

Automating
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Automating Treatment Planning in Radiation Therapy

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February 04, 2021

Acknowledgments

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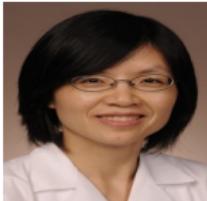
Steve Jiang, UTSW



Nick Gans, UTARI



Xuejun Gu, UTSW



Dan Nguyen, UTSW



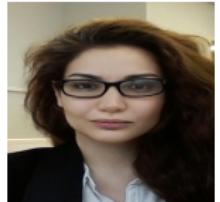
Rod Wiersma, Penn



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Funding Sources

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Talk Outline

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

Research Significance

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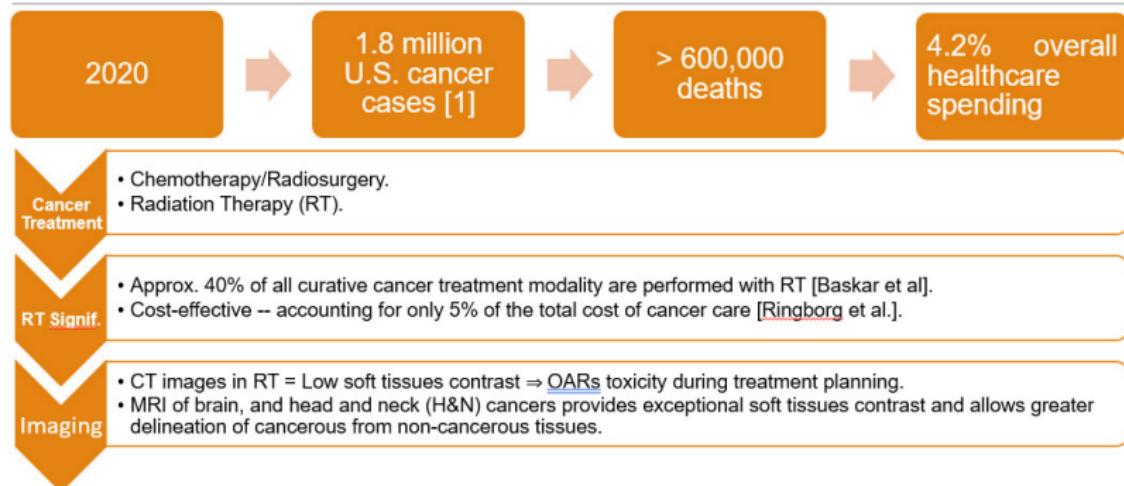
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IMRT Treatment Planning (Beam Delivery)

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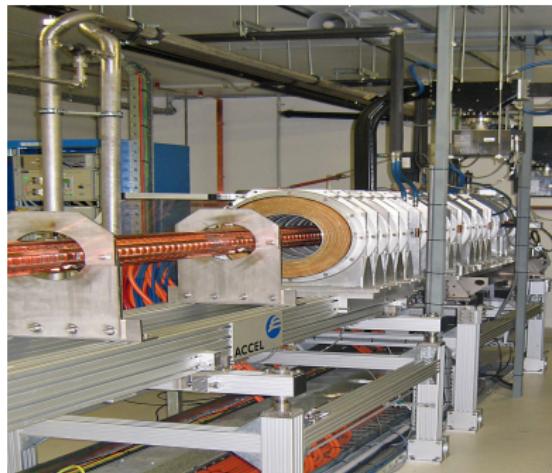
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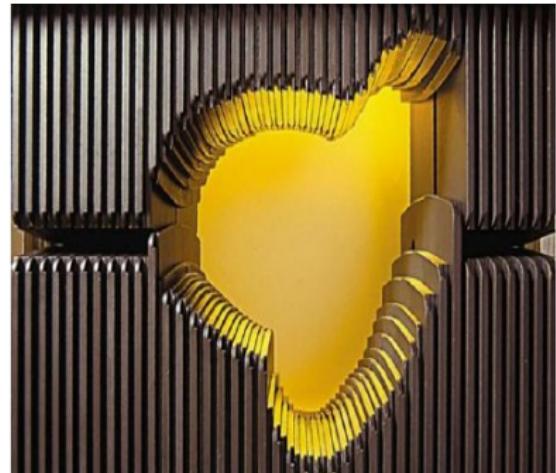
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The Australian Synchrotron.



Multi-leaf collimator (Varian)

Radiation Delivery Couch and Gantry

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Varian's TrueBeam Radiotherapy System.

Part I.A: Beam Orientation Optimization (BOO)

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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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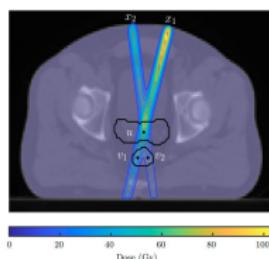
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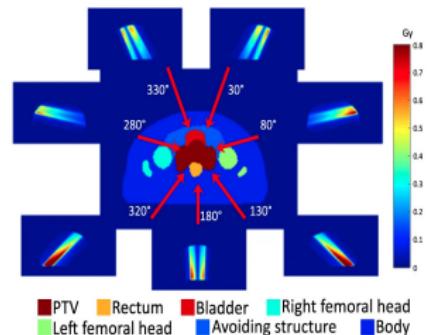
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Prostate CT slice



Prostate before
BOO



Fluence Map

Treatment Plan Flowchart

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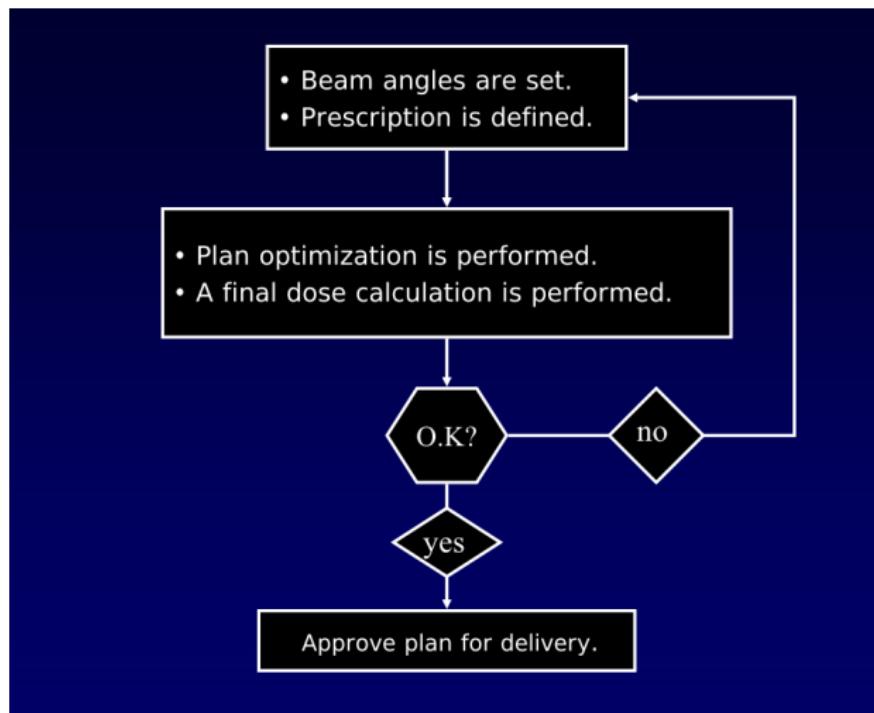
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Reprinted from "IMRT Optimization Algorithms. David Shepard. Swedish Cancer Institute. AAPM 2007."

Current Approaches

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References

- 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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- 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.

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- 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 64×64

State Representation: Prostate Organ Masks

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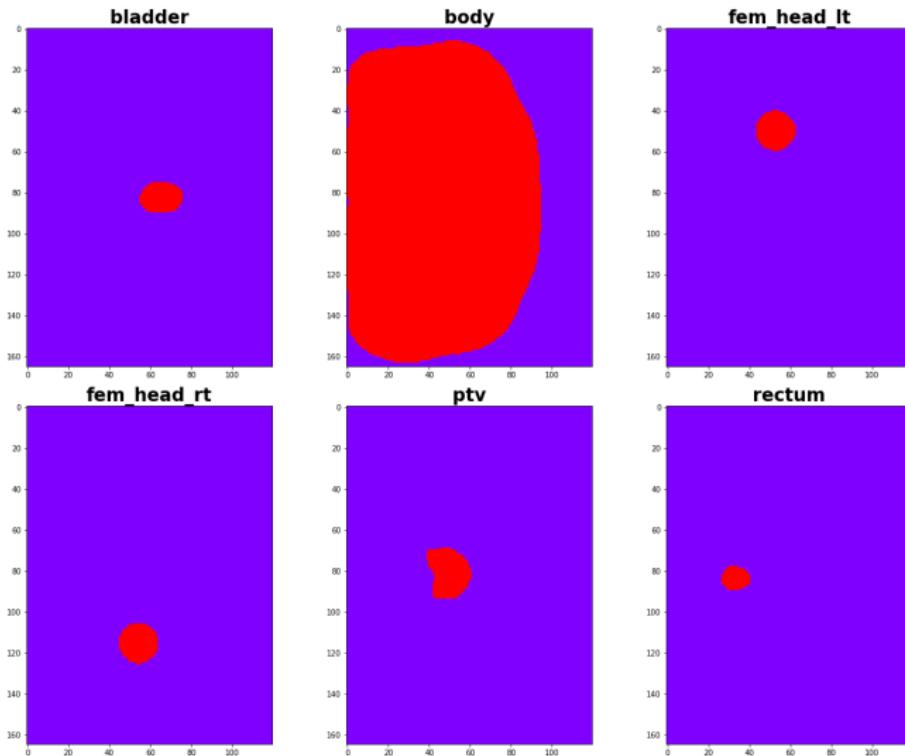
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State Representation: Beam Angles

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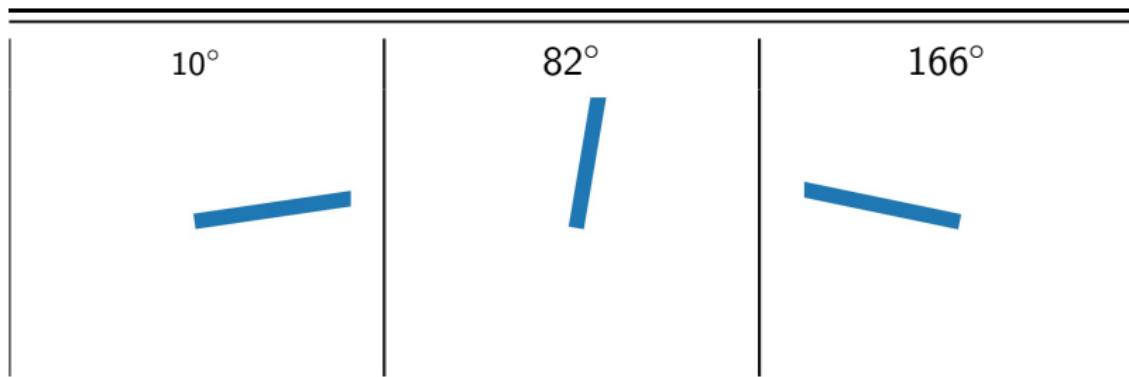
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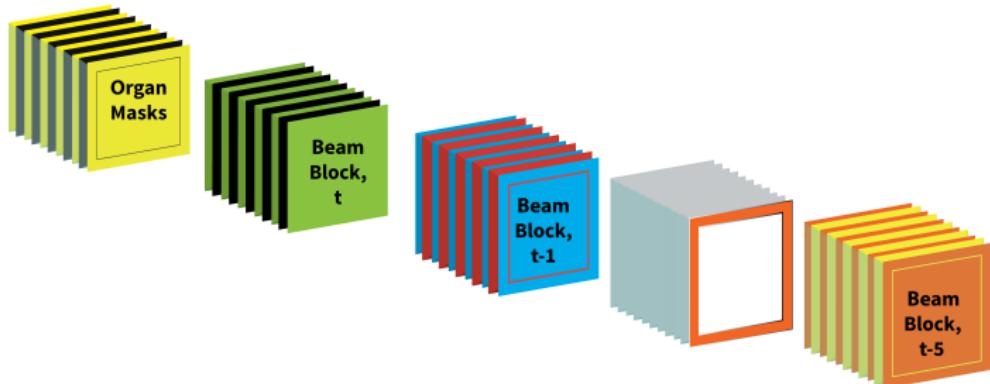
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State Representation



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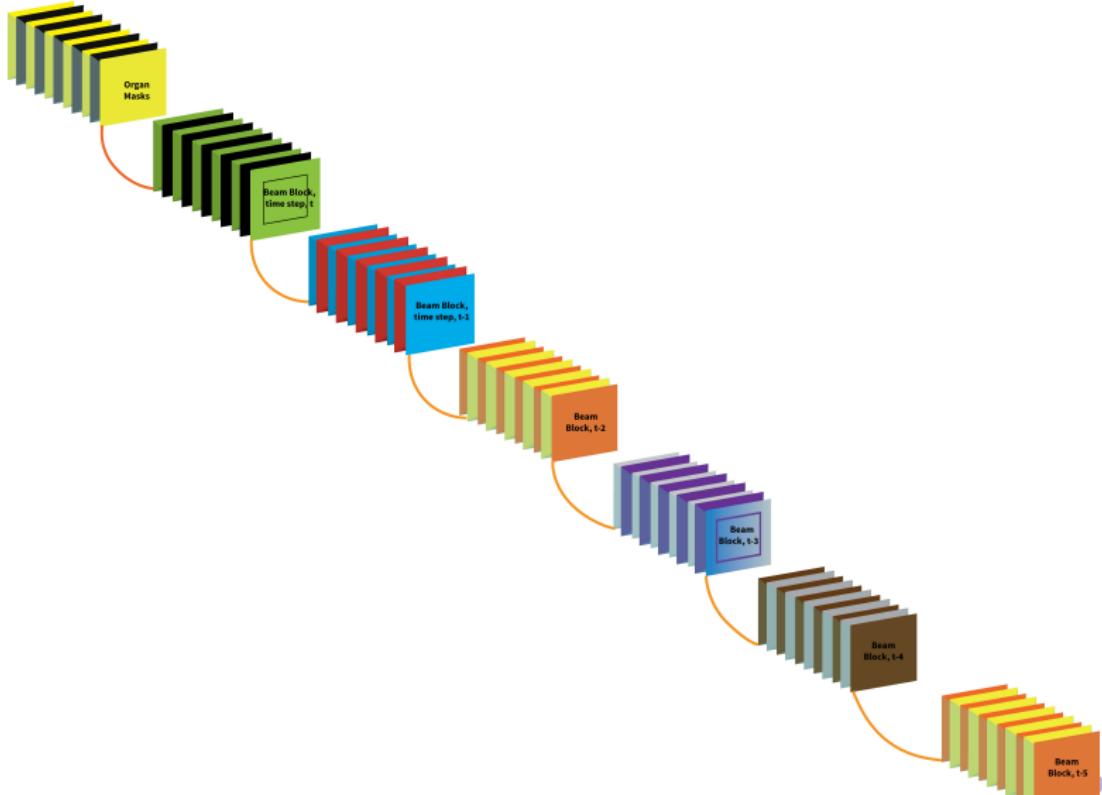
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Tree Representation and Game Simulation

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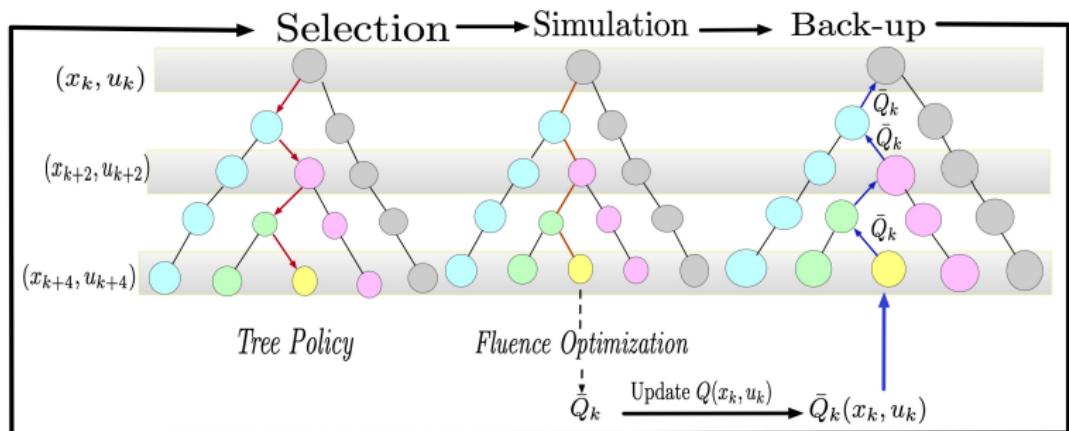
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Tree Composition

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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_i for every bixel, j , at every φ° , 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:

$$\mathbf{Ax} = \left\{ \sum_s \frac{w_s}{v_s} \mathcal{D}_{ij}^s \mathbf{x}_s \mid \mathcal{D}_{ij} \in \mathbb{R}^{n \times l}, n > l \right\}$$

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 γ is a parameter that controls the step length.

Training and Validation Loss

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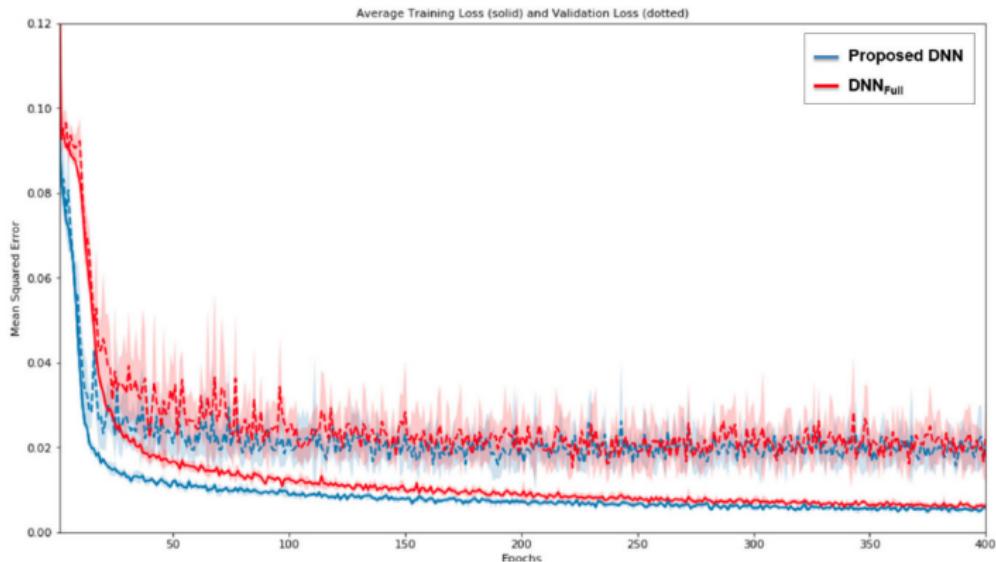
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Average training (solid) and validation (dotted) loss function (MSE) values across six cross-validation folds for the network (blue) and full network.

BOO Results: Testing of self-play network

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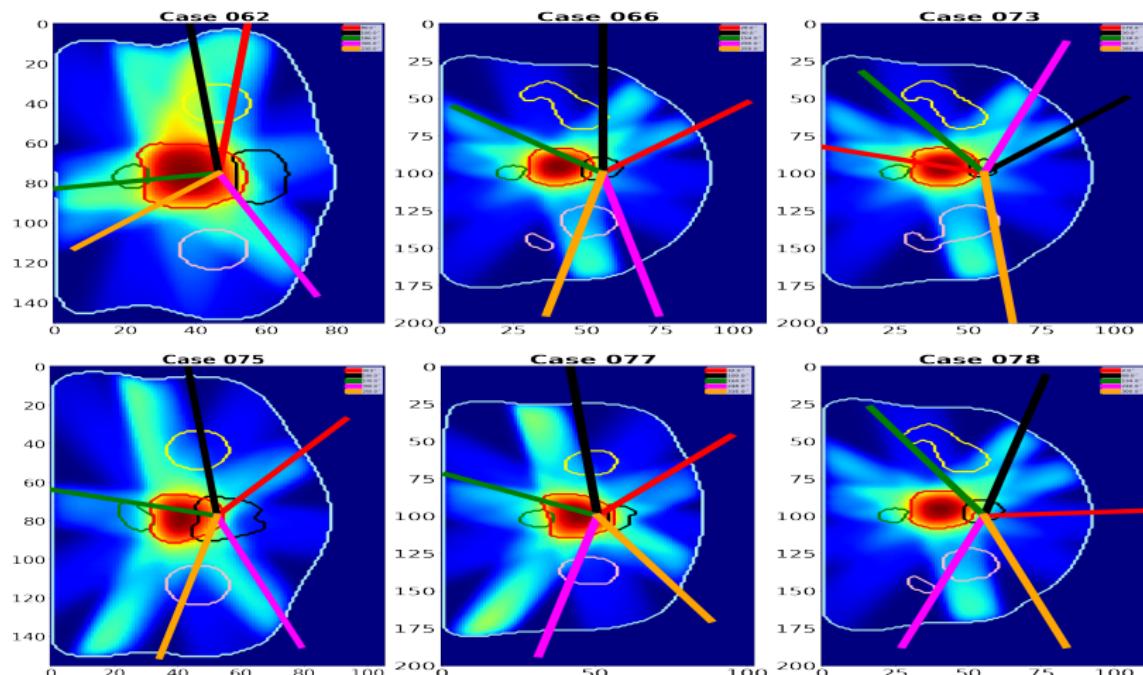
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Dose Washes of Column Generation vs Neural Network

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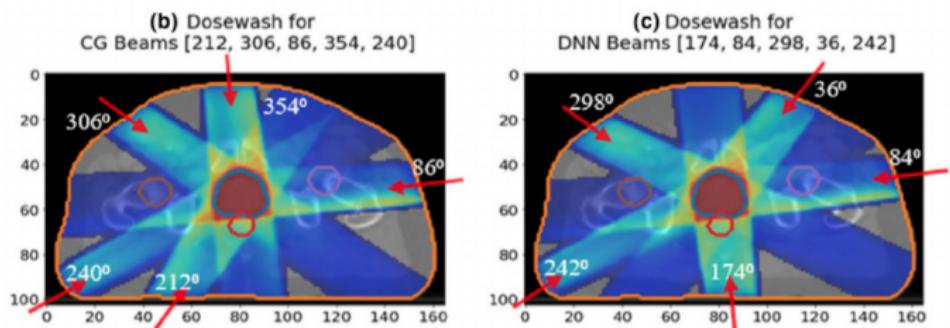
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Dose-Volume Histogram of CG vs DNN architectures [Sadeghnejad Barkousaraie, Azar and Ogunmolu, Olalekan and Jiang, Steve and Nguyen, Dan (2019)].

Dose Volume Histograms

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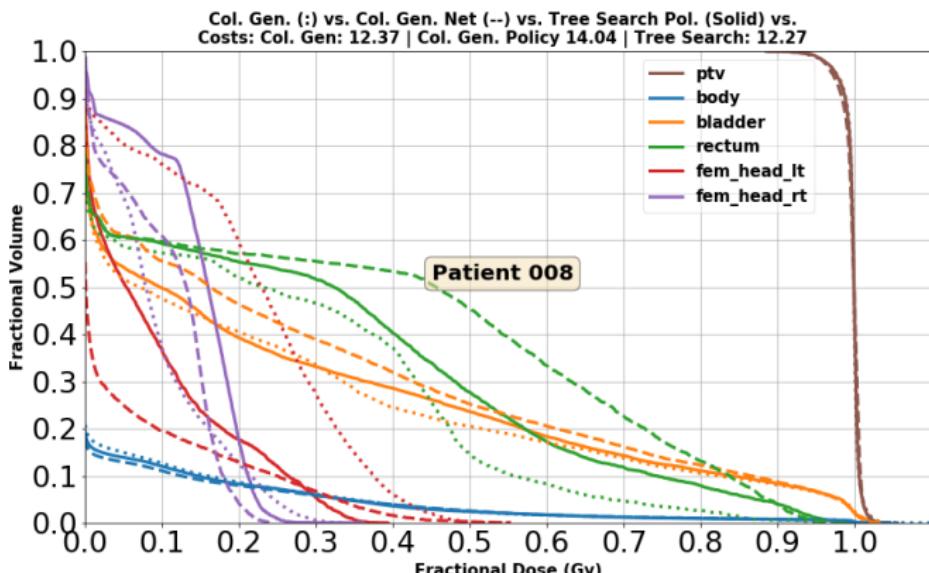
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- Finding the good beam angle candidates is orders of magnitude faster than the current approaches
 - Based on a neural network generative model of an MDP
 - Sparse lookahead search builds tree with nodes labeled by state-action pairs in an alternating 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.

Head Stabilization in Radiation Therapy (RT)

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- Head Stabilization in Cancer Radiation Therapy
 - Intensity-Modulated RT (IMRT)

Varian's TrueBeam Radiotherapy System.

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Correcting Head Motion: RT and MRI-LINACs

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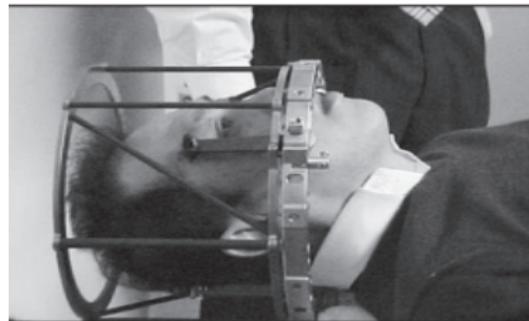
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(a) The BRW SRS Frame [Chelvarajah et al. (2004)]



(b) Thermoplastic masks



(c) Frame With MRI Coils (PSOM)

4-D Motion Correction Stage

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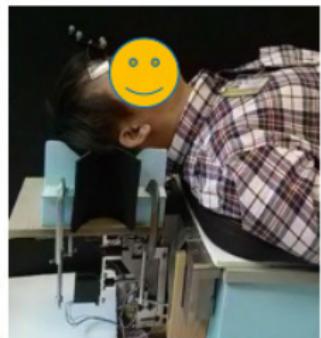
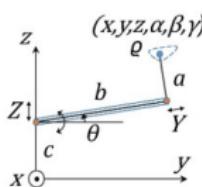
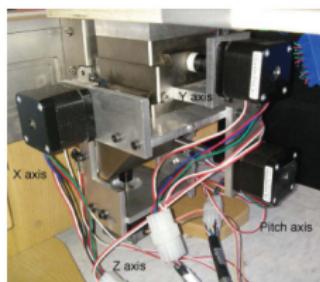
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Liu et al. (2015)

4-DOF Motion Controller Block Diagram

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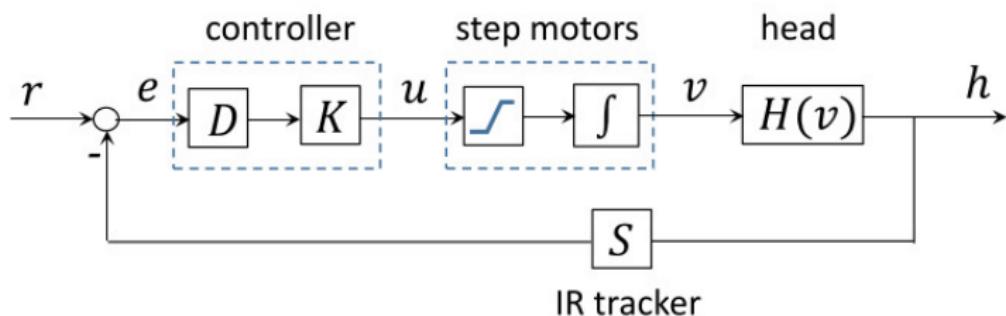
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Liu et al. (2015)

Phantom Feedback Motion Correction Results

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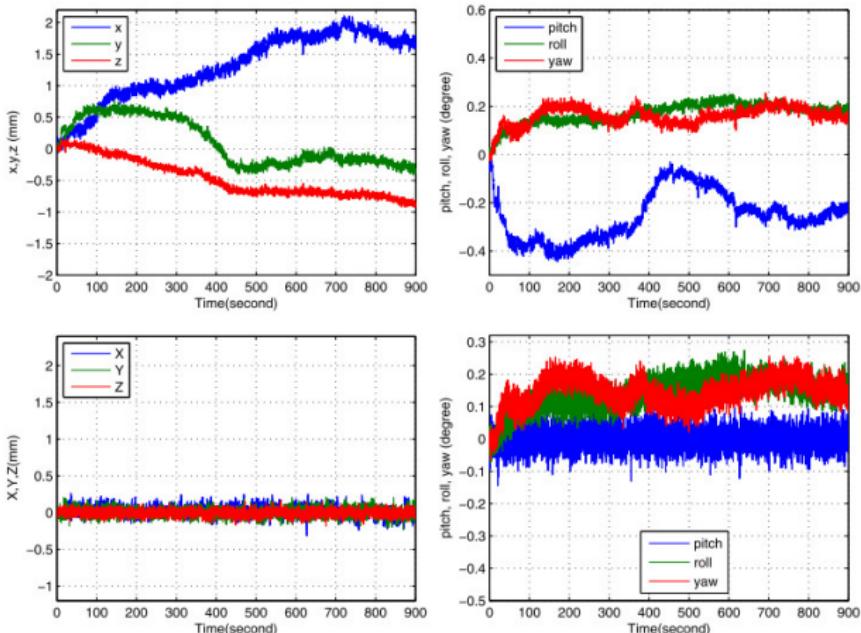
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Time response of feedback control without (left) and with (right) decoupling control [Liu et al. (2015)].

Human Volunteer Feedback Motion Correction Results

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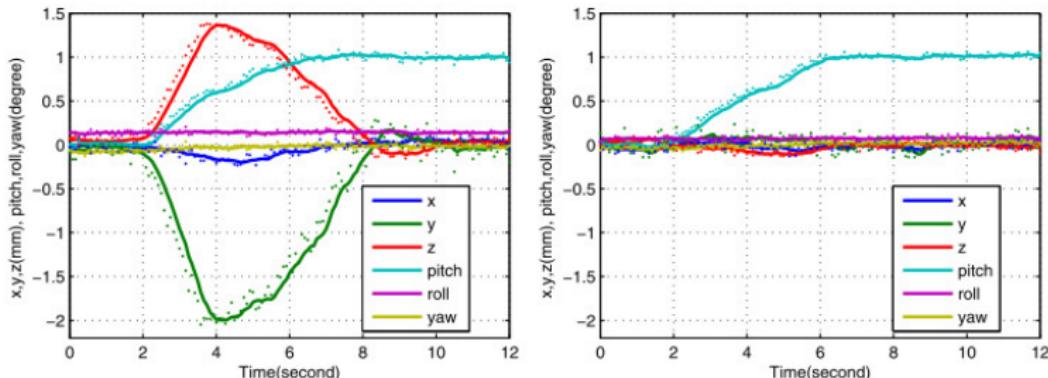
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Head Motion Without and With Motion Correction. Left: Coupled Axes; Right: Decoupled Axes.

SRS: Wiersma Stewart-Gough Platform

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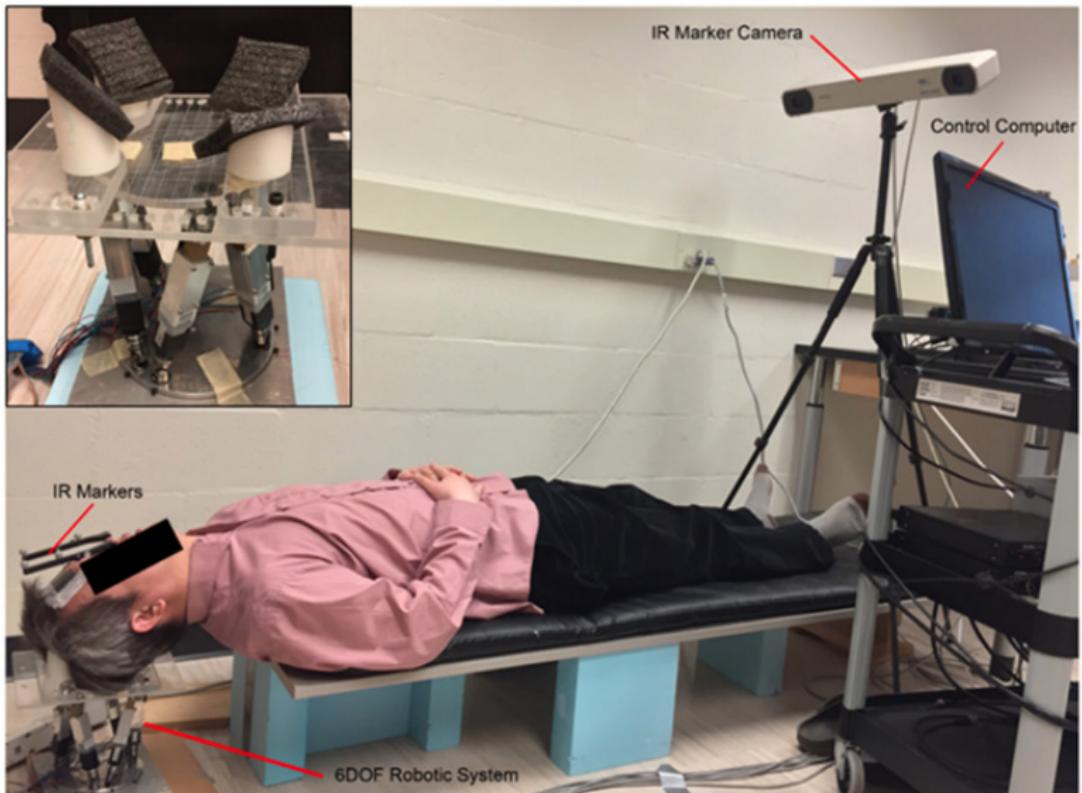
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6-DOF Motion Correction Results

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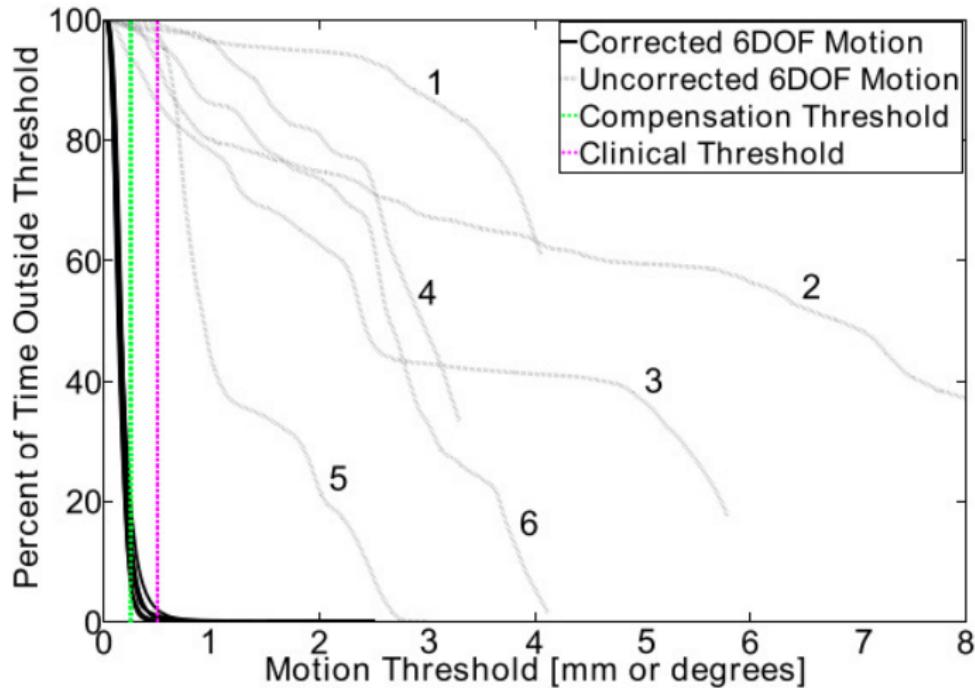
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Drawbacks of current solutions

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- Rigid patient's body assumption
- Non-compliant immobilization devices
- Invasiveness during radiosurgery/RT
- Attenuation of photon beams

Robotic Radiosurgery

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

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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)



Radiation Delivery Couch and Gantry

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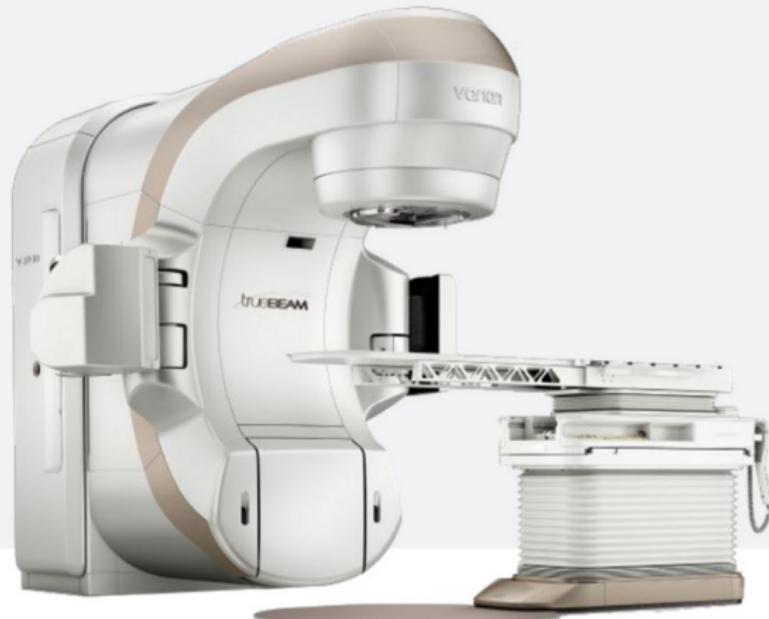
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Varian's TrueBeam Radiotherapy System.

Next-Gen RT Treatment with MRI-LINACs

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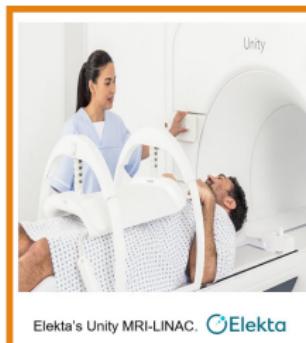
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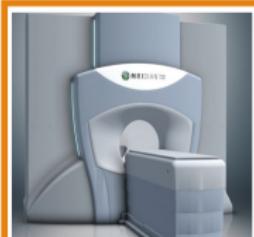
References



Elekta's Unity MRI-LINAC.



MagnetTx



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 univolved, online, and real-time cancer RT treatment [Raaymakers et al., Raaymakers et al.]
 - 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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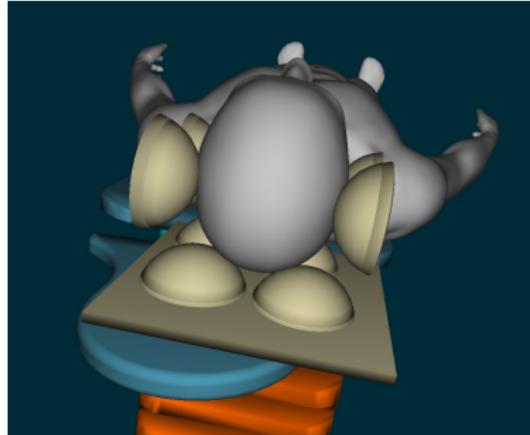
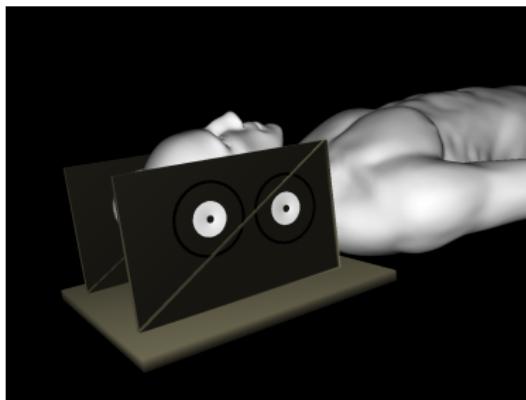
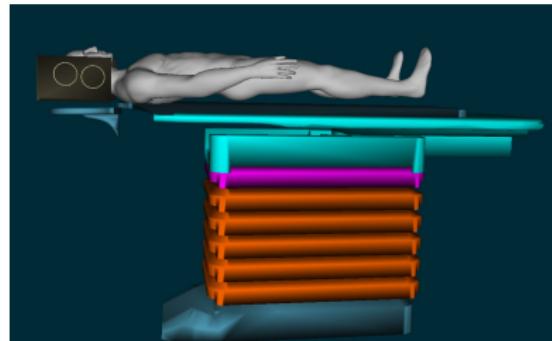
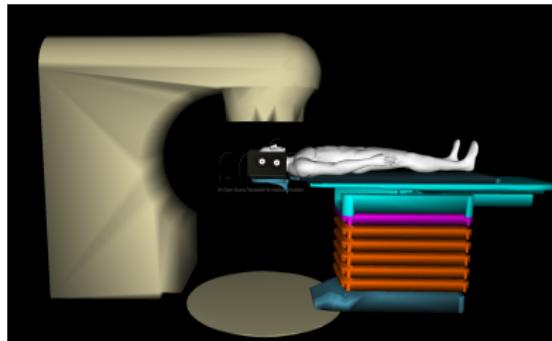
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Cephalopods-inspired CCOARSE Actuator Design

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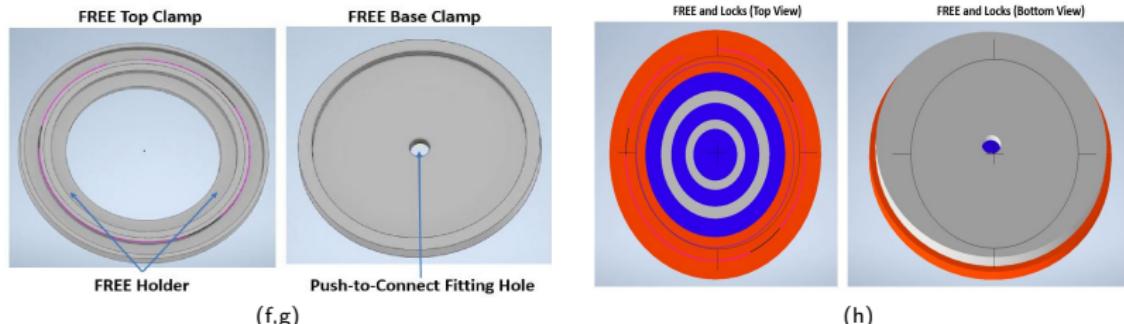
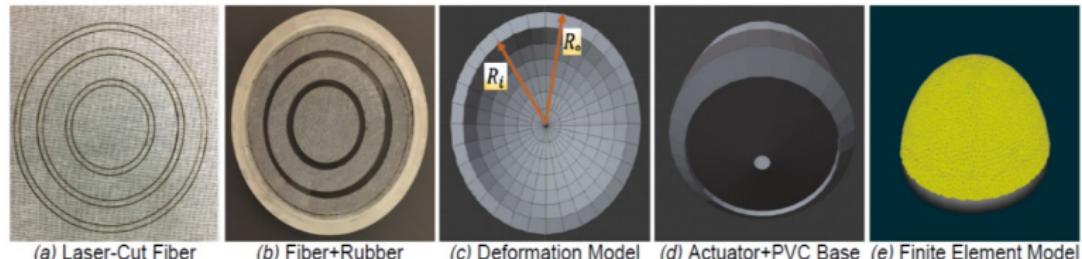
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Circumferentially Constrained And Radially Symmetric Elastomers [Pikul et al. (2019)].



CCOARSE Actuator Schematic

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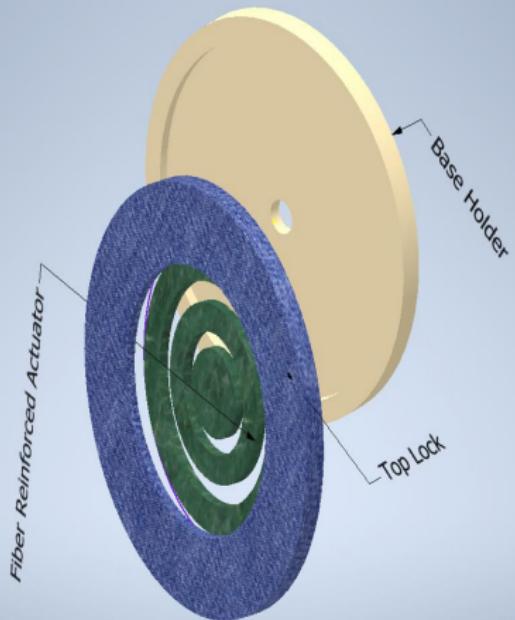
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Nonlinear Elastic Deformation Analysis

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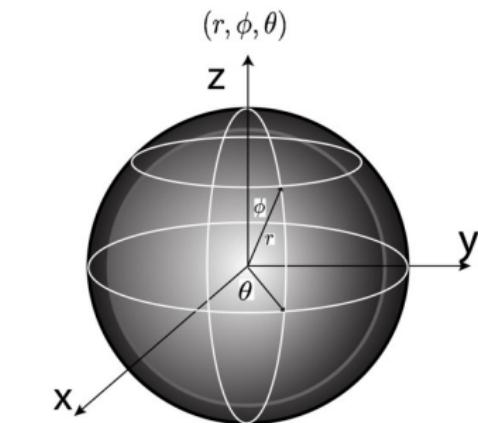
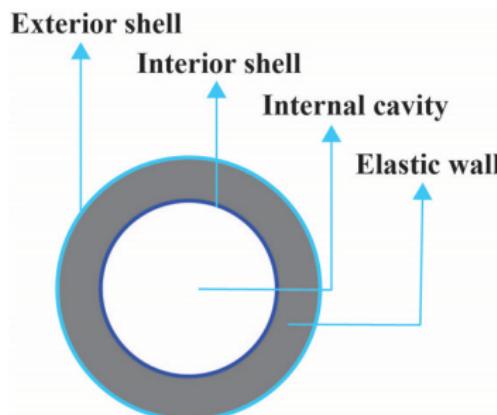
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IAB SHELLS AND AIR CAVITY/DEFORMATION ANALYSIS



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

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
 - $P(r) = \int_{r_i}^{r_o} [2C_1\left(\frac{r}{R^2} - \frac{R^4}{r^5}\right) + 2C_2\left(\frac{r^3}{R^4} - \frac{R^2}{r^3}\right)] dr$
 - $P(r) = \int_{R_i}^{R_o} [2C_1\left(\frac{1}{r} - \frac{R^6}{r^7}\right) - 2C_2\left(\frac{R^4}{r^5} - \frac{r}{R^2}\right)] dr$
 - $r^3 = R^3 + r_i^3 - R_i^3 \text{ and } r_o^3 = R_0^3 + r_i^3 - R_i^3$

Volumetric Deformation Results (Simulation)

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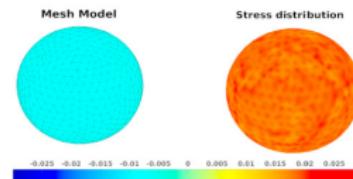
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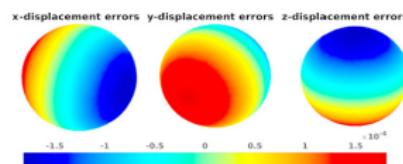
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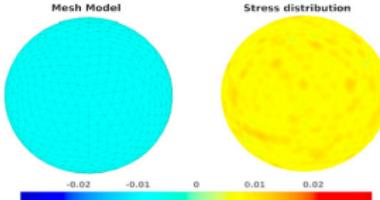
(a) Left: Mesh model. Right: Stress distribution on outer skin.



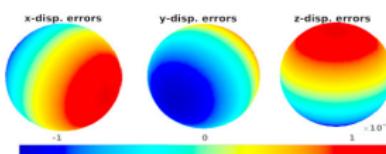
(b) Displacement errors along x, y, z coordinates.

Inputs				Outputs			
C_1	C_2	R_i	r_i	R_o	r_o	P	ΔV
1.1e4	2.2e4	.027	.03	.03	.033	.76	≈ 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	ΔV
1.1e4	2.2e4	.025	.03	.03	.028	-.34	≈ 0

Fig. 7: Volumetric Deformation (Compression).

Pneumatic Control and Deformation Scheme

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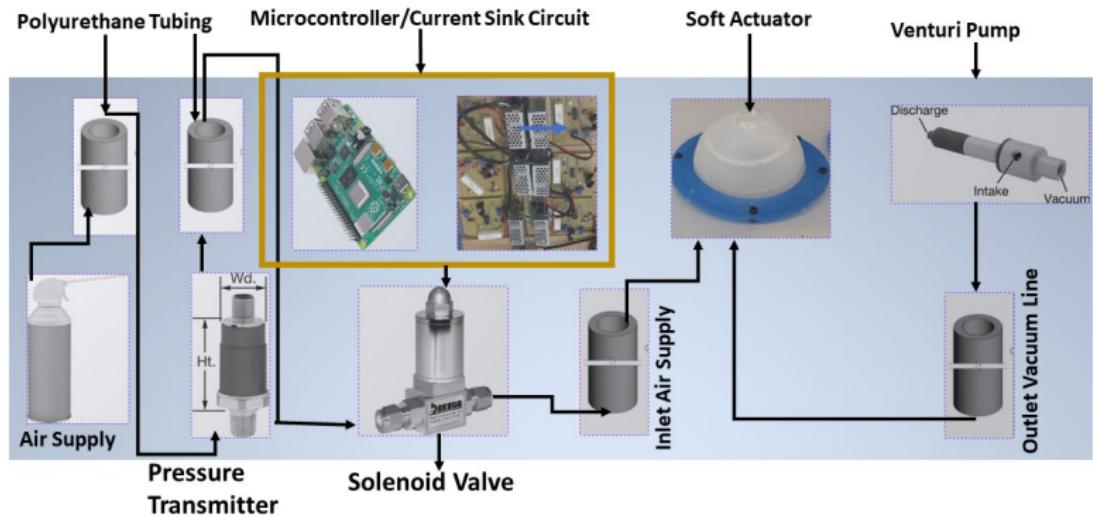
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Volumetric Deformation Results (Actual)

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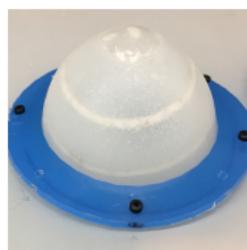
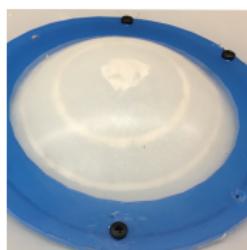
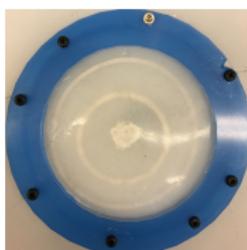
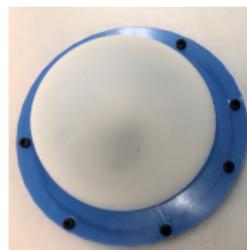
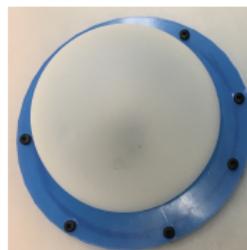
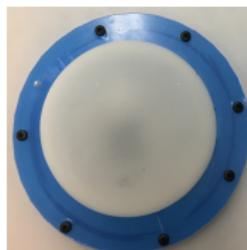
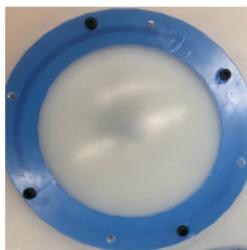
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Mechanism Setup

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Mechanism Setup with Phantom

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Head Motion Control (Independent Actuation)

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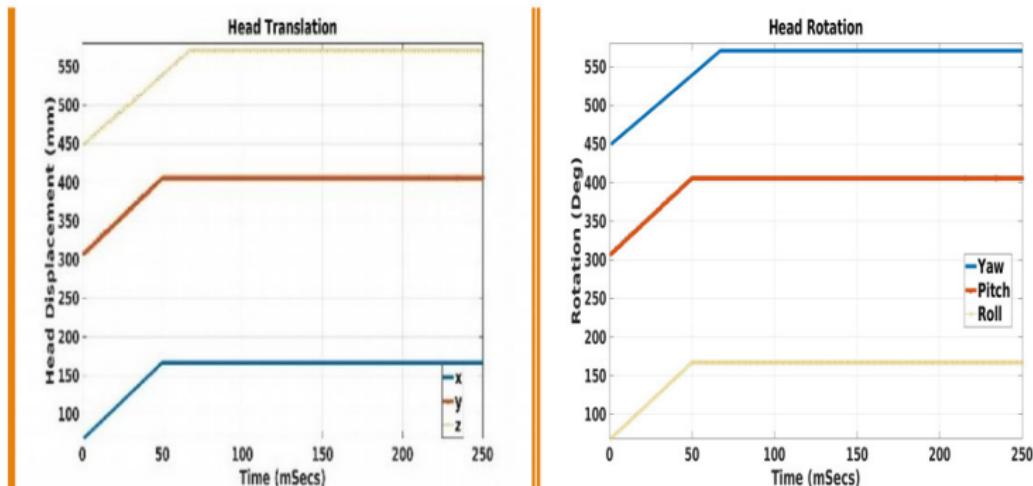
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Head Translation along x, y, z for a task of raising the head by a certain threshold above the table

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

Ongoing Work: 6-DOF Closed-loop Control

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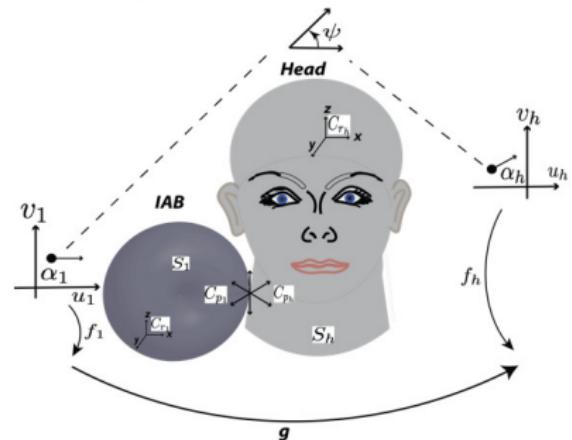
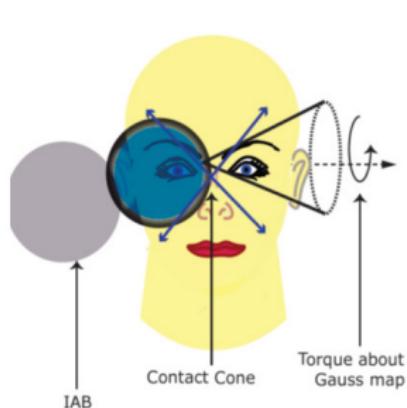
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Continuum Mechanical Model Validation/Differential Geometry/Newton-Euler Dynamics



Pneumatic Actuated Soft Robots for Head Motion Compensation

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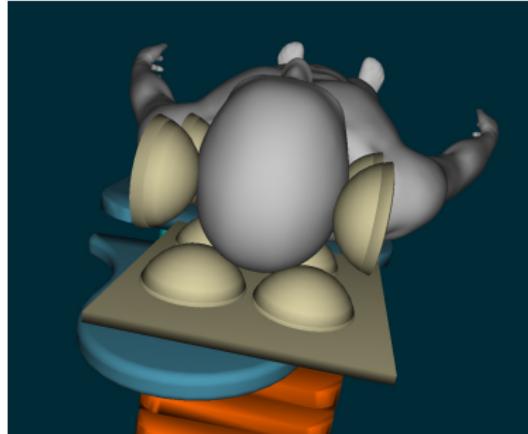
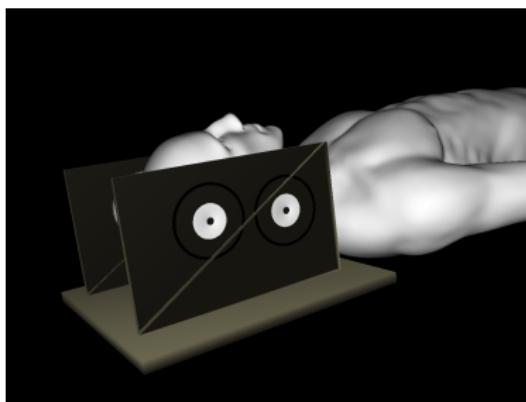
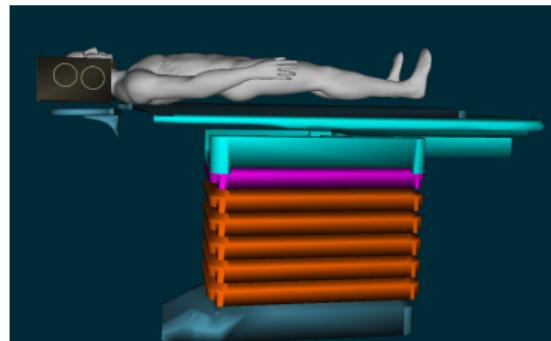
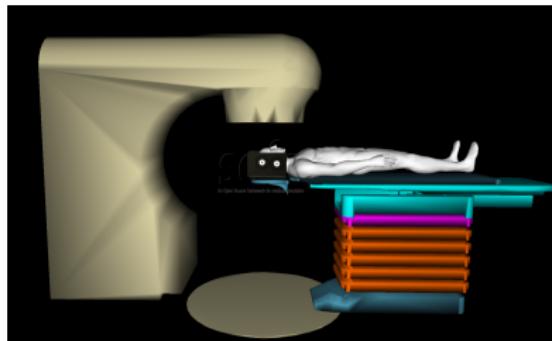
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3-DOF Simulation Testbed

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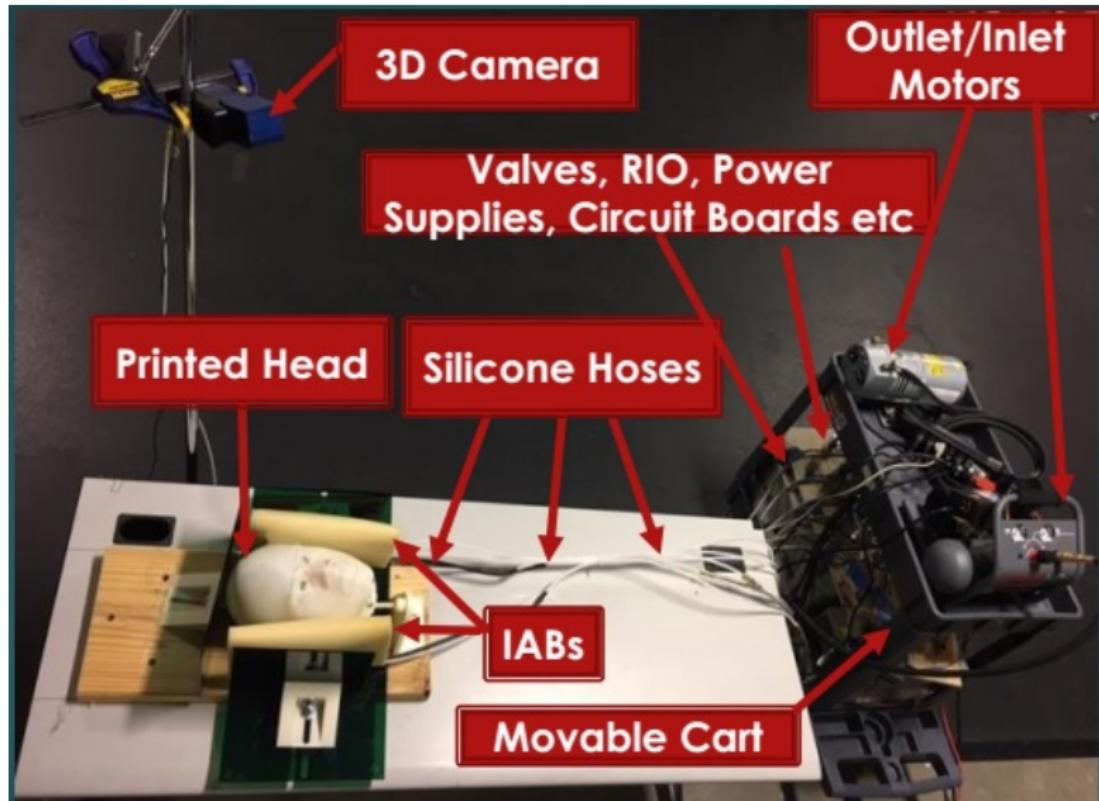
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Control Design Goals

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- Stabilize z , pitch, and roll states, *i.e.*

$$\mathbf{x} = \begin{pmatrix} z \\ \theta \\ \phi \end{pmatrix}$$

- By solving an adaptive state feedback controller, optimal regulation, and minimize parametric uncertainties

Control Design Goals

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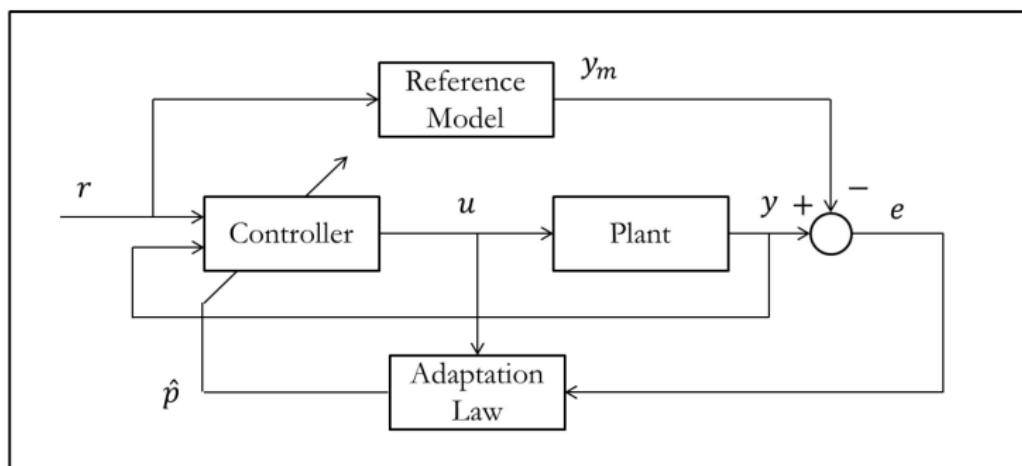
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- Provide closed loop tracking given a desired trajectory, r
- Robustify system to (non-)parametric uncertainties



Indirect MRAC system. (Source mdpi.com)

Model Reference Adaptive Control

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- Model head and bladder dynamics as
 - $\dot{x} = Ax + B\Lambda(u - f(x, u)) + w(k)$
- Approximate $f(x, u)$ by a neural network with continuous memory states
- Derive adaptive adjustment mechanism from Lyapunov analysis for Adaptive Control Parks (1966)
 - $u = \underbrace{\hat{K}_x^T x}_{\text{state feedback}} + \underbrace{\hat{K}_r^T r}_{\text{optimal regulator}} + \underbrace{\hat{f}(x, u)}_{\text{approximator}}$

Neural Network Architecture

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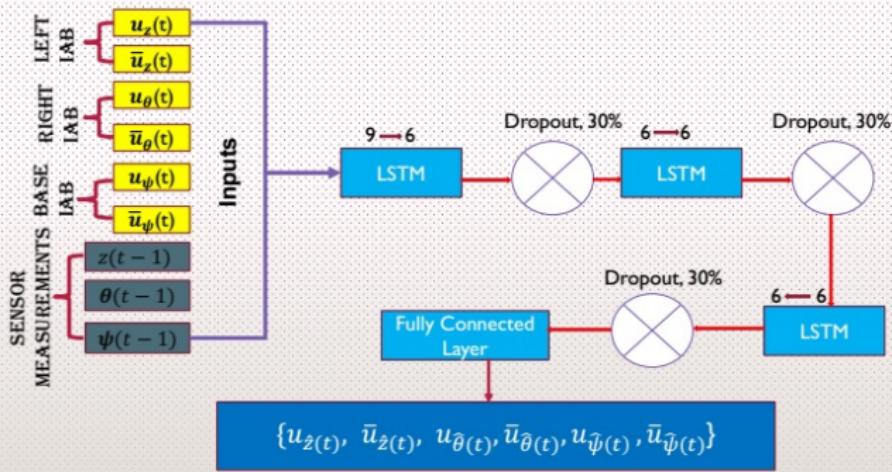
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Neural Net Architecture



Lyapunov Redesign: Theorem

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- For correct adaptive gains, $\hat{\mathbf{K}}_x$ and $\hat{\mathbf{K}}_r$, $\mathbf{e}(k)$ is **uniformly ultimately bounded**, and the state \mathbf{x} converges to a neighborhood of \mathbf{r} .
- Choose a \mathbf{V} in terms of \mathbf{e} ; $\tilde{\mathbf{K}}_x^T$, $\tilde{\mathbf{K}}_r^T$; and parameter error $\varepsilon_f(\mathbf{x}(k))$ space

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

Stability Results: Ogunmolu et al. (2017)

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

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

Results: Z and Pitch Motions

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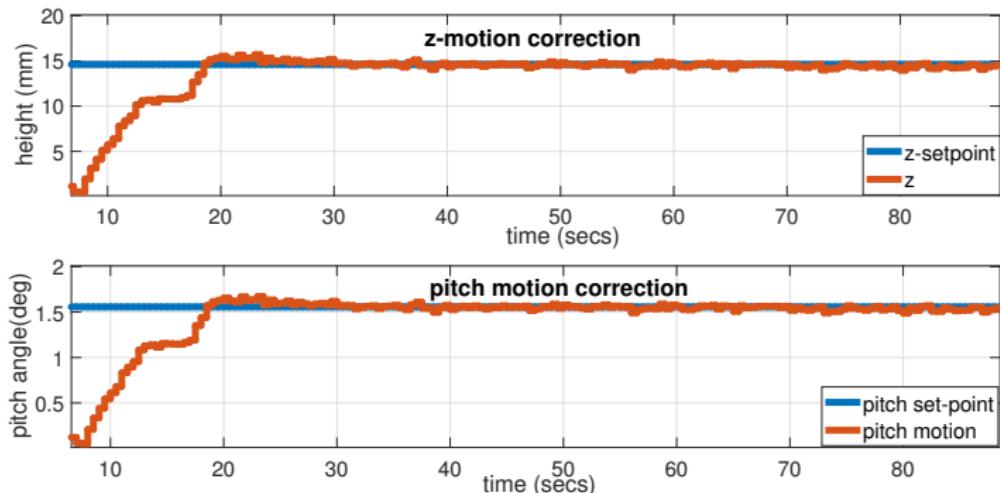
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Goal command: $(z, \theta, \phi) = (14\text{mm}, 1.6^\circ, 45^\circ)^T$.

Results: Roll Motion

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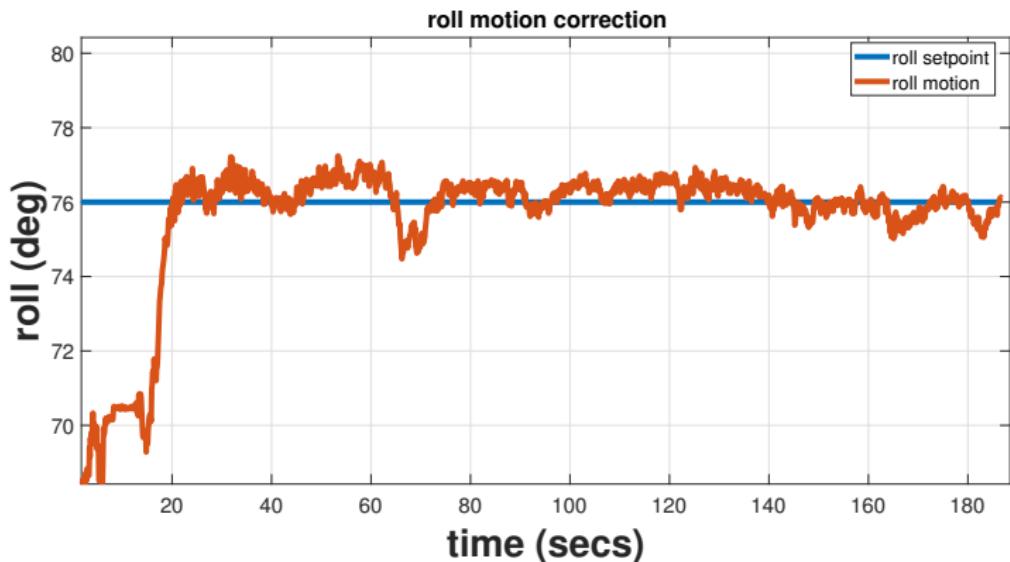
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Head roll tracking.

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- Non-invasive soft robot for head motion compensation ✓
- Photons-transparent as opposed to rigid/electro-mechanical devices/robots ✓
- Adaptable under MRI coils for newer MRI-LINACs ✓

Part III: Robustness Margins and Robust Deep Policies

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- Robustness Margins and Robust Deep Policies for Nonlinear Control

The robustness conundrum

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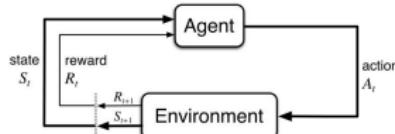
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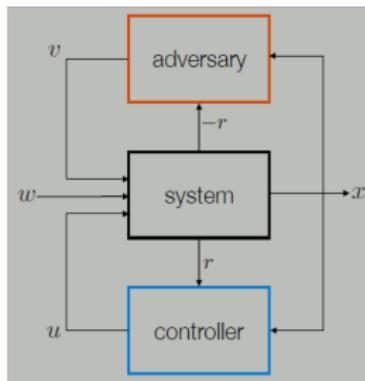
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- How to know *a priori* a policy's robustness limits?



- 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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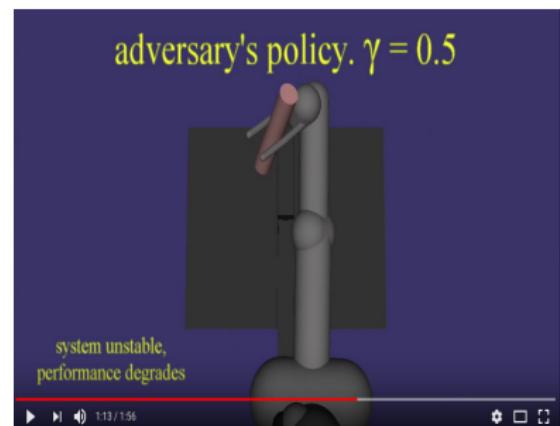
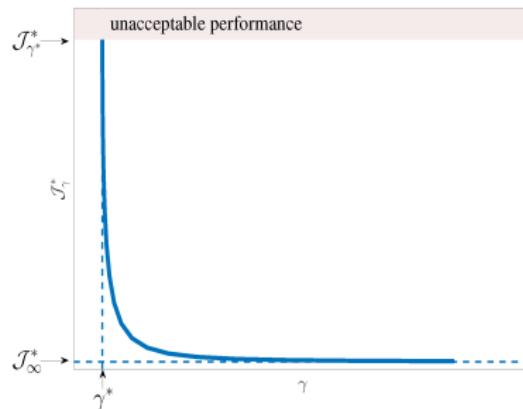
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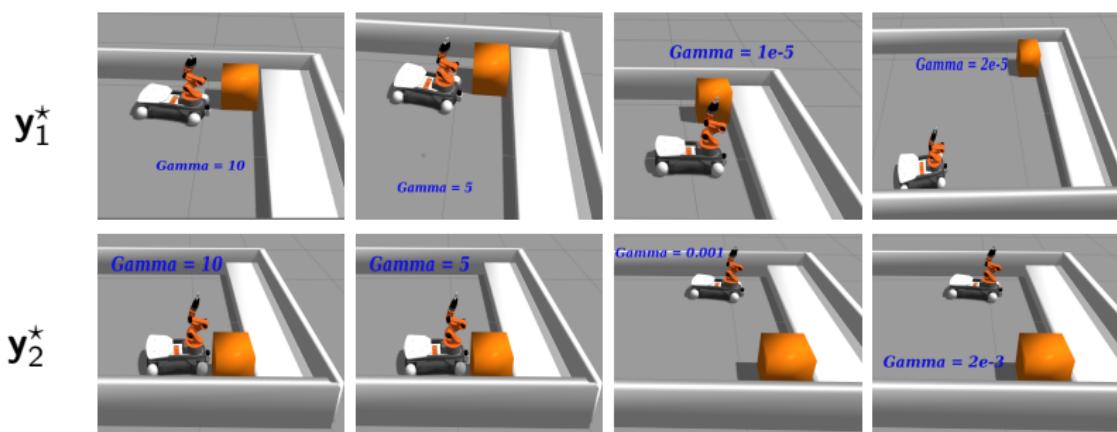
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Results: Iterative Dynamic Game



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

Future Work: MRI/RT Immobilization

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- Explore multiple parallel robot mechanisms for head motion correction.
- Adopt iterative dynamic game approach [Ogunmolu et al. (2018)] for solving robust controller for head stabilization.
- Build on Freeman and Kokotovic's point-wise min-norm robust control lyapunov function to realize a meaningful value function in deep policies [Freeman and Kokotovic (1996)].

Conclusions

- Designed a non-invasive soft robot for head motion compensation in IMRT/emerging MRI-LINACs ✓
- Photons-transparent; Adaptable under MRI coils for newer MRI-LINACs ✓
- Fast inference of beam orientations in treatment planning:
Approx 60 secs beams prediction time✓
- Adapted H_{∞} control methods for quantifying the brittleness of deep policies✓
- Devised a min-max-trained deep saddle policy for mitigating model mismatch, transfer errors, and policy sensitivity e.t.c. ✓

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End of Slides/Questions?

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A vote of thanks to many of my past undergraduate interns, colleagues, and other researchers not limited to James Pikul (Penn MEAM), Rachel Thompson (MIT), Xinmin Liu (UChicago/Penn), Jethro Tan (PFN), Iretiayo Akinola (Columbia University), Audrey Sedal (TTIC), Namhyung Lee (KAIST), UTSW MAIA lab, and UTD Robotec lab colleagues e.t.c.