustness Margins and Robust Deep Policies for Nonlinear Control

# Research Significance

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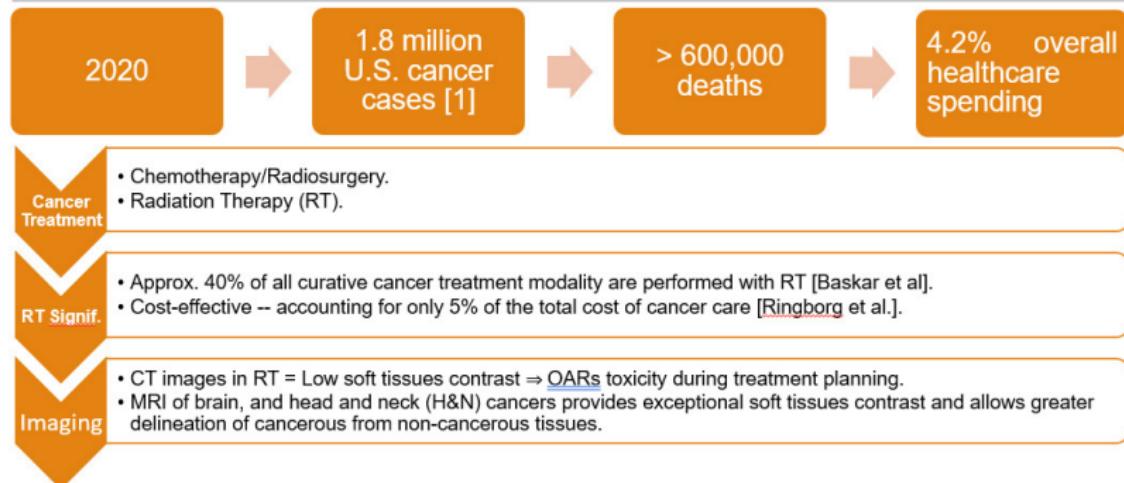
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# IMRT Treatment Planning (Beam Delivery)

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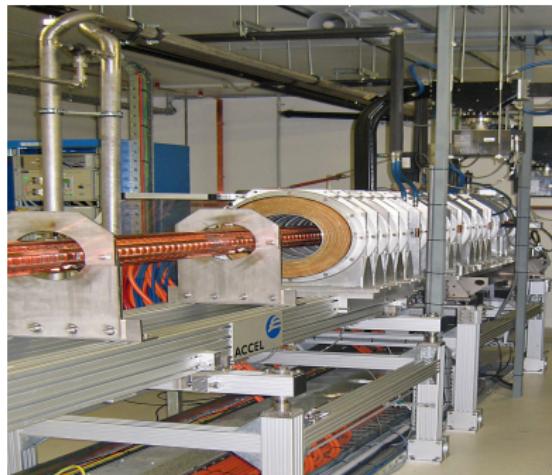
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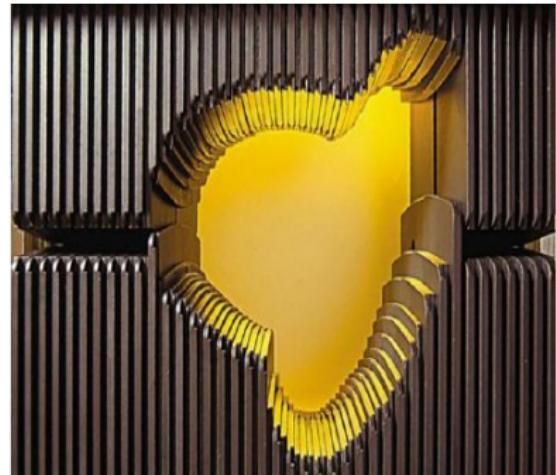
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The Australian Synchrotron.



Multi-leaf collimator (Varian)

# Radiation Delivery Couch and Gantry

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Varian's TrueBeam Radiotherapy System.

# Head Stabilization in RT

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- Head Stabilization in Cancer Radiation Therapy
  - Magnetic Resonance Imaging-Linear Accelerator Systems (MRI-LINACs)

# Robotic Radiosurgery

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## A Patient Head Motion-Correction Mechanism for MRI-LINAC RT

OLALEKAN OGUNMOLU

DEPARTMENT OF RADIATION ONCOLOGY, PENN SCHOOL OF MEDICINE

- Current Collaborators: Rodney Wiersma & Xinmin Liu (UChicago → UPenn)
- Past Collaborators: Steve Jiang, Xuejun Gu, (UT Southwestern); Nick Gans (UT Dallas, UT Arlington)

# Relevant Publications

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- **Ogunmolu, Olalekan**, Xinmin Liu, Nicholas Gans, and Rodney D. Wiersma. "Mechanism and Model of a Soft Robot for Head Stabilization in Cancer Radiation Therapy." In *2020 IEEE International Conference on Robotics and Automation (ICRA)*, pp. 4609-4615. IEEE, 2020.
- **Ogunmolu, Olalekan**, and Rodney D. Wiersma. "Kinematics and Kinetics of a Continuum Parallel Soft Robot for MRI-LINAC Motion Correction." Working Paper, In *IEEE Transactions on Robotics*, IEEE 2020.
- **Ogunmolu, Olalekan** and Rodney D. Wiersma. "A Real-Time Patient Head Motion Correction Mechanism for MRI-Linac Systems." In *2020 Virtual Joint AAPM/COMP Meeting*, AAPM 2020.
- **Ogunmolu, Olalekan**, Xinmin Liu, Rodney D. Wiersma. "Auto-Determination of the Dextrous WorkSpace in Robotic Stereotactic Radiosurgery." In *2020 Virtual Joint AAPM/COMP Meeting*, AAPM 2020.

# Correcting Head Motion: RT and MRI-LINACs

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(a) The BRW SRS Frame [Chelvarajah et al. (2004)]



(b) Thermoplastic masks



(c) Frame With MRI Coils (PSOM)

# 4-D Motion Correction Stage

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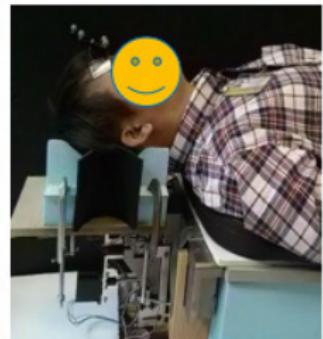
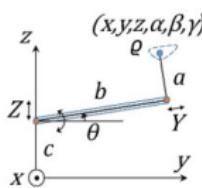
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Liu et al. (2015)

# 4-DOF Motion Controller Block Diagram

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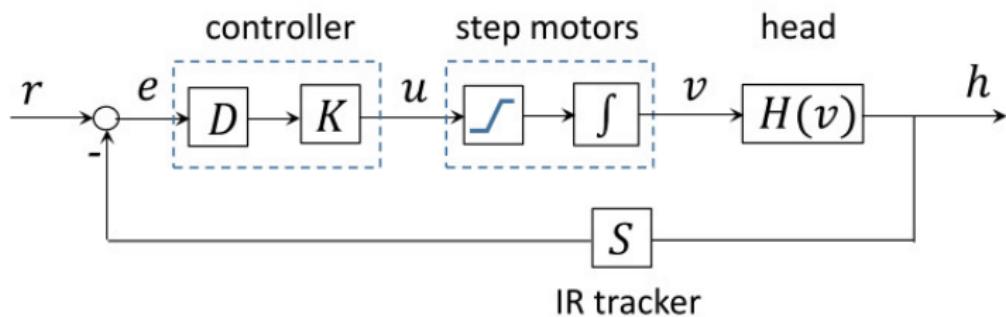
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Liu et al. (2015)

# Phantom Feedback Motion Correction Results

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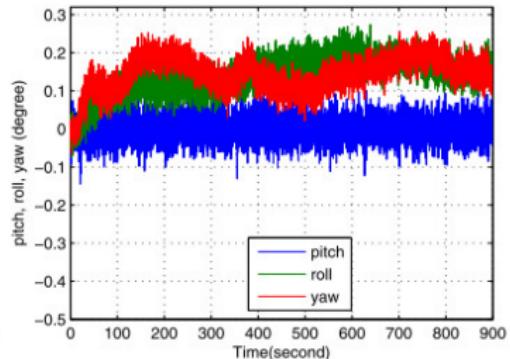
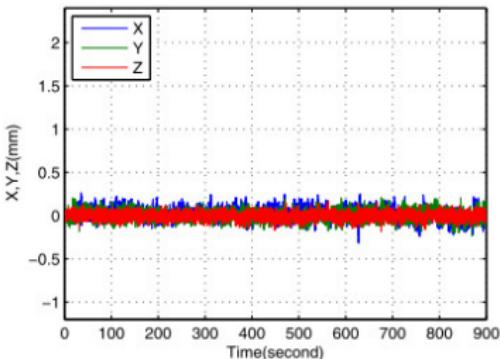
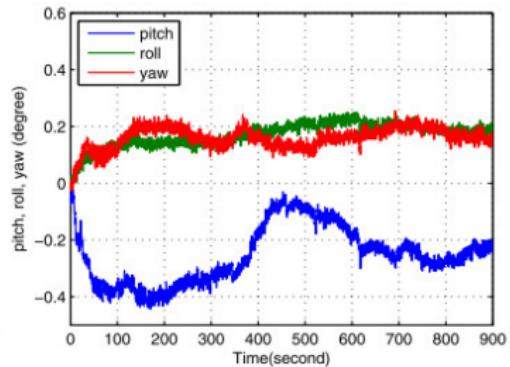
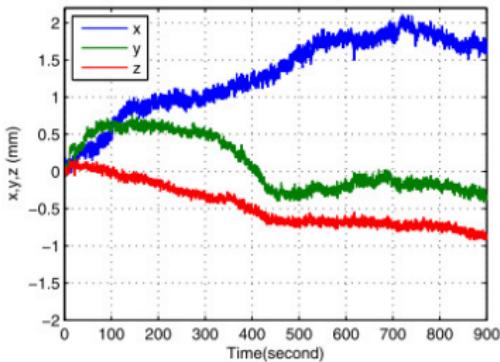
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# Head Motion Without and With Motion Correction

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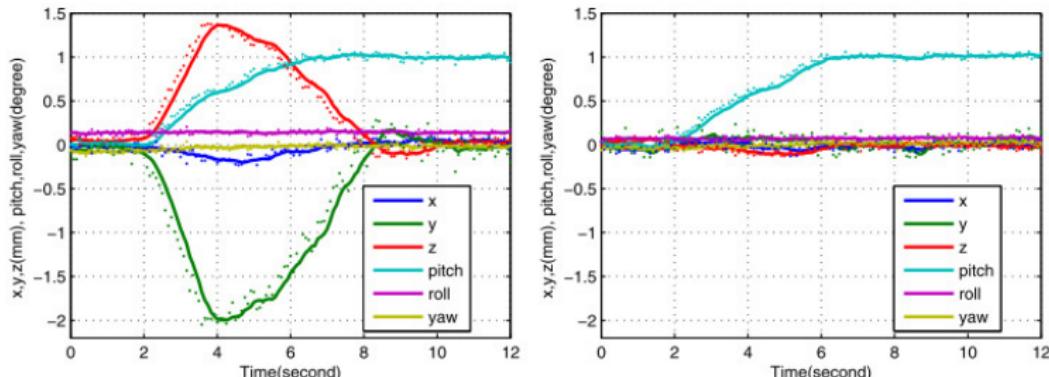
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Human Volunteer Results. Left: Coupled Axes; R: Decoupled Axes.

# SRS: Wiersma Stewart-Gough Platform

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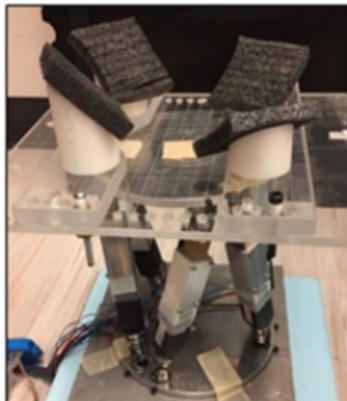
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# 6-DOF Motion Correction Results

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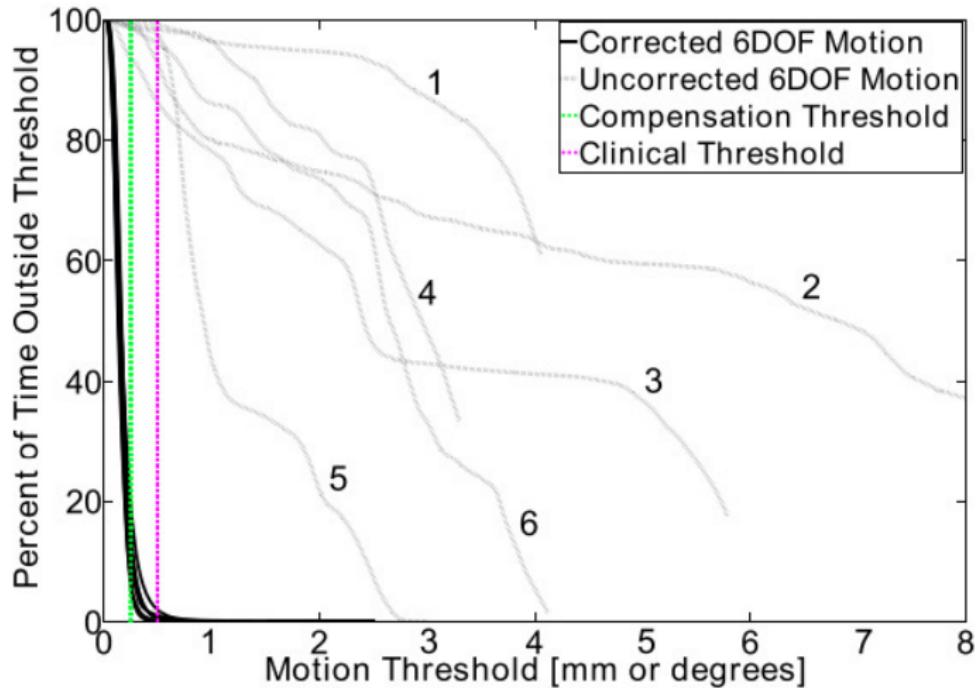
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# Next-Gen RT Treatment with MRI-LINACs

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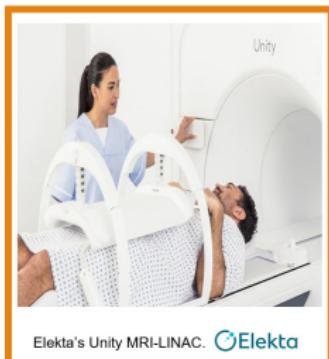
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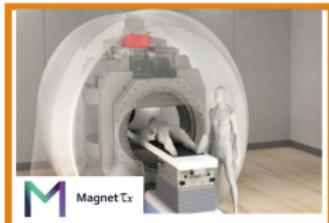
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Elekta's Unity MRI-LINAC.



MRIDIAN by ViewRay: MR image guidance Radiation on table Adaptive Radiotherapy.



## MRI in LINAC RT

- Next generation precision beam delivery.
- High speed, high resolution MLC.
- Online plan adaptation capabilities.

• MRI that offers superior soft tissues visualization integrated with linear accelerator (LINAC) RT Offers unrivaled, online, and real-time cancer R

- Commercialized in systems such as
  - Elekta AB's (Sweden) 1.5T diagnostic imaging system [Raaymakers et al.];
  - Viewray's MRIdian system [Mutic et al.]; or
  - the MagnetTx's (Canada) Aurora RT system [Fallone et al.] among others.

• Random and involuntary patient motion often occurs during image acquisition leading to

- Artifacts → Poor image quality.
- Incomplete irradiation of the tumor target.
- Exposure of healthy tissues to radiation toxicity.
  - ❖ These lower the accuracy of online and real-time precise radiation dose delivery.
  - ❖ Affects clinical efficacy.

# Pneumatic Actuated Soft Robots for Head Motion Compensation

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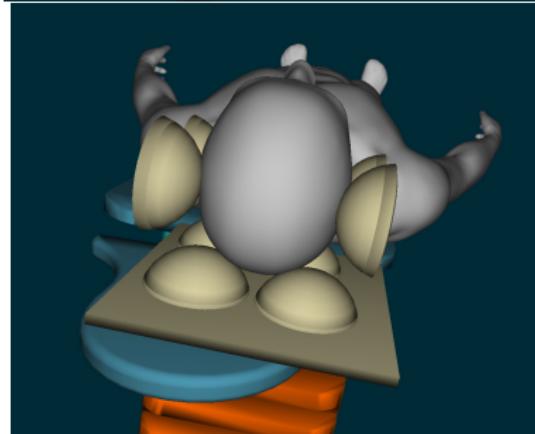
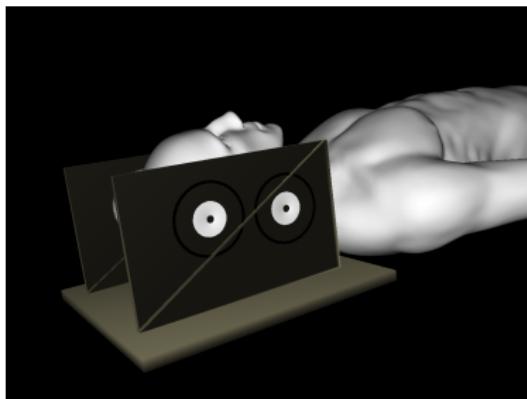
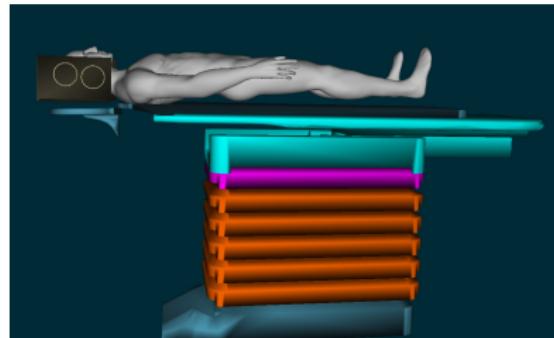
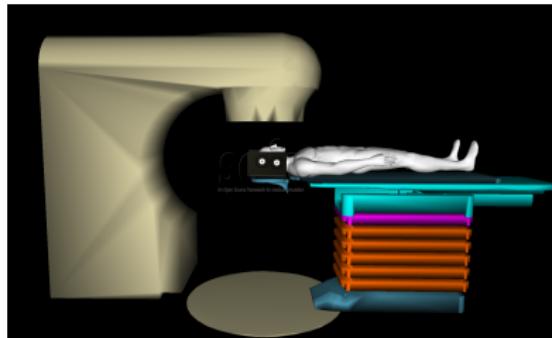
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# Cephalopods-inspired CCOARSE Actuator Design

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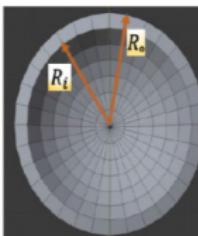
Circumferentially Constrained And Radially Symmetric Elastomers [Pikul et al. (2019)].



(a) Laser-Cut Fiber



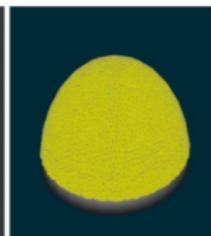
(b) Fiber+Rubber



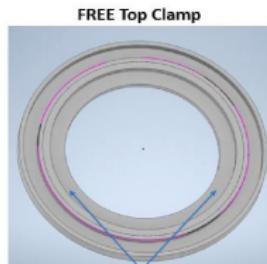
(c) Deformation Model



(d) Actuator+PVC Base



(e) Finite Element Model

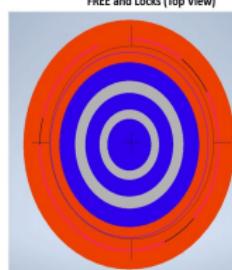


FREE Top Clamp

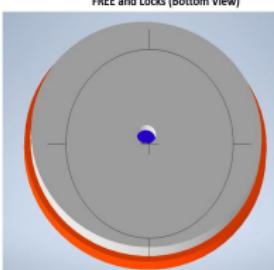


FREE Base Clamp

(f,g)



FREE and Locks (Top View)



(h)

# CCOARSE Actuator Schematic

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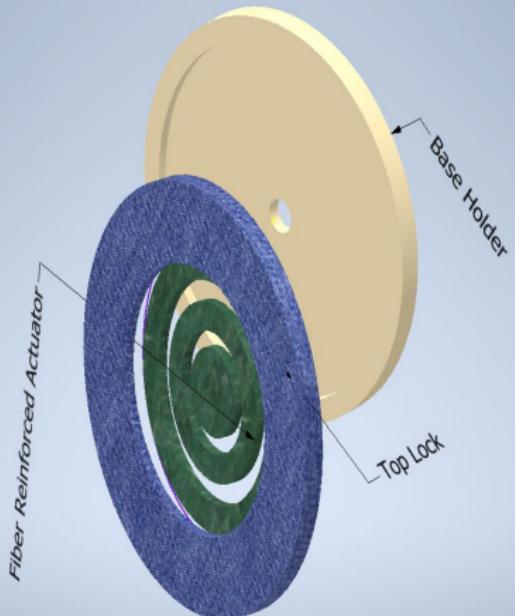
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# Pneumatic Control and Deformation Scheme

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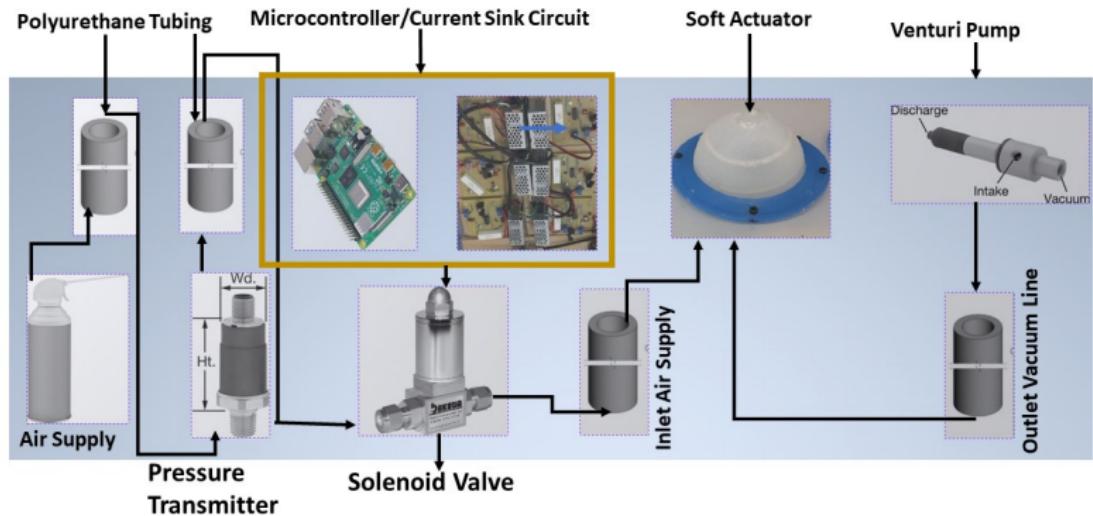
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# Nonlinear Elastic Deformation Analysis

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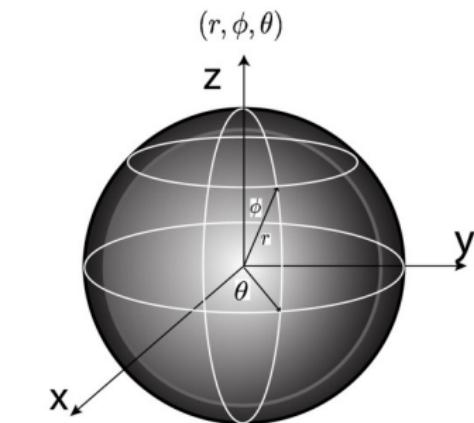
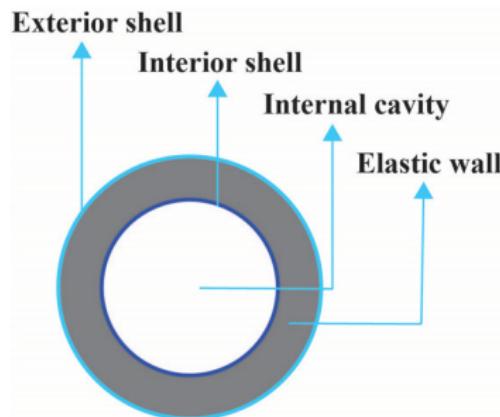
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## IAB SHELLS AND AIR CAVITY/DEFORMATION ANALYSIS



$$r_i \leq r \leq r_o, \quad 0 \leq \theta \leq 2\pi, \quad 0 \leq \phi \leq \pi$$

# Soft IK via Boundary Value Problem

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- Using the following boundary conditions for the Cauchy Stress,
  - $\sigma_{rr}|_{R=R_0} = -P_{atm}, \sigma_{rr}|_{R=R_i} = -P_{atm} - P$
- And together with Cauchy's first law, we find that
  - $\sigma_{rr}(r) = - \int_{r_i}^{r_o} [2C_1\left(\frac{r}{R^2} - \frac{R^4}{r^5}\right) + 2C_2\left(\frac{r^3}{R^4} - \frac{R^2}{r^3}\right)] dr$
  - $\sigma_{rr}(r) = \int_{R_i}^{R_o} [2C_1\left(\frac{1}{r} - \frac{R^6}{r^7}\right) - 2C_2\left(\frac{R^4}{r^5} - \frac{r}{R^2}\right)] dr$
- With  $\sigma_{rr}|_{R=R_i} = -P_{atm} - P$  and setting  $P_{atm} = 0$ , we find
  - $P(r) = \int_{r_i}^{r_o} [2C_1\left(\frac{r}{R^2} - \frac{R^4}{r^5}\right) + 2C_2\left(\frac{r^3}{R^4} - \frac{R^2}{r^3}\right)] dr$
  - $P(r) = \int_{R_i}^{R_o} [2C_1\left(\frac{1}{r} - \frac{R^6}{r^7}\right) - 2C_2\left(\frac{R^4}{r^5} - \frac{r}{R^2}\right)] dr$
  - $r^3 = R^3 + r_i^3 - R_i^3 \text{ and } r_o^3 = R_o^3 + r_i^3 - R_i^3$

# Volumetric Deformation Results (Simulation)

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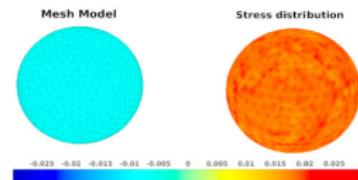
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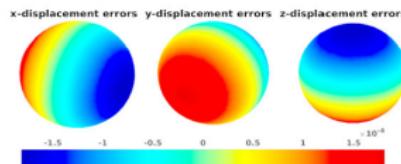
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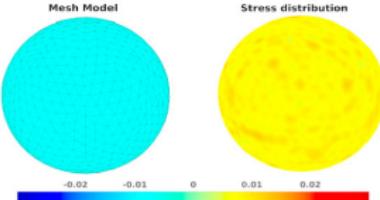
(a) Left: Mesh model. Right: Stress distribution on outer skin.



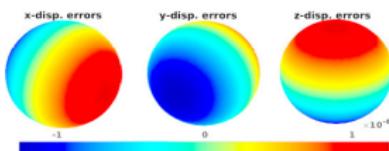
(b) Displacement errors along  $x, y, z$  coordinates.

Inputs				Outputs			
$C_1$	$C_2$	$R_i$	$r_i$	$R_o$	$r_o$	$P$	$\Delta V$
1.1e4	2.2e4	.027	.03	.03	.033	.76	$\approx 0$

Fig. 6: Volumetric Deformation (Expansion).



(a) Left: Mesh model. Right: Stress distribution on outer skin.



(b) Displacement errors along  $x, y, z$  coordinates.

Inputs				Outputs			
$C_1$	$C_2$	$R_i$	$r_i$	$R_o$	$r_o$	$P$	$\Delta V$
1.1e4	2.2e4	.025	.03	.03	.028	-.34	$\approx 0$

Fig. 7: Volumetric Deformation (Compression).

# Volumetric Deformation Results (Actual)

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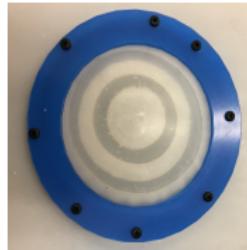
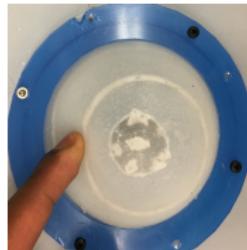
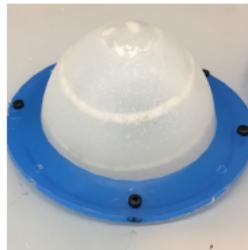
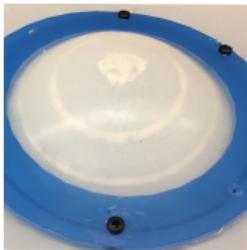
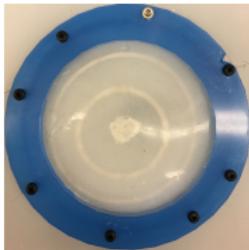
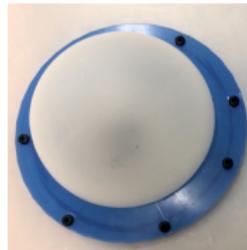
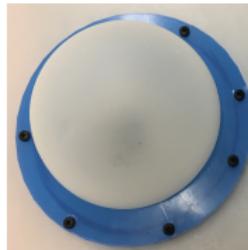
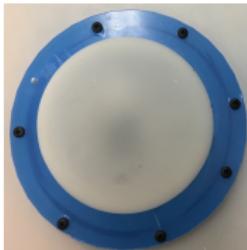
Column Generation

iDG

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# Tension/Compression Analysis

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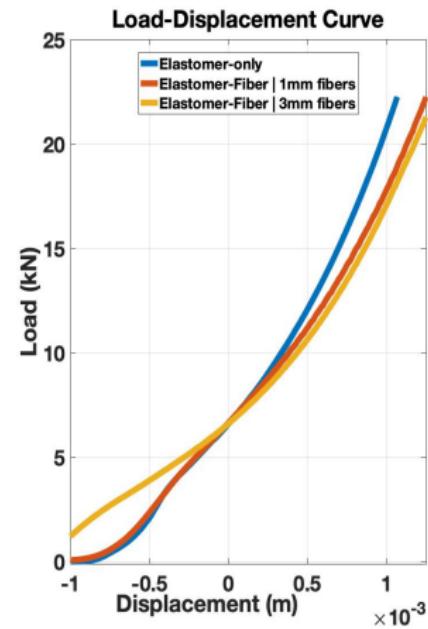
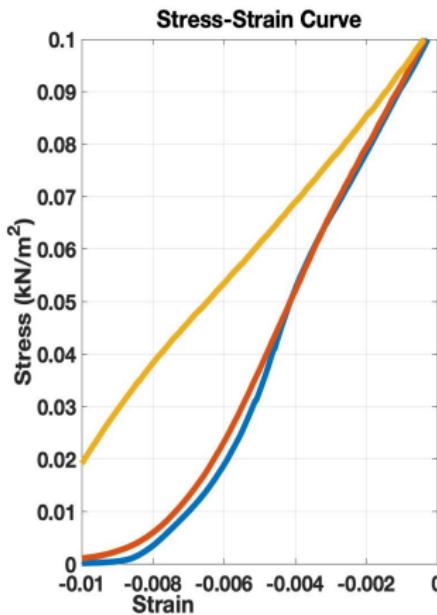
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# Head Motion Control (Independent Actuation)

Automating Treatment Planning in Radiation Therapy

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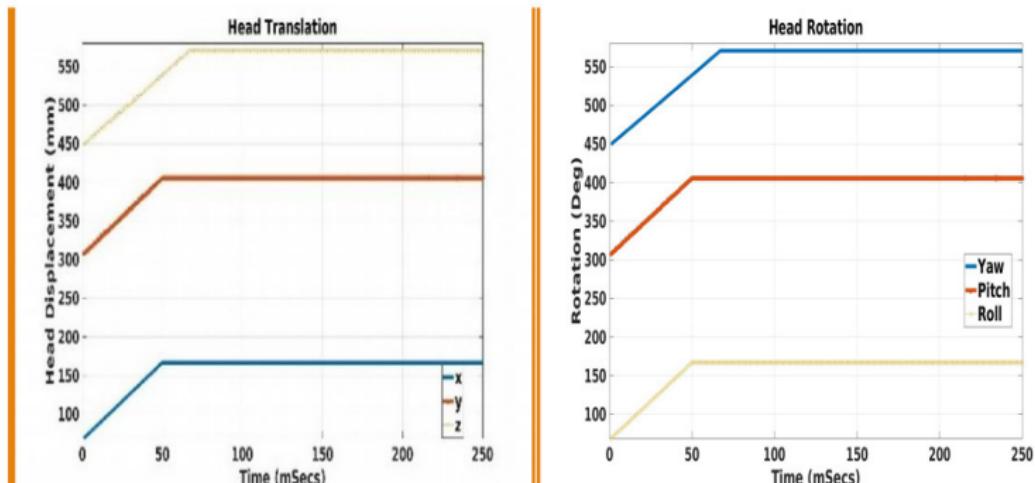
Column Generation

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Head Translation along  $x, y, z$  for a task of raising the head by a certain threshold above the table

Head rotation in Euler angles for a task of tilting the head about the  $x, y, z$  axes on the treatment table.

# Ongoing/Future work

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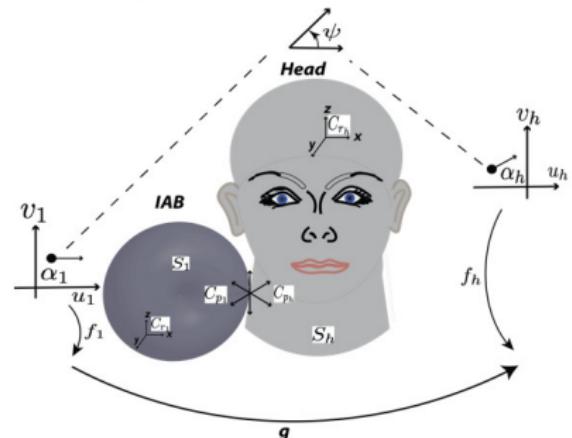
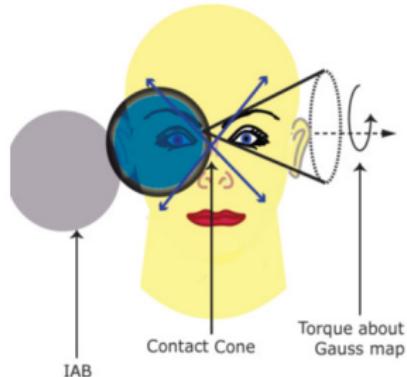
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Continuum Mechanical Model Validation/Differential Geometry/Newton-Euler Dynamics



# Part II.B: Head Stabilization in Radiation Therapy (RT)

Automating Treatment Planning in Radiation Therapy

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- Head Stabilization in Cancer Radiation Therapy
  - Intensity-Modulated RT (IMRT): Earlier PhD Work

# Relevant Publications

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- **Ogunmolu, Olalekan**, Gans, Nicholas, Jiang, Steve, and Gu, Xuejun. "SU-E-J-12: An Image-Guided Soft Robotic Patient Positioning System for Maskless Head-And-Neck Cancer Radiotherapy: A Proof-Of-Concept Study." *Medical Physics* 42, no. 6Part7 (2015): 3266-3266.
- **Ogunmolu, Olalekan P.**, Xuejun Gu, Steve Jiang, and Nicholas R. Gans. "A real-time, soft robotic patient positioning system for maskless head-and-neck cancer radiotherapy: an initial investigation." In *2015 IEEE International Conference on Automation Science and Engineering (CASE)*, pp. 1539-1545. IEEE, 2015.
- **Ogunmolu, Olalekan P.**, Xuejun Gu, Steve Jiang, and Nicholas R. Gans. "Vision-based control of a soft robot for maskless head and neck cancer radiotherapy," In *2016 IEEE International Conference on Automation Science and Engineering (CASE)*, pp. 180-187.IEEE, 2016.
- **Ogunmolu, Olalekan**, Adwait Kulkarni, Yonas Tadesse, Xuejun Gu, Steve Jiang, and Nicholas Gans. "Soft-neuroadapt: A 3-dof neuro-adaptive patient pose correction system for frameless and maskless cancer radiotherapy." In *2017 IEEE/RSJ International Conference on Intelligent Robots and Systems (IROS)*, pp. 3661-3668. IEEE, 2017.
- Almubarak, Yara, Joshi, Aniket, **Ogunmolu, Olalekan**, Gu, Xuejun, Jiang, Steve, Gans, Nicholas, and Tadesse, Yonas. "Design and development of soft robot for head and neck cancer radiotherapy." In *Electroactive Polymer Actuators and Devices (EAPAD) XX*, vol. 10594, p. 1059418. International Society for Optics and Photonics, 2018.

# Simulation Testbed

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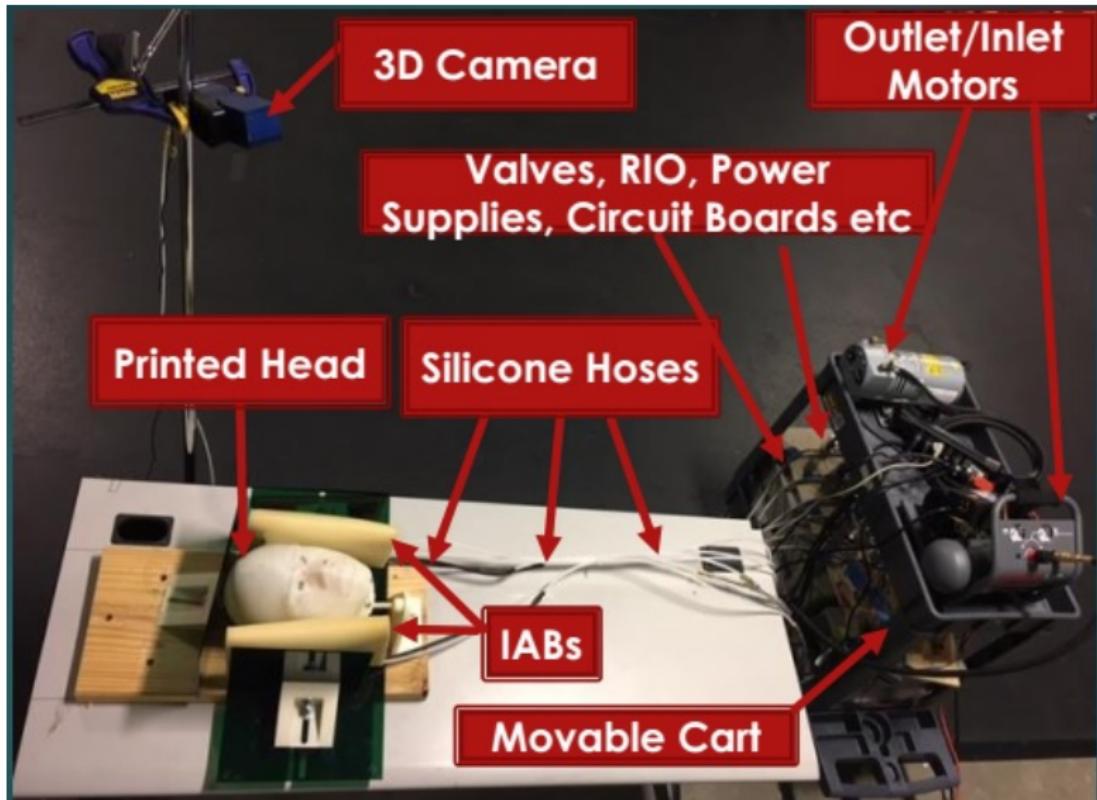
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# Control Proposals

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- Solve a state feedback and feedforward regulation problem
- An adaptation model based on past states and controls:
  - $Z^N = \{u(k), u(k-1), \dots, u(k-n_u), y(k), \dots, y(k-n_y)\}$
- Design Goal:
  - Stabilize states,  $\mathbf{y} = [z, \theta, \phi]^T$
  - i.e.  $z$ , pitch, and roll.

# Model Reference Adaptive Control

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iDG Results

- Model head and bladder dynamics
  - $\dot{\mathbf{y}} = \mathbf{A}\mathbf{y} + \mathbf{B}\Lambda(\mathbf{u} - f(\mathbf{y}, \mathbf{u})) + \mathbf{w}(k)$
  - $\mathbf{A}, \Lambda$  unknown,  $\mathbf{B}, \text{sgn}\Lambda$  known
- Approximate  $f(\mathbf{y}, \mathbf{u})$  by a neural network with continuous memory states
  - $\hat{f}(\mathbf{y}(k), \mathbf{u}(k-d))$  is realized with a *long-short term memory* cell (Horchreiter and Schmidhuber, '91, '97)
  - **purpose:** remember good adaptation gains

# Adaptive Neuro-Control Scheme

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- Derive adaptive adjustment mechanism from Lyapunov analysis for Adaptive Control (Parks, P., 1966)
- $u = \underbrace{\hat{K}_y^T y}_{\text{state feedback}} + \underbrace{\hat{K}_r^T r}_{\text{optimal regulator}} + \underbrace{\hat{f}(y, u)}_{\text{approximator}}$

# Neural Network Model

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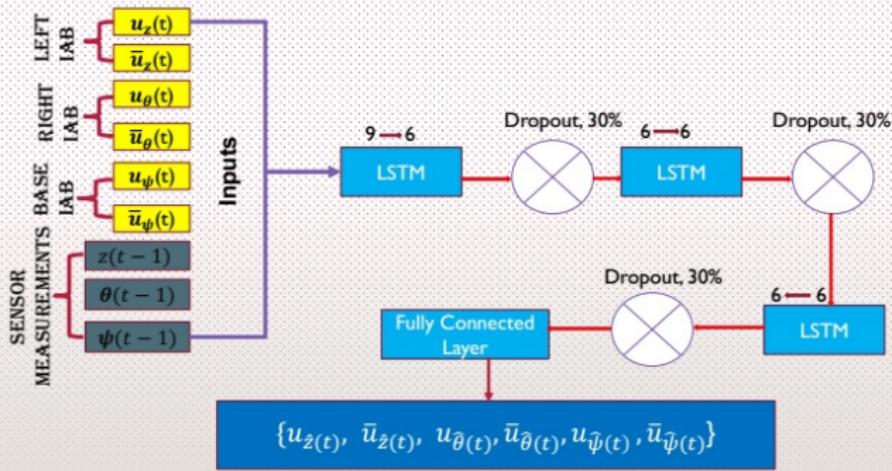
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## Neural Net Architecture



# Lyapunov Redesign: Theorem

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- Given correct choice of adaptive gains  $\hat{\mathbf{K}}_y$  and  $\hat{\mathbf{K}}_r$ , the error state vector,  $\mathbf{e}(k)$  with closed loop time derivative  $\dot{\mathbf{e}}$ , is ***uniformly ultimately bounded***, and the state  $\mathbf{y}$  will converge to a neighborhood of  $\mathbf{r}$ .
- Choose a Lyapunov function candidate  $\mathbf{V}$  in terms of the generalized error state space  $\mathbf{e}$ , gains,  $\tilde{\mathbf{K}}_y^T$ ,  $\tilde{\mathbf{K}}_r^T$ , and parameter error  $\varepsilon_f(\mathbf{y}(k))$  space

$$\mathbf{V}(\mathbf{e}, \tilde{\mathbf{K}}_y, \tilde{\mathbf{K}}_r^T) = \mathbf{e}^T \mathbf{P} \mathbf{e} + \text{tr}(\tilde{\mathbf{K}}_y^T \Gamma_y^{-1} \tilde{\mathbf{K}}_y^T | \Lambda |) + \text{tr}(\tilde{\mathbf{K}}_r^T \Gamma_r^{-1} \tilde{\mathbf{K}}_r^T | \Lambda |)$$

# Stability Results

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See Proof in *Ogunmolu et al. IROS 2018*. In the end, we have

$$\begin{aligned}\dot{\mathbf{V}}(\cdot) &= -\mathbf{e}^T \mathbf{Q} \mathbf{e} - 2\mathbf{e}^T \mathbf{P} \mathbf{B} \boldsymbol{\Lambda} \boldsymbol{\varepsilon}_f \\ &\leq -\lambda_{low} \|\mathbf{e}\|^2 + 2\|\mathbf{e}\| \|\mathbf{P} \mathbf{B}\| \lambda_{high}(\boldsymbol{\Lambda}) \boldsymbol{\varepsilon}_{max}\end{aligned}$$

- $\lambda_{low}, \lambda_{high} \equiv$  minimum and maximum eigenvalues of  $\mathbf{Q}$  and  $\boldsymbol{\Lambda}$  respectively.
- $\dot{\mathbf{V}}(\cdot)$  is thus negative definite outside the compact set
  - $\chi = \left( \mathbf{e} : \|\mathbf{e}\| \leq \frac{2\|\mathbf{P} \mathbf{B}\| \lambda_{high}(\boldsymbol{\Lambda}) \boldsymbol{\varepsilon}_{max}(\mathbf{y})}{\lambda_{low}(\mathbf{Q})} \right)$ 
    - i.e. the error  $\mathbf{e}$  is uniformly ultimately bounded, or  $\mathbf{y}(t) \rightarrow 0$  as  $t \rightarrow \infty$ .

# Results

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- Solving the general form of the Lyapunov equation, we have

$$\mathbf{P} = \begin{bmatrix} -\frac{170500}{2668} & 0 & 0 \\ 0 & -\frac{170500}{2668} & 0 \\ 0 & 0 & -\frac{170500}{2668} \end{bmatrix}$$

- Solenoid valves operate in pairs

- set

$$\mathbf{B} = \begin{bmatrix} 1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 1 \end{bmatrix}$$

- $\mathbf{B}$  maps to the 3-axes controllers

$$[u_z \quad u_\theta \quad u_\psi]^T$$

- non-zero terms are the max. duty-cycle to valves

# Results: Z and Pitch Motions

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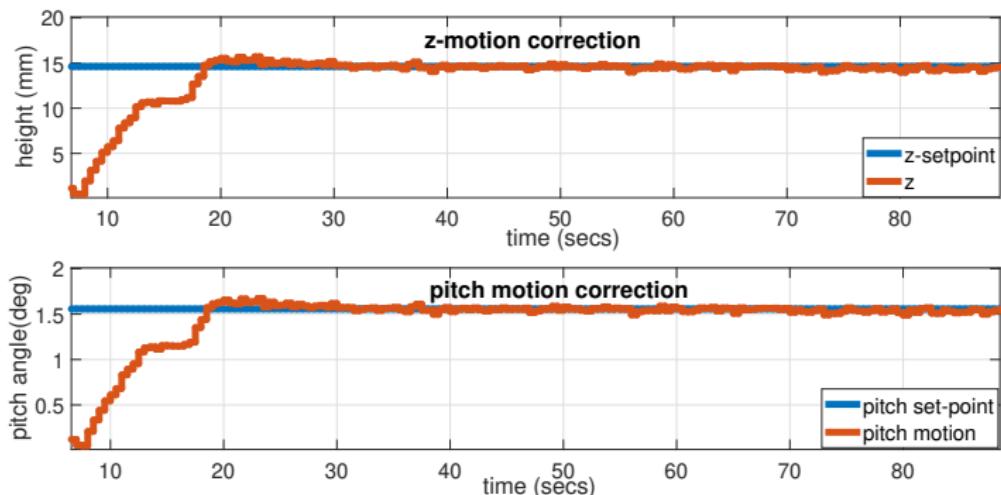
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Goal command:  $(z, \theta, \phi) = (2.5\text{mm}, 0.25^\circ, 35^\circ)$  to  $(14\text{mm}, 1.6^\circ, 45^\circ)^T$ .

# Results: Roll Motion

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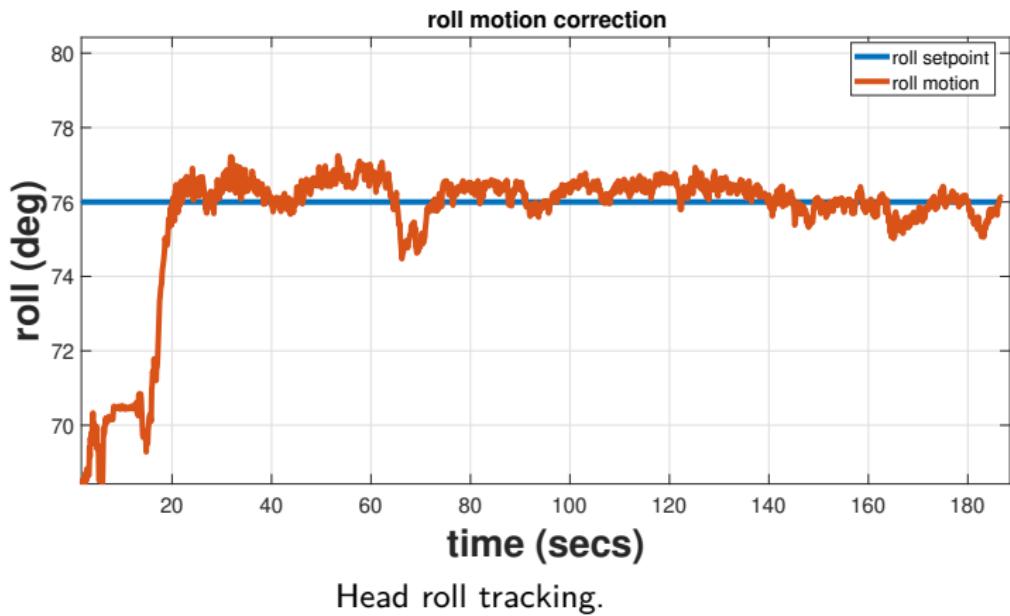
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# Part I.A: Beam Orientation Optimization (BOO)

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## ■ Beam Orientation Optimization (BOO)

- Monte Carlo Tree Search and Neuro-Dynamic Programming for BOO

# BOO Relevant Works

Automating Treatment Planning in Radiation Therapy

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- Sadeghnejad Barkousaraie, Azar, **Olalekan Ogunmolu**, Steve Jiang, and Dan Nguyen. "A fast deep learning approach for beam orientation optimization for prostate cancer treated with intensity-modulated radiation therapy." In *Medical physics: International Journal of Medical Physics Research and Practice*, 47, no. 3 (2020): 880-897.
- **Ogunmolu, Olalekan**, Michael Folkerts, Dan Nguyen, Nicholas Gans, and Steve Jiang. "Deep BOO! Automating Beam Orientation Optimization in Radiation Therapy." In *Algorithm Foundations of Robotics XIII*, Merida, Mexico. Published in *Springer's Proceedings in Advanced Robotics (SPAR) Book*, 2020.
- Barkousaraie, Azar Sadeghnejad, **Olalekan Ogunmolu**, Steve Jiang, and Dan Nguyen. "Using Supervised Learning and Guided Monte Carlo Tree Search for Beam Orientation Optimization in Radiation Therapy." In *Workshop on Artificial Intelligence in Radiation Therapy*, pp. 1-9. Springer, Cham, 2019.
- Azar Sadeghnejad Barkousaraie, **Olalekan Ogunmolu**, Steve Jiang, and Dan Nguyen. "A Fast Deep Learning Approach for Beam Orientation Selection Using Supervised Learning with Column Generation on IMRT Prostate Cancer Patients." *Medical Physics (AAPM)* 46 (6), E237-E237, San Antonio, TX, July 2019.
- **Olalekan Ogunmolu**, Azar Sadeghnejad Barkousaraie, Nicholas Gans, Steve Jiang, and Dan Nguyen. "An Approximate Policy Iteration Scheme for Beam Orientation Selection in Radiation Therapy." *Medical Physics (AAPM)* 46 (6), E386-E386 San Antonio, TX, July 2019.
- Azar Sadeghnejad Barkousaraie, **Olalekan Ogunmolu**, Steve Jiang, and Dan Nguyen. "A Reinforcement Learning Application of Guided Monte Carlo Tree Search Algorithm for Beam Orientation Selection in Radiation Therapy." *Medical Physics (AAPM)* 46 (6), E236-E236, San Antonio, TX, July 2019.

# Contributions

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## Relevant Publications

Ogunmolu, Olalekan, Michael Folkerts, Dan Nguyen, Nicholas Gans, and Steve Jiang. "Deep BOO! Automating Beam Orientation Optimization in Radiation Therapy." In *Algorithm Foundations of Robotics XIII*, Merida, Mexico. Published in *Springer's Proceedings in Advanced Robotics (SPAR) Book*, 2020.

- A sparse tree lookout strategy for games with large state spaces guides transition between beam angle sets
- Tree lookout strategy guided by a deep neural network policy

# BOO Process: Fluence Map Optimization

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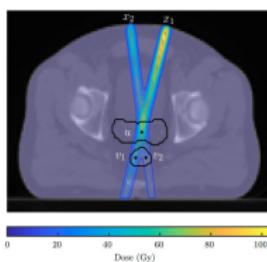
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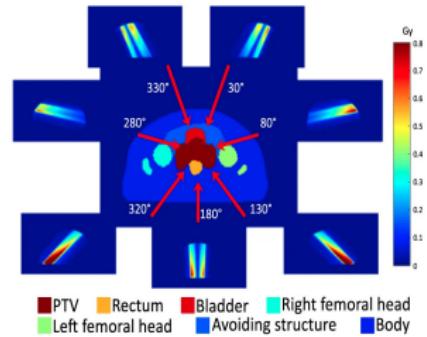
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Prostate CT slice



Prostate before BOO



Fluence Map

# Treatment Plan Flowchart

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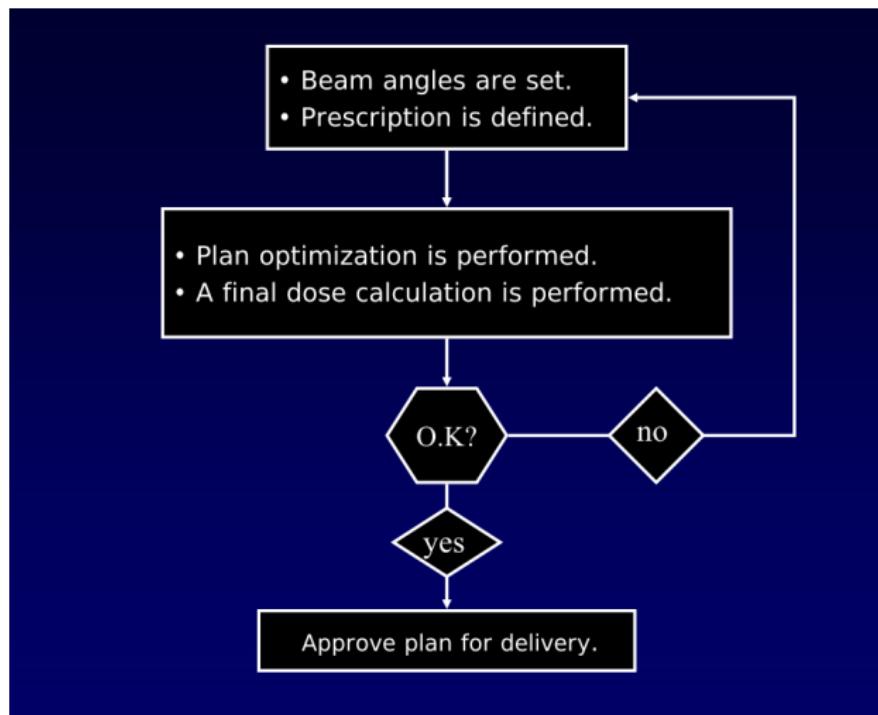
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Reprinted from "IMRT Optimization Algorithms. David Shepard. Swedish Cancer Institute. AAPM 2007."

# Current Approaches

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iDG Results

- Stochastic optimization approaches: simulated annealing; genetic algorithms and gradient search, or a combination of genetic and gradient search algorithms.
- Mixed-integer programming, branch and cut/bound algorithms, beam angle elimination algorithms.
- Commercial planners use some highly non-convex objective (actual function is proprietary and unknown to public).

# IMRT/BOO Motivation

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iDG Results

- Beam orientations largely manually chosen or adopted from a standard protocol for clinical use.
- Pre-solve the dose influence matrices for each beam orientation.
- Then solve FMO.
- Time consuming (hours for dose fluence), and minutes for (FMO); Still solution is often not optimal.

# Approach

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iDG Results

- A Tower Neural Network generates a policy that guides MCTS simulations for two players in a zero-sum Markov game
  - Produces a *utility (value) function* & a subjective *probability distribution*
- Each player in a two-player Markov game finds an alternating best response to the current player's average strategy
  - driving the neural network policy's weights toward an approximate **saddle equilibrium** [Heinrich et al. (2015)].
  - aids network in finding an *approximately optimal* beam angle candidate set that meets a dosimetric requirements.

# Data Preprocessing

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- 77 anonymized patient CT scans,  $D$ , and their dose influence matrices,  $\mathcal{D}_{ij}$
- Scans shaped,  $D \times N \times H \times W$  from prostate cases in previous treatment plans
- Each slice resized to  $64 \times 64$

# State Representation: Prostate Organ Masks

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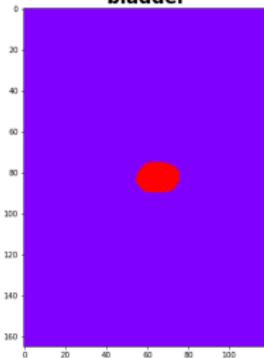
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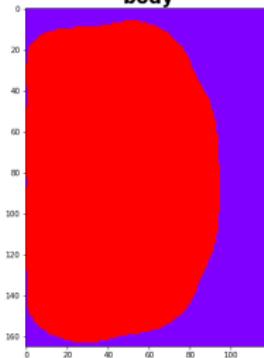
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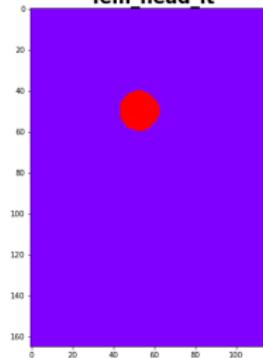
bladder



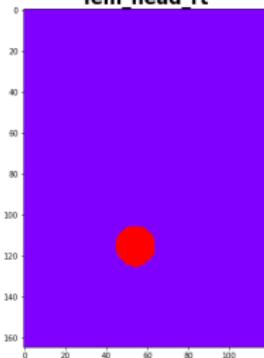
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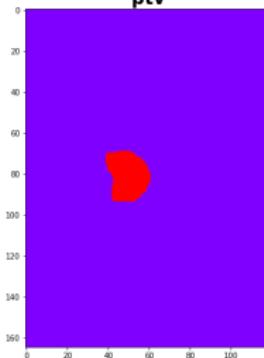
fem\_head\_lt



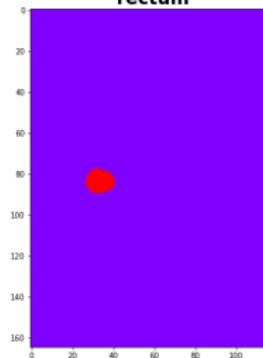
fem\_head\_rt



ptv



rectum



# State Representation: Beam Angles

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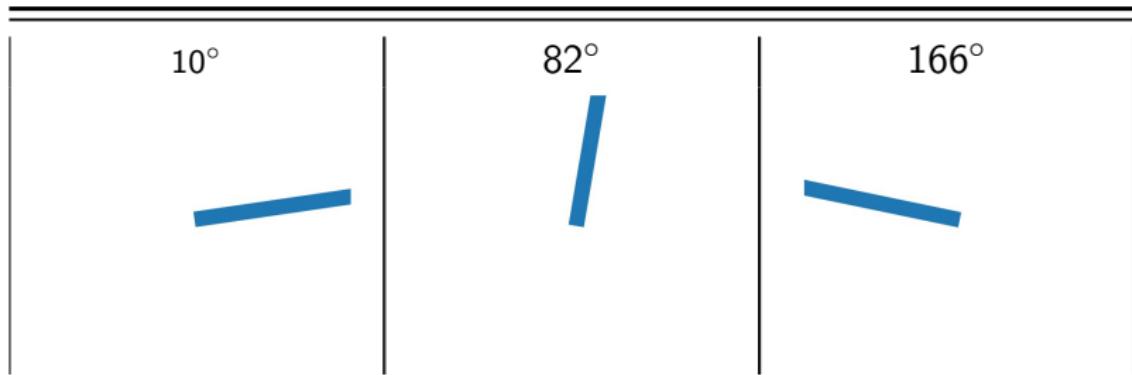
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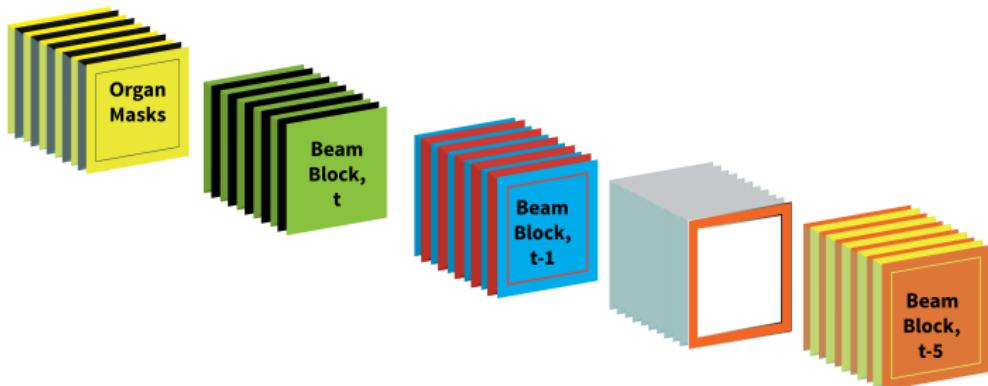
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# State Representation



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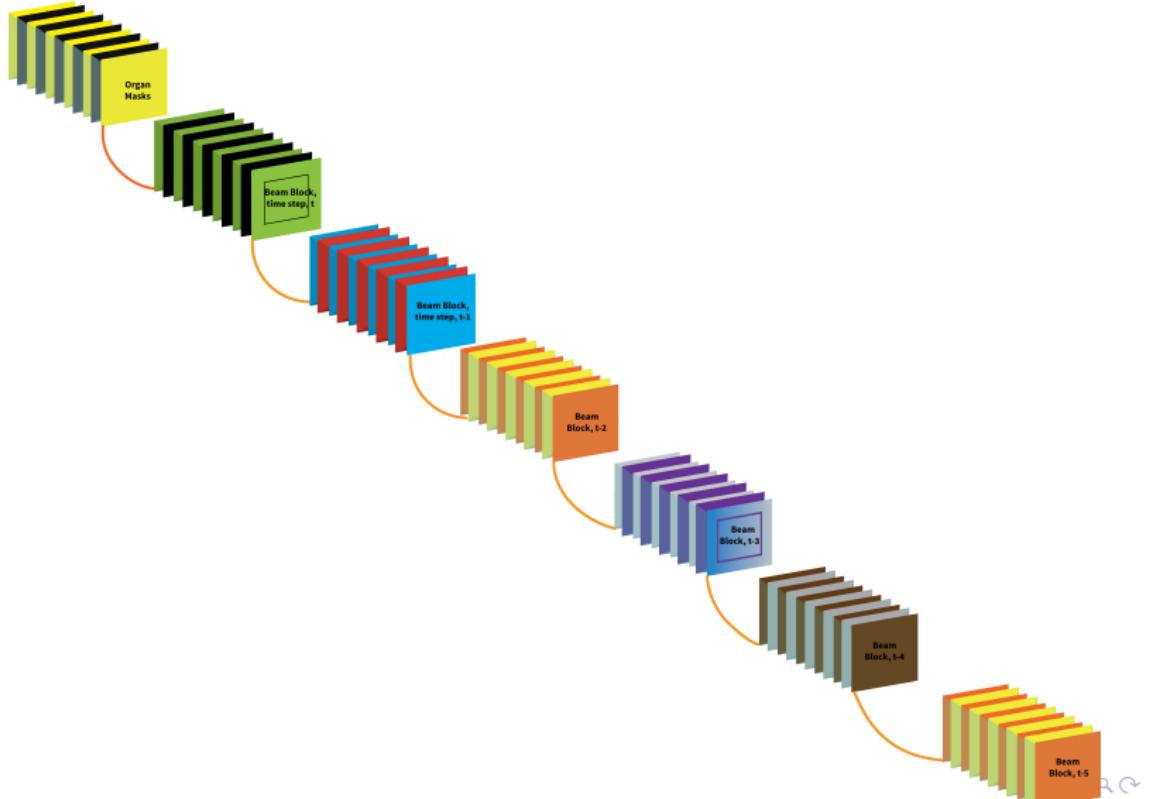
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# Tree Representation and Game Simulation

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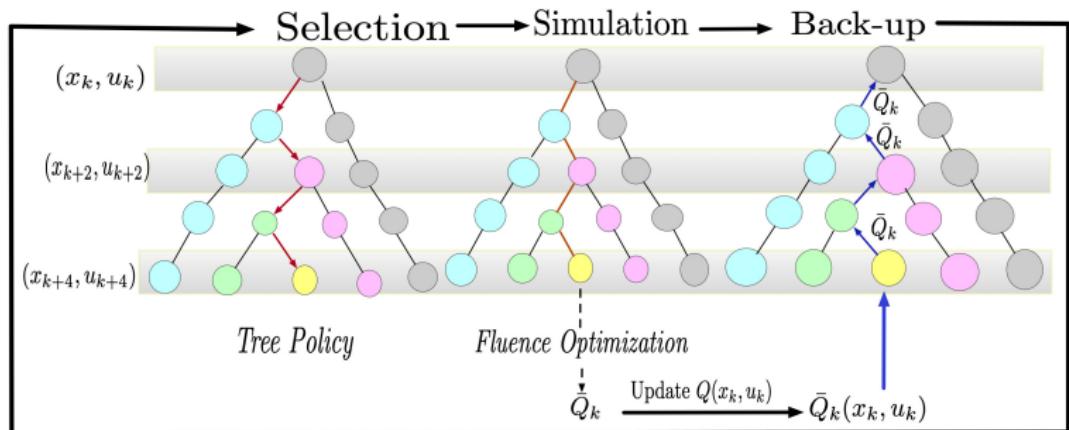
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# Tree Composition

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Every **node** of the tree,  $x$ , has the following fields:

- a pointer to the parent that led to it,  $x.p$ ;
- the beamlets,  $x_b$ , stored at that node;  $b = \{1, \dots, m\}$ ;
- a set of move probabilities prior,  $p(s, a)$ ;
- a pointer  $x.r$ , to the reward  $r_t$ , for the state  $x_t$ ;
- a pointer to the state-action value  $Q(s, a)$  and its upper confidence bound  $U(s, a)$ ;
- a visit count  $N(s, a)$ , that indicates the number of times that node was visited; and
- a pointer  $x.child$ ; to each of its children nodes.

# Game Simulation: Mixed Strategies

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- Each player,  $p_1, p_2$ , bases its decision on a random event's outcome
  - generating a **mixed strategy** determined by **averaging the outcome** of individual plays.
- Both players constitute a two-player **stochastic action selection strategy**:  $\pi(s, a) = Pr(a|s) := \{\pi^{p_1}, \pi^{p_2}\}$  that gives the probability of selecting moves in any given state
- Suppose the game simulation starts from an initial condition  $s_0$ .

# Saddle Point Strategy Formulation

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- The **saddle point strategies** for an optimal control sequence pair  $\{a_t^{p_1^*}, a_t^{p_2^*}\}$  can be recursively obtained by optimizing a state-action value cost,  $\mathcal{J}_t(s, a)$

$$V_t^*(s) = Q_t^*(s_t, \pi_t^{p_1}, \pi_t^{p_2}) = \min_{\pi^{p_1} \in \Pi^{p_1}} \max_{\pi^{p_2} \in \Pi^{p_2}} Q_t^*(s_t, \pi^{p_1}, \pi^{p_2})$$
$$\forall s_t \in \mathcal{S}, \pi^{p_1} \in \Pi^{p_1}, \pi^{p_2} \in \Pi^{p_2}.$$

such that

$$v_{p_1}^* \leq v^* \leq v_{p_2}^* \quad \forall \{\pi_t^{p_1}, \pi_t^{p_2}\}_{0 \leq t \leq T}.$$

where  $v_{p_i}^*$  are the respective optimal values for each player.

# Fluence Map Optimization

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- $\mathcal{X} \implies$  total discretized voxels of interest (*VOI's*) in a target volume
- $\mathcal{B}_1 \cup \mathcal{B}_2 \cup \dots \cup \mathcal{B}_n \subseteq \mathcal{B} \implies$  beam partition subset
- $\mathcal{D}_{ij}(\theta_k) \implies$  matrix that describes each dose influence,  $d_i$ 
  - Computed by calculating each  $d_j$  for every bixel,  $j$ , at every  $\varphi^\circ$ , resolution, where  $j \in \mathcal{B}_k$

# Methods: FMO problem definition

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## ■ Cost

$$\frac{1}{v_s} \sum_{s \in \text{OARs}} \|(\underline{b}_s - \underline{w}_s \mathcal{D}_{ij}^s \mathbf{x}_s)_+\|_2^2 + \frac{1}{v_s} \sum_{s \in \text{PTVs}} \|(\bar{w}_s \mathcal{D}_{ij}^s \mathbf{x}_s - b_s)_+\|_2^2 \quad (1)$$

■ Pre-calculated dose term:  $\mathbf{A}\mathbf{x} = \{\sum_s \frac{w_s}{v_s} \mathcal{D}_{ij}^s \mathbf{x}_s \mid \mathcal{D}_{ij} \in \mathbb{R}^{n \times l}, n > l\}$

# Methods: FMO

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- Rewriting the objective

$$\min \frac{1}{2} \|Ax - b\|_2^2 \quad \text{subject to } x \geq 0.$$

- With Lagrangian:

$$L(x, \lambda) = \min \frac{1}{2} \|Ax - b\|_2^2 - \lambda^T x.$$

- Introducing an auxiliary variable  $z$ , we have

$$\min_x \frac{1}{2} \|Ax - b\|_2^2, \quad \text{subject to } z = x, \quad z \geq 0,$$

# Methods: FMO by way of ADMM

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- Solving either the  $\mathbf{x}$  and  $\mathbf{z}$  sub-problems, we have

$$\mathbf{x}^{k+1} = (\mathbf{A}^T \mathbf{A} + \rho \mathbf{I})^{-1} (\mathbf{A}^T \mathbf{b} + \rho \mathbf{z}^k - \boldsymbol{\lambda}^k). \quad (2)$$

- And using the soft-thresholding operator,  $S_{\boldsymbol{\lambda}/\rho}$ , we find that

$$\mathbf{z}^{k+1} = S_{\boldsymbol{\lambda}/\rho} (\mathbf{x}^{k+1} + \boldsymbol{\lambda}^k), \quad (3)$$

where  $S_{\boldsymbol{\lambda}/\rho}(\tau) = (\mathbf{x} - \boldsymbol{\lambda}/\rho)_+ - (-\tau - \boldsymbol{\lambda}/\rho)_+$ .  $\boldsymbol{\lambda}$  is updated as

$$\boldsymbol{\lambda}^{k+1} = \boldsymbol{\lambda}^k - \gamma (\mathbf{z}^{k+1} - \mathbf{x}^{k+1}), \quad (4)$$

where  $\gamma$  is a parameter that controls the step length.

# BOO Results: Testing of self-play network

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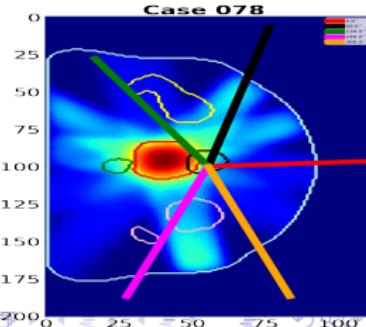
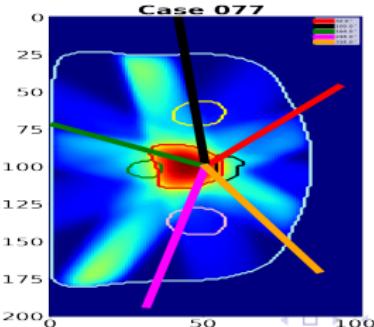
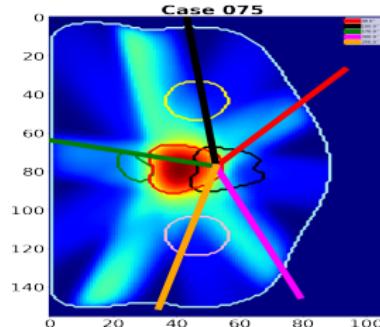
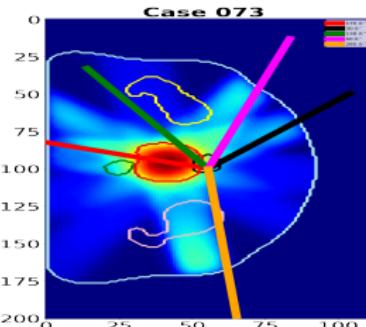
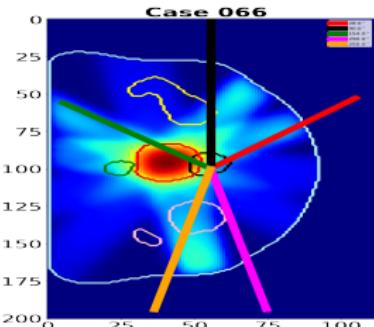
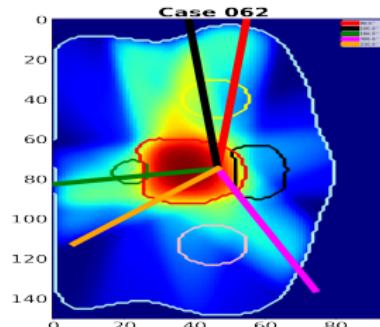
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## Inference Regime



# Part I.B: Supervised Column Generation Pretraining for BOO

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## ■ Beam Orientation Optimization (BOO)

- Monte Carlo Tree Search and Neuro-Dynamic Programming for BOO
- → Column Generation as Pretraining for Deep Neural Network BOO

### Relevant Publication

- Sadeghnejad Barkousaraie, Azar, Olalekan Ogunmolu, Steve Jiang, and Dan Nguyen. "A fast deep learning approach for beam orientation optimization for prostate cancer treated with intensity-modulated radiation therapy." In *Medical physics: International Journal of Medical Physics Research and Practice*, 47, no. 3 (2020): 880-897.

# Column Generation as Pretraining for DNN

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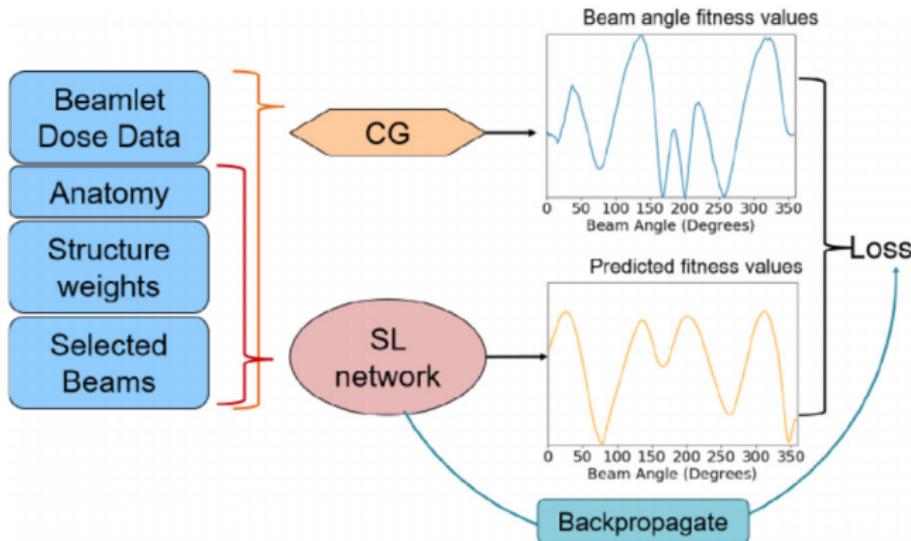
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# Network Structure

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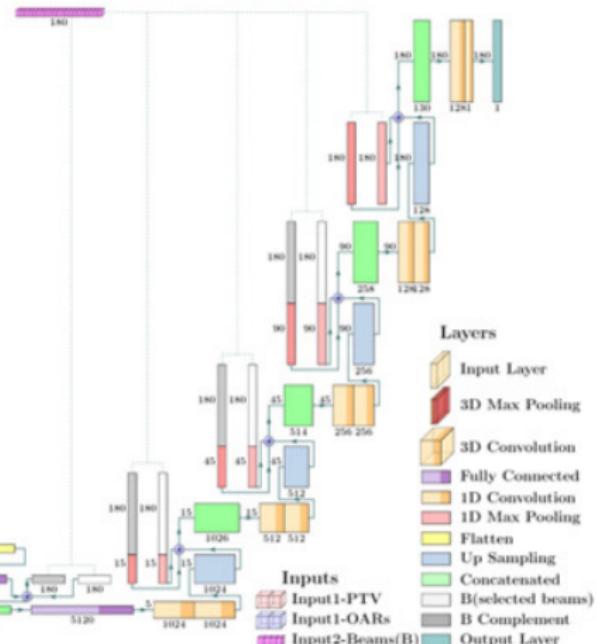
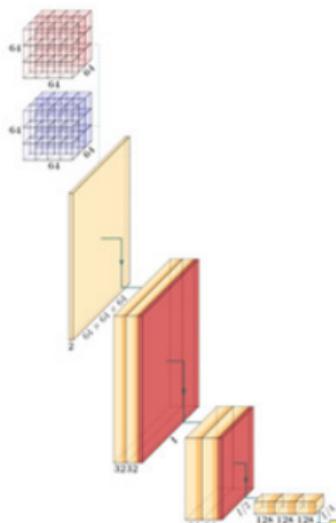
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# Training and Validation Loss

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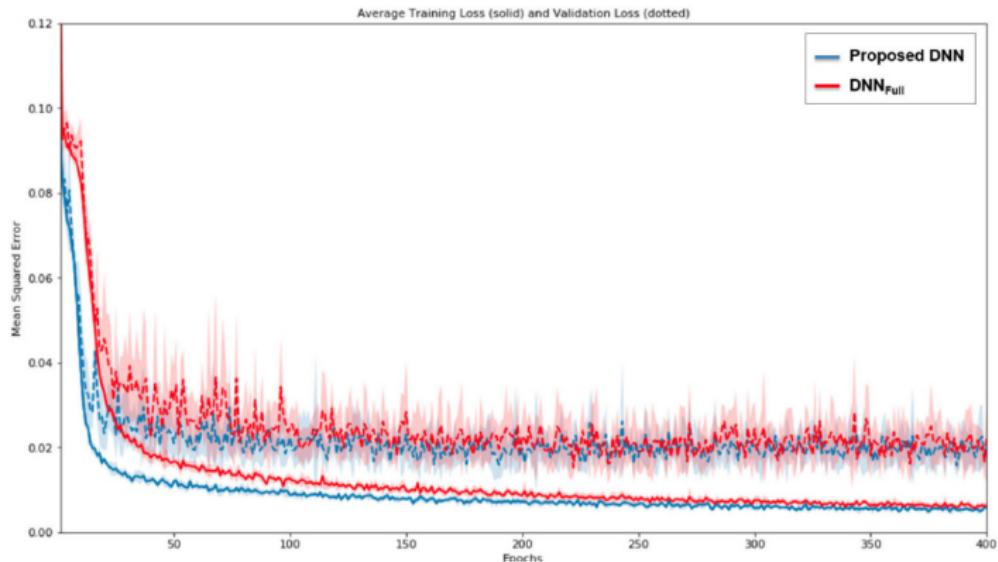
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*Average training (solid) and validation (dotted) loss function (MSE) values across six cross-validation folds for the network (blue) and full network.*

# Inference: Column Generation vs U-Net

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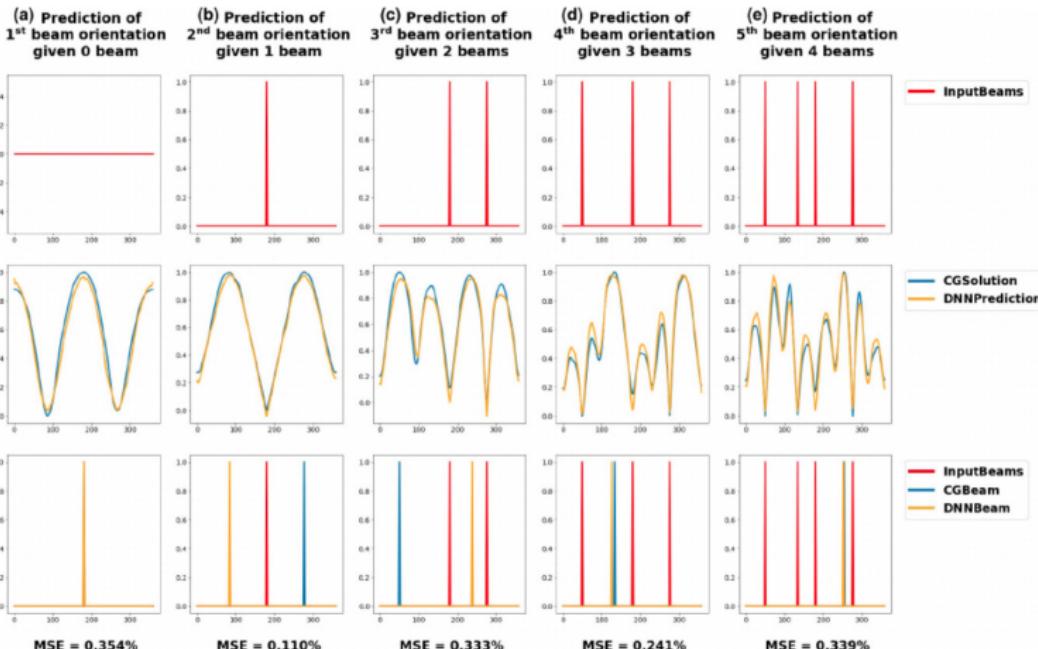
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- (a) Prediction of 1st beam orientation given no beam. (b) Prediction of 2nd beam orientation given 1 beam.  
(c) Prediction of 3rd beam orientation given 2 beams. (d) Prediction of 4th beam orientation given 3 beams.  
(e) Prediction of 5th beam orientation given 4 beams.

# Dose Washes of Column Generation vs Neural Network

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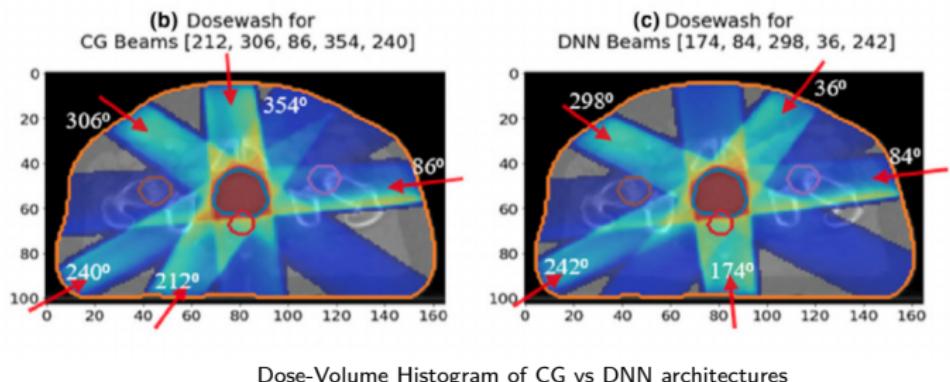
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# Dose Volume Histograms

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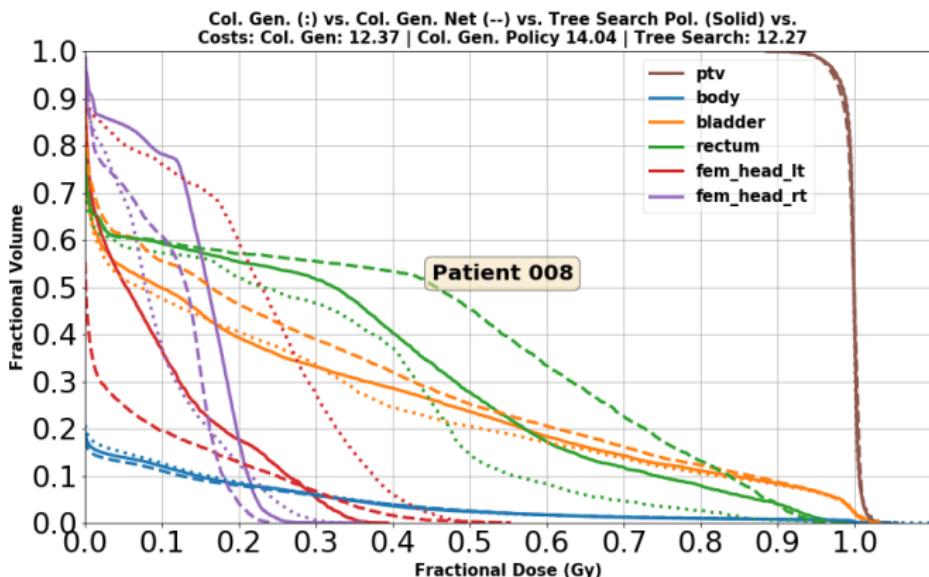
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# Conclusions

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- Finding the good beam angle candidates is orders of magnitude faster than the current approaches
  - Based on a neural network generative model of an MDP
  - Sparse lookahead search builds tree with nodes labeled by state-action pairs in an alternating manner (2-3 minutes).
  - Tree built stagewise from root to nodes has fixed depth; sample rewards stored on edges connecting state-action with state nodes
- Beam angles prediction takes between 2-3 minutes with MCTS vs 1 minute with Column Generation Pretraining.

# Part III: Robustness Margins and Robust Deep Policies

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- Robustness Margins and Robust Deep Policies for Nonlinear Control

# Iterative Dynamic Game

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## Relevant Papers

- Ogunmolu, Olalekan, Nicholas Gans, and Tyler Summers. "Minimax iterative dynamic game: Application to nonlinear robot control tasks." In *2018 IEEE/RSJ International Conference on Intelligent Robots and Systems (IROS)*, pp. 6919-6925. IEEE, 2018.
- Ogunmolu, Olalekan, Nicholas Gans, and Tyler Summers. "Robust zero-sum deep reinforcement learning." *arXiv preprint arXiv:1710.00491* (2017).
- Summers, Tyler, Olalekan Ogunmolu, Nicholas Gans. "Robustness Margins and Robust Guided Policy Search for Deep Reinforcement Learning." In *IEEE/RSJ International Conference on Robots and Intelligent Systems,(Abstract Only Track)*, vol. 8. 2017.

# The robustness conundrum

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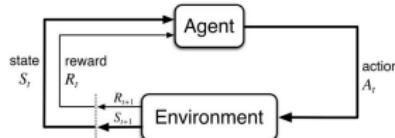
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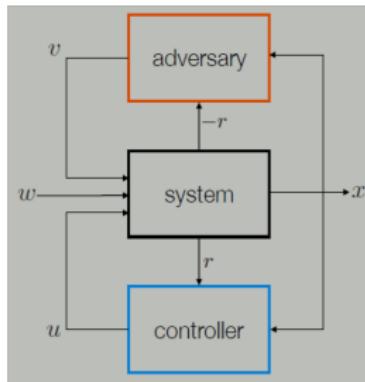
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- How to know *a priori* a policy's robustness limits?



- How to inculcate robustness into multistage decision policies?



# Problem Setup

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- To quantify the brittleness, we optimize the stage cost

$$\max_{\mathbf{v}_t \sim \psi \in \Psi} \left[ \sum_{t=0}^T \underbrace{c(\mathbf{x}_t, \mathbf{u}_t)}_{\text{nominal}} - \gamma \underbrace{g(\mathbf{v}_t)}_{\text{adversarial}} \right]$$

- To mitigate lack of robustness, we optimize the *cost-to-go*

$$\mathcal{J}_t(\mathbf{x}_t, \pi, \psi) = \min_{\mathbf{u}_t \sim \pi} \max_{\mathbf{v}_t \sim \psi} \left( \sum_{t=0}^{T-1} \ell_t(\mathbf{x}_t, \mathbf{u}_t, \mathbf{v}_t) + L_T(\mathbf{x}_T) \right),$$

- and seek a saddle point equilibrium policy that satisfies

$$\mathcal{J}_t(\mathbf{x}_t, \pi^*, \psi) \leq \mathcal{J}_t(\mathbf{x}_t, \pi^*, \psi^*) \leq \mathcal{J}_t(\mathbf{x}_t, \pi, \psi^*),$$

# Results: Brittleness Quantification

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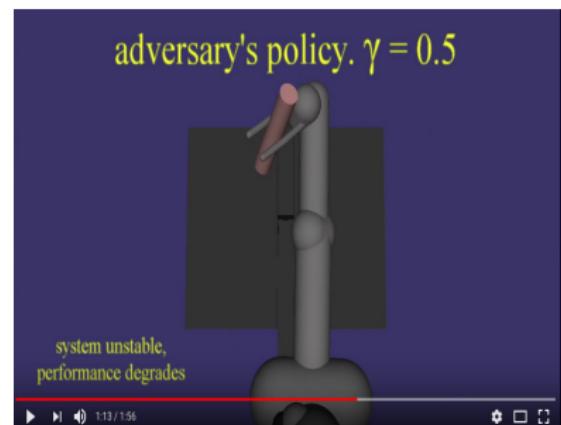
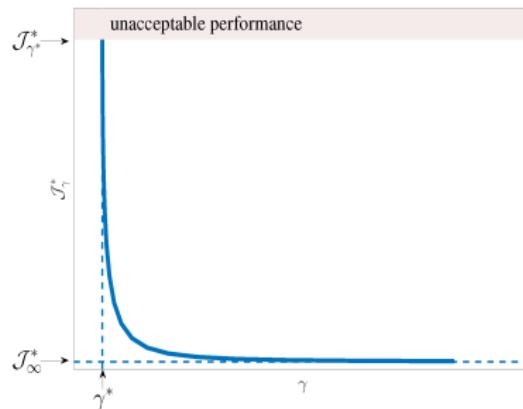
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# Results: Iterative Dynamic Game

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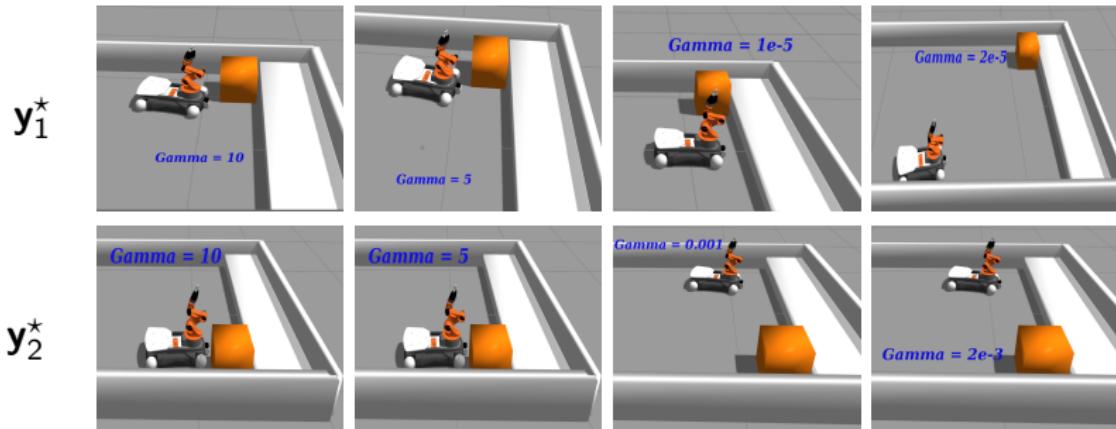


Table: \*

End pose of the KUKA platform with our iDG formulation given different  
goal states and  $\gamma$ -values

# End of Slides

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**Thank you!**

# Future Work: MRI/RT Immobilization

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- Explore multiple parallel robot mechanisms for head motion correction
- Adopt best practices from one of the SOTA modeling approaches viz
  - *constant curvature approach* [Godage et al. (2016)],
  - the *continuous Cosserat approach* [Renda et al. (2014)], and
  - the *multi-body hyper-redundant model* [Kang et al. (2012)].

# Future Work

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iDG Results

- Robust Stabilization via inverse optimality
  - Imbibing robust Lyapunov stability into deep optimal controllers
    - Build on Freeman and Kokotovic's point-wise min-norm robust control lyapunov function to realize a meaningful value function (Int. Journal of Optimal Control, 1996)
    - Simplify algorithm for real-time control
  - Carry out numerical and experimental verification and validation
  - Important in multistage decision policies, reinforcement learning controllers

## Automating Treatment Planning in Radiation Therapy

Lekan Ogunmolu

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### iDG

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- Radhini Chelvarajah, Brigid Leighton, Linda Martin, Wayne Smith, and Rachael Beldham-Collins. Cranial immobilisation—is there a better way? *Radiographer*, 51(1):29–33, 2004.
- Xinmin Liu, Andrew H Belcher, Zachary Grelewicz, and Rodney D Wiersma. Robotic stage for head motion correction in stereotactic radiosurgery. In *2015 American Control Conference (ACC)*, pages 5776–5781. IEEE, 2015.
- Andrew Belcher. *Patient Motion Management with 6-DOF Robotics for Frameless and Maskless Stereotactic Radiosurgery*. PhD thesis, The University of Chicago, 2017.
- Olalekan Ogunmolu and Rodney Wiersma. A Real-Time Patient Head Motion Correction Mechanism for MRI-Linac Systems. In *Joint AAPM / COMP Meeting, Virtual*, 2020.
- James Pikul, Itai Cohen, and Robert Shepherd. Stretchable surfaces with programmable texture, May 2 2019. US Patent App. 16/161,029.
- Johannes Heinrich, Marc Lanctot, and David Silver. Fictitious self-play in extensive-form games. In *International Conference on Machine Learning*, pages 805–813, 2015.
- Isuru S Godage, Gustavo A Medrano-Cerda, David T Branson, Emanuele Guglielmino, and Darwin G Caldwell. Dynamics for variable length multisection continuum arms. *The International Journal of Robotics Research*, 35(6):695–722, 2016.
- Federico Renda, Michele Giorelli, Marcello Calisti, Matteo Cianchetti, and Cecilia Laschi. Dynamic model of a multibending soft robot arm driven by cables. *IEEE Transactions on Robotics*, 30(5):1109–1122, 2014.
- Rongjie Kang, David T Branson, Emanuele Guglielmino, and Darwin G Caldwell. Dynamic modeling and control of an octopus inspired multiple continuum arm robot. *Computers & Mathematics with Applications*, 64(5):1004–1016, 2012.