

Automating
Treatment
Planning in
Radiation
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BOO Motivation

Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues

Approach

iDG Results

Future Work

Publications

References

Automating Treatment Planning in Radiation Therapy

Lekan Ogunmolu

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University of Pennsylvania, Philadelphia, PA

February 04, 2021

Funding Sources

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Treatment
Planning in
Radiation
Therapy

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BOO
MCTS
BOO Motivation
Approach

Head
Stabilization
IMRT
MRI-LINAC

iDG
Robustness issues
Approach
iDG Results

Future Work
Publications
References



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Talk Outline

Automating
Treatment
Planning in
Radiation
Therapy

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BOO

MCTS
BOO Motivation
Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues
Approach

iDG Results

Future Work

Publications

References

- 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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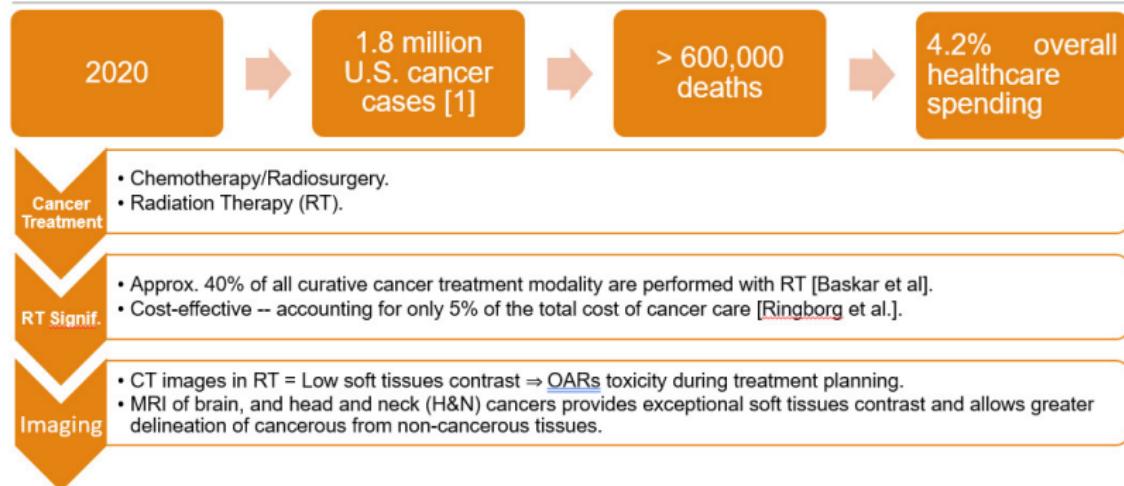
MCTS
BOO Motivation
Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG
Robustness issues
Approach
iDG Results

Future Work
Publications
References



IMRT Treatment Planning (Beam Delivery)

Automating
Treatment
Planning in
Radiation
Therapy

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MCTS

BOO Motivation

Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues

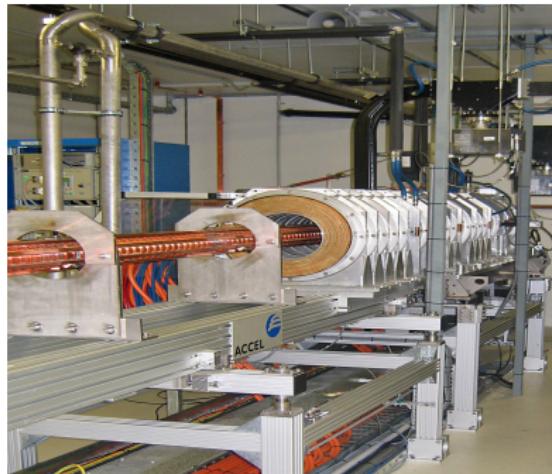
Approach

iDG Results

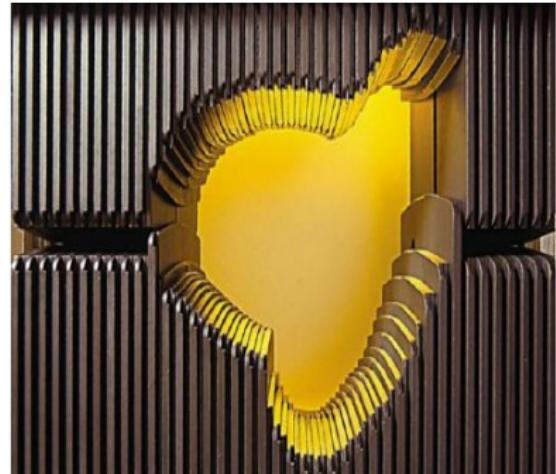
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Publications

References



The Australian Synchrotron.



Multi-leaf collimator (Varian)

Radiation Delivery Couch and Gantry

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Treatment
Planning in
Radiation
Therapy

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MCTS
BOO Motivation
Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG

Robustness issues
Approach
iDG Results

Future Work

Publications

References



Varian's TrueBeam Radiotherapy System.

Part I.A: Beam Orientation Optimization (BOO)

Automating
Treatment
Planning in
Radiation
Therapy

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BOO

MCTS

BOO Motivation
Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues

Approach

iDG Results

Future Work

Publications

References

■ Beam Orientation Optimization (BOO)

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

Contributions

Automating
Treatment
Planning in
Radiation
Therapy

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BOO
MCTS

BOO Motivation
Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG

Robustness issues
Approach
iDG Results

Future Work
Publications

References

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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MCTS

BOO Motivation

Approach

Head Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues

Approach

iDG Results

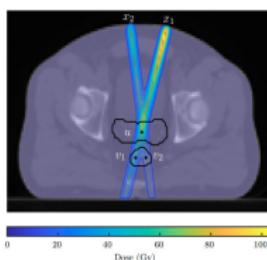
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Publications

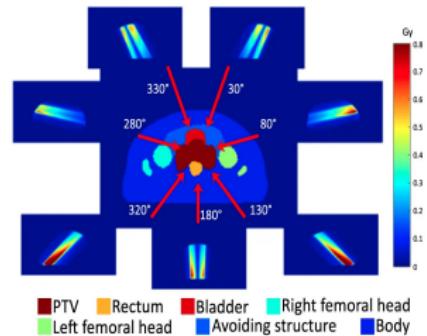
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Prostate CT slice



Prostate before
BOO



Fluence Map

Treatment Plan Flowchart

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Planning in
Radiation
Therapy

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BOO Motivation

Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues

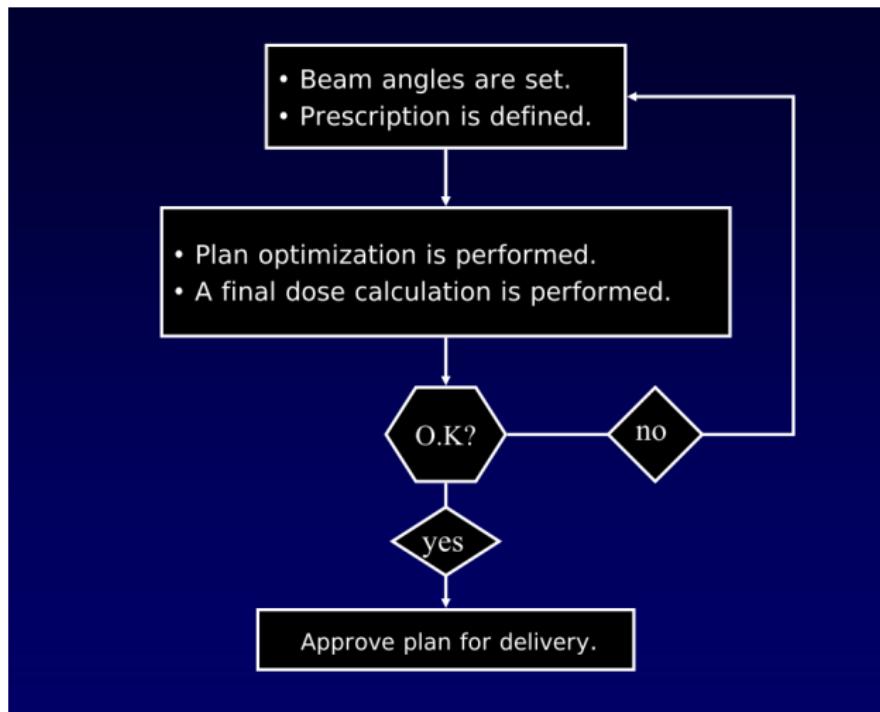
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iDG Results

Future Work

Publications

References



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

Current Approaches

Automating
Treatment
Planning in
Radiation
Therapy

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Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG
Robustness issues
Approach

iDG Results

Future Work
Publications

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

Automating
Treatment
Planning in
Radiation
Therapy

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MCTS
BOO Motivation
Approach

Head
Stabilization
IMRT
MRI-LINAC

iDG
Robustness issues
Approach
iDG Results

Future Work
Publications
References

- 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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Treatment
Planning in
Radiation
Therapy

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BOO
MCTS
BOO Motivation
Approach
Head
Stabilization
IMRT
MRI-LINAC

iDG
Robustness issues
Approach
iDG Results

Future Work
Publications
References

- 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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Radiation
Therapy

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BOO Motivation

Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues

Approach

iDG Results

Future Work

Publications

References

- 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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Planning in
Radiation
Therapy

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BOO Motivation
Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG

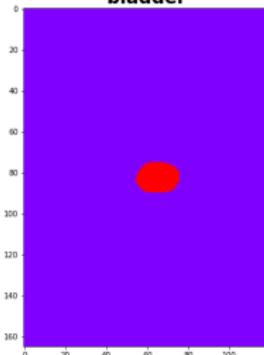
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Approach

iDG Results

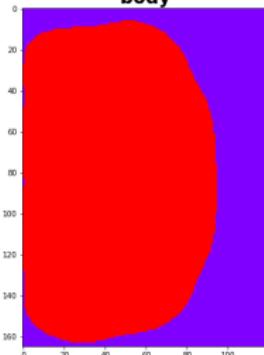
Future Work
Publications

References

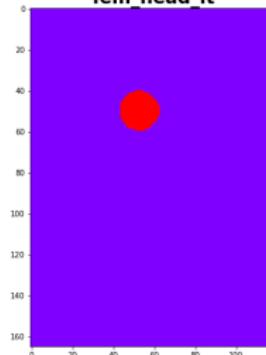
bladder



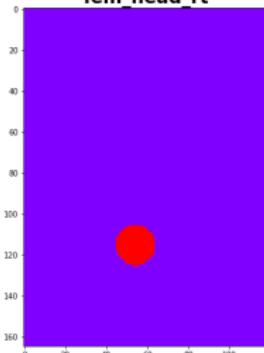
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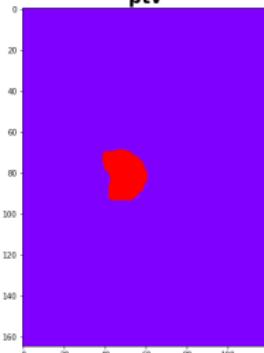
fem_head_lt



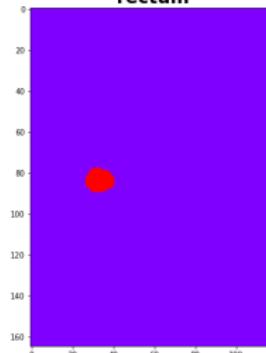
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ptv



rectum



State Representation: Beam Angles

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Planning in
Radiation
Therapy

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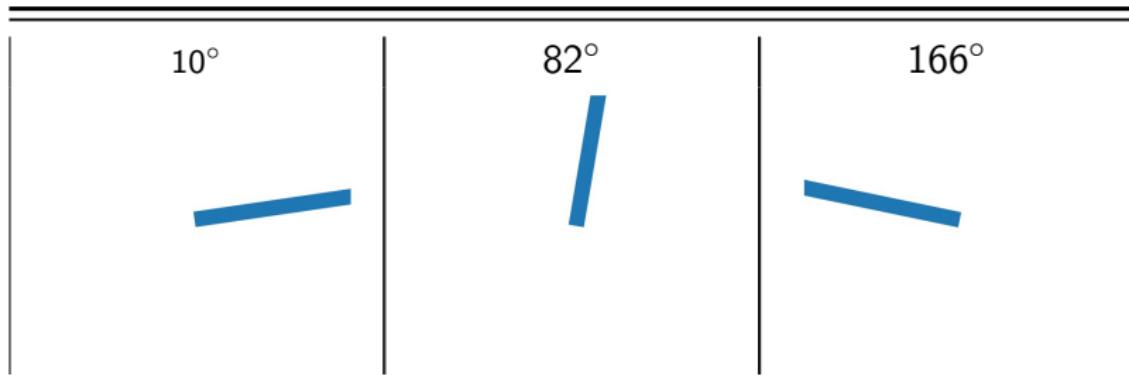
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MCTS
BOO Motivation
Approach

Head
Stabilization

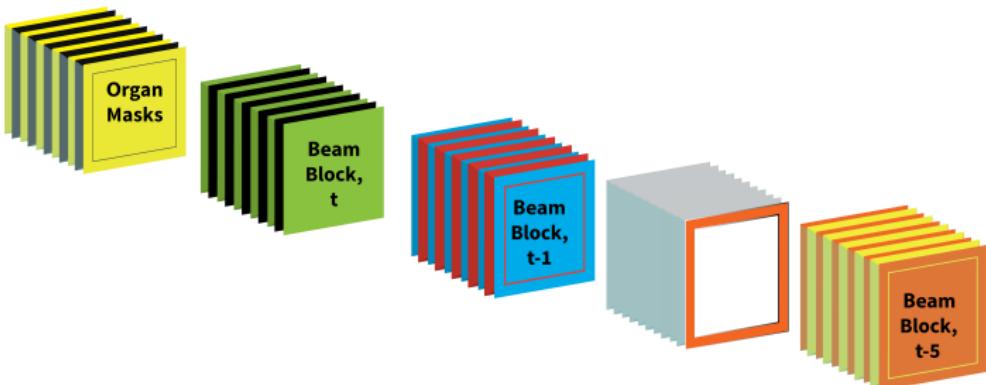
IMRT
MRI-LINAC

iDG
Robustness issues
Approach
iDG Results

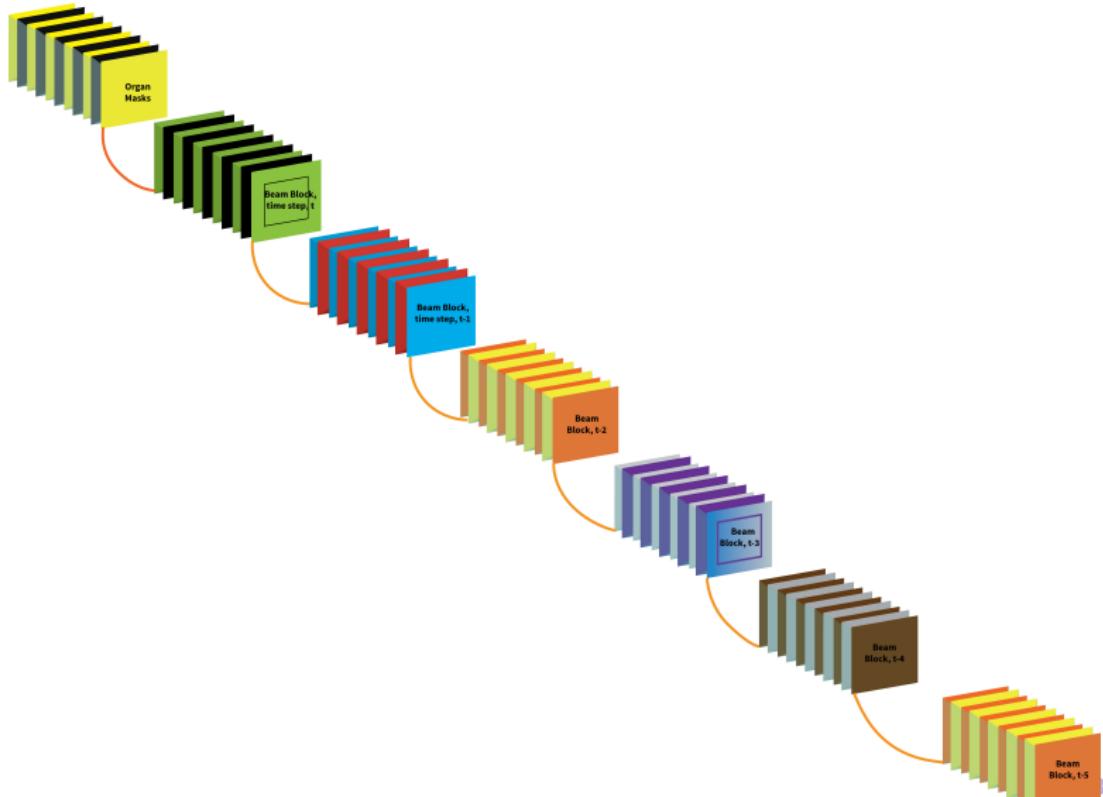
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Publications
References



State Representation



State Representation



Tree Representation and Game Simulation

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Planning in
Radiation
Therapy

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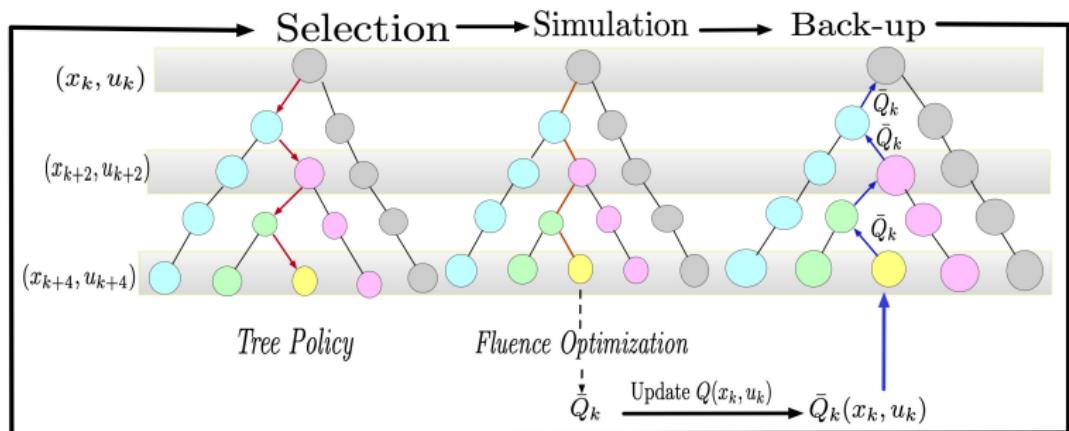
BOO
MCTS
BOO Motivation
Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG
Robustness issues
Approach
iDG Results

Future Work
Publications
References



Tree Composition

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Treatment
Planning in
Radiation
Therapy

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BOO Motivation
Approach

Head
Stabilization
IMRT
MRI-LINAC

iDG
Robustness issues
Approach
iDG Results

Future Work
Publications
References

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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Therapy

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BOO Motivation
Approach

Head
Stabilization
IMRT
MRI-LINAC

iDG
Robustness issues
Approach
iDG Results

Future Work
Publications
References

- 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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Therapy

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Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG

Robustness issues
Approach
iDG Results

Future Work
Publications

References

- 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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Therapy

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Approach

Head
Stabilization

IMRT
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Robustness issues
Approach
iDG Results

Future Work
Publications
References

- $\mathcal{X} \implies$ 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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Planning in
Radiation
Therapy

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BOO Motivation
Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues
Approach
iDG Results

Future Work

Publications

References

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

Methods: FMO

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Treatment
Planning in
Radiation
Therapy

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BOO

MCTS
BOO Motivation
Approach

Head
Stabilization
IMRT
MRI-LINAC

iDG
Robustness issues

Approach

iDG Results

Future Work

Publications

References

- 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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Planning in
Radiation
Therapy

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BOO
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BOO Motivation
Approach

Head
Stabilization
IMRT
MRI-LINAC

iDG
Robustness issues
Approach
iDG Results

Future Work
Publications
References

- 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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Treatment
Planning in
Radiation
Therapy

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MCTS

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Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues

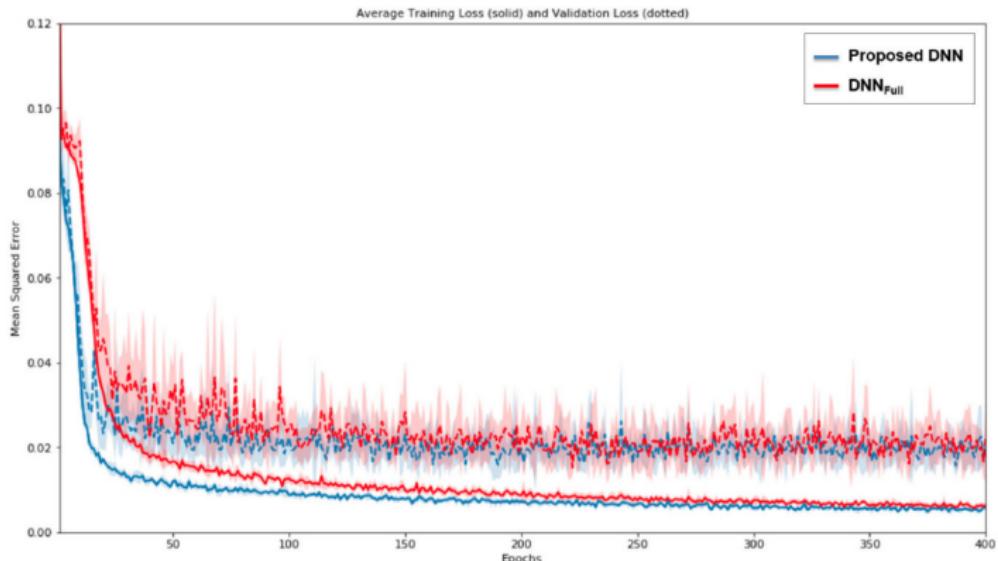
Approach

iDG Results

Future Work

Publications

References



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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Planning in
Radiation
Therapy

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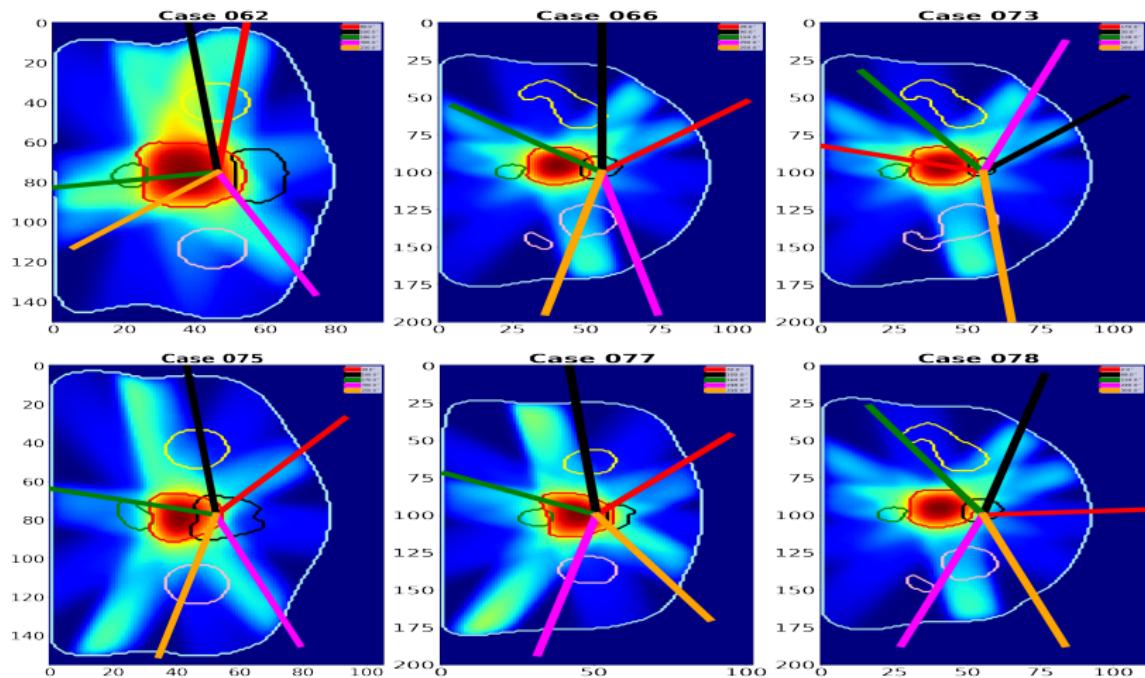
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MCTS
BOO Motivation
Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG
Robustness issues
Approach
iDG Results

Future Work
Publications
References



Dose Washes of Column Generation vs Neural Network

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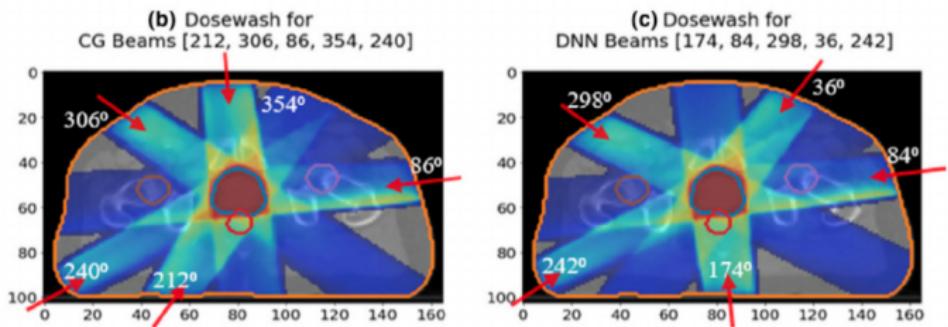
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Head Stabilization
IMRT
MRI-LINAC

iDG
Robustness issues Approach
iDG Results

Future Work
Publications
References



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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Treatment
Planning in
Radiation
Therapy

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MCTS
BOO Motivation
Approach

Head
Stabilization

IMRT

MRI-LINAC

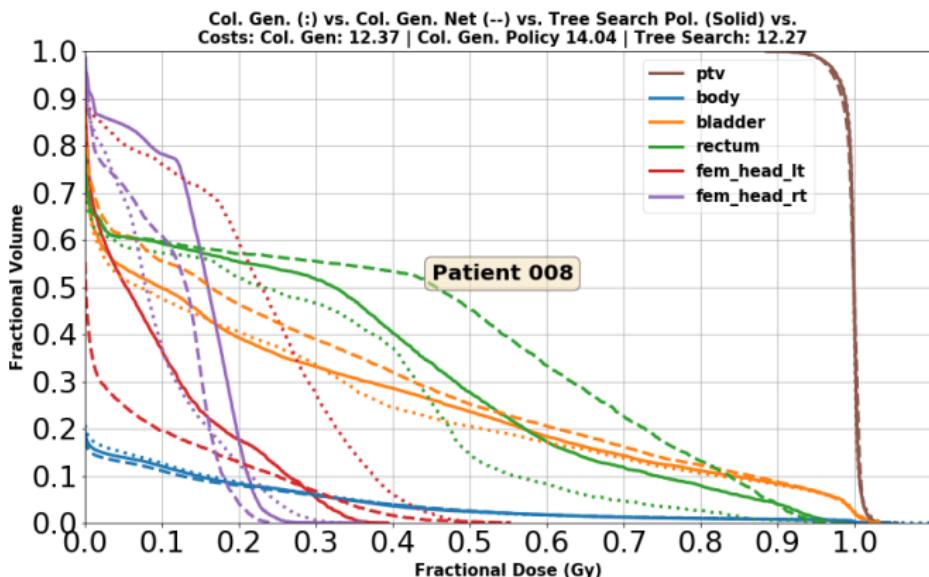
iDG

Robustness issues
Approach
iDG Results

Future Work

Publications

References



Conclusions

Automating
Treatment
Planning in
Radiation
Therapy

Lekan
Ogunmolu

BOO

MCTS
BOO Motivation
Approach

Head
Stabilization
IMRT

MRI-LINAC

iDG

Robustness issues
Approach
iDG Results

Future Work

Publications

References

- 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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Treatment
Planning in
Radiation
Therapy

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BOO
MCTS
BOO Motivation
Approach

Head
Stabilization
IMRT
MRI-LINAC

iDG
Robustness issues
Approach
iDG Results

Future Work
Publications
References

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

Varian's TrueBeam Radiotherapy System.

Automating
Treatment
Planning in
Radiation
Therapy

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BOO

MCTS
BOO Motivation

Approach

Head
Stabilization
IMRT

MRI-LINAC

iDG

Robustness issues
Approach
iDG Results

Future Work

Publications

References



Correcting Head Motion: RT and MRI-LINACs

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Treatment
Planning in
Radiation
Therapy

Lekan
Ogunmolu

BOO

MCTS

BOO Motivation

Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues

Approach

iDG Results

Future Work

Publications

References



(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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Treatment
Planning in
Radiation
Therapy

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BOO Motivation

Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues

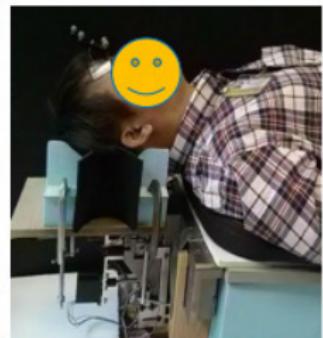
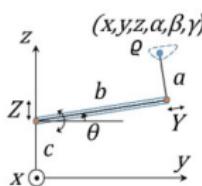
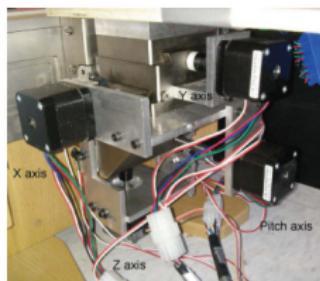
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iDG Results

Future Work

Publications

References



Liu et al. (2015)

4-DOF Motion Controller Block Diagram

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Planning in
Radiation
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Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG

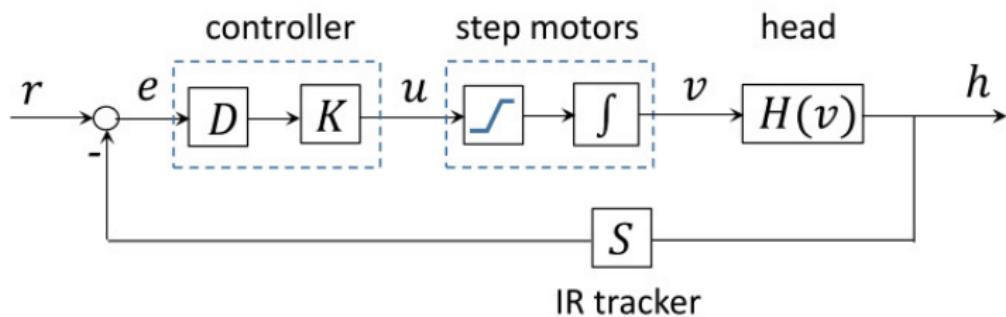
Robustness issues
Approach

iDG Results

Future Work

Publications

References



Liu et al. (2015)

Phantom Feedback Motion Correction Results

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Treatment
Planning in
Radiation
Therapy

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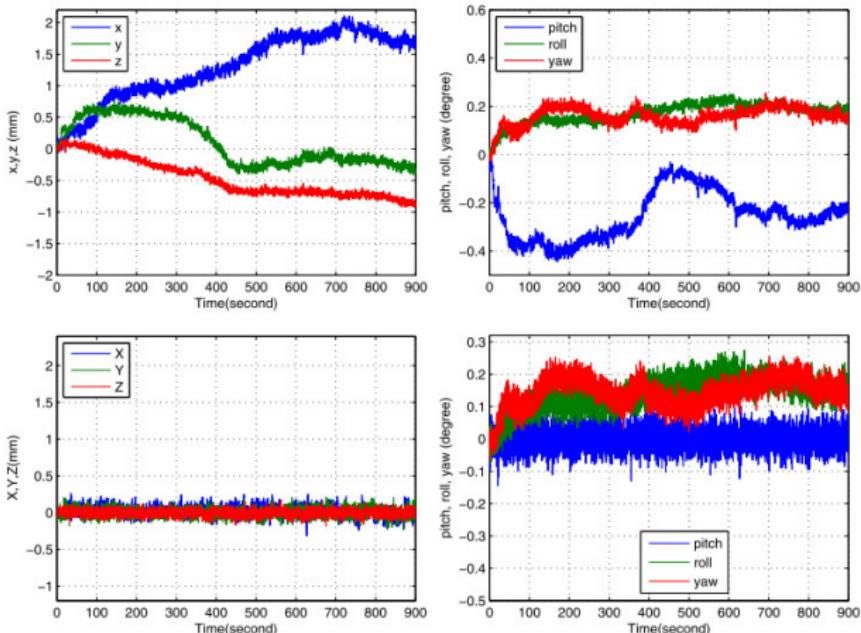
BOO
MCTS
BOO Motivation
Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG
Robustness issues
Approach
iDG Results

Future Work
Publications
References



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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BOO

MCTS

BOO Motivation Approach

Head Stabilization

IMRT

MRI-LINAC

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Robustness issues

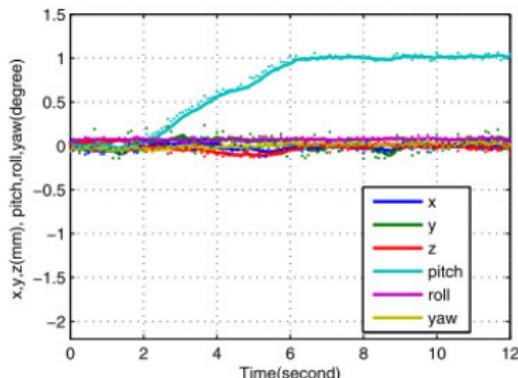
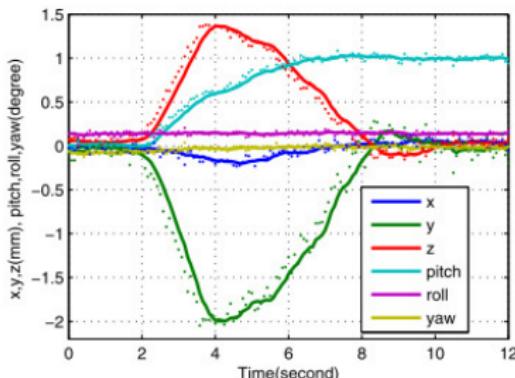
Approach

iDG Results

Future Work

Publications

References



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

SRS: Wiersma Stewart-Gough Platform

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Head Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues

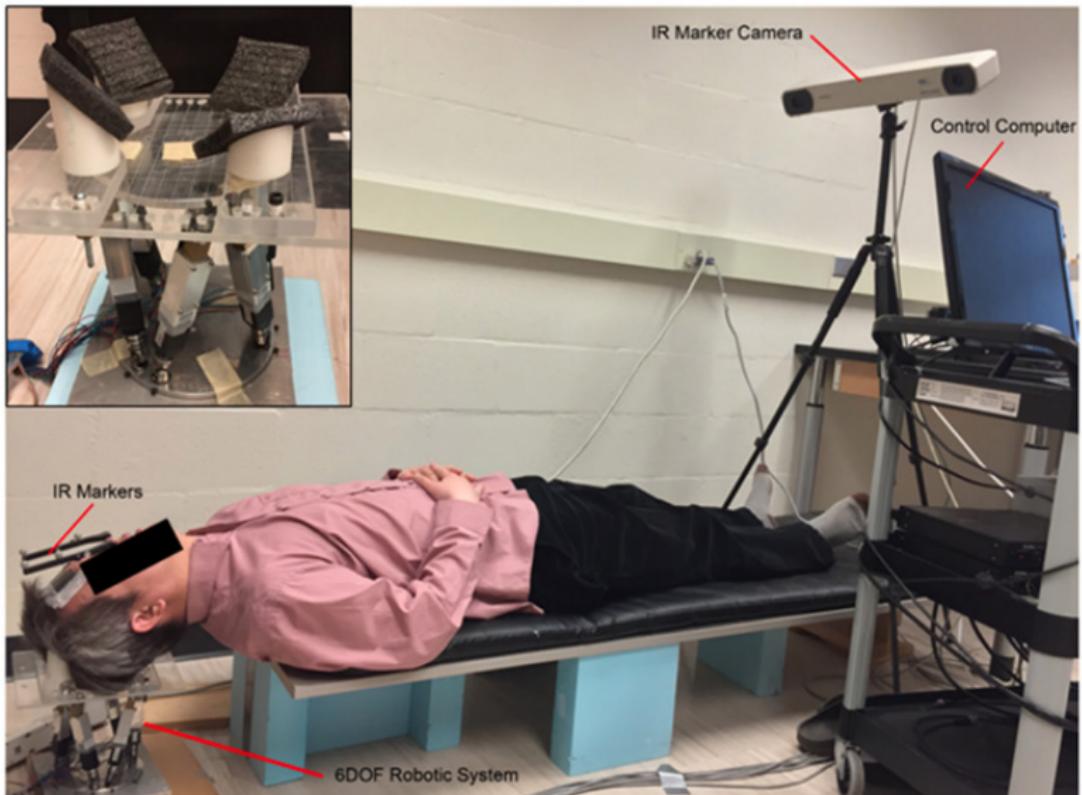
Approach

iDG Results

Future Work

Publications

References



6-DOF Motion Correction Results

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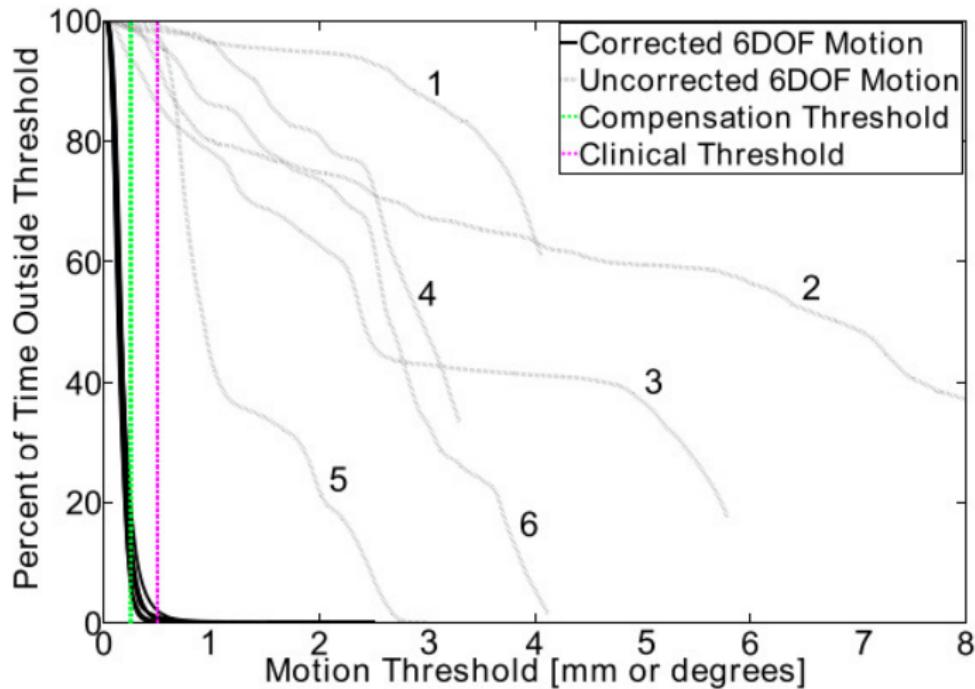
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Stabilization

IMRT
MRI-LINAC

iDG
Robustness issues
Approach
iDG Results

Future Work
Publications

References



Drawbacks of current solutions

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Radiation
Therapy

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Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG

Robustness issues
Approach
iDG Results

Future Work

Publications

References

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

Robotic Radiosurgery

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Treatment
Planning in
Radiation
Therapy

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Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues

Approach

iDG Results

Future Work

Publications

References



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)

Radiation Delivery Couch and Gantry

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Radiation
Therapy

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Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG

Robustness issues
Approach
iDG Results

Future Work

Publications

References



Varian's TrueBeam Radiotherapy System.

Next-Gen RT Treatment with MRI-LINACs

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Treatment
Planning in
Radiation
Therapy

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Approach

Head
Stabilization
IMRT

MRI-LINAC

iDG

Robustness issues

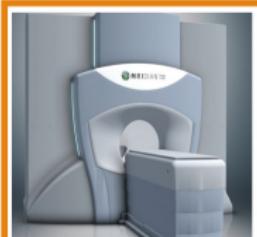
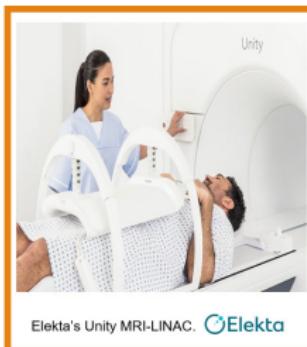
Approach

iDG Results

Future Work

Publications

References



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 univiewed, 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 [Motic 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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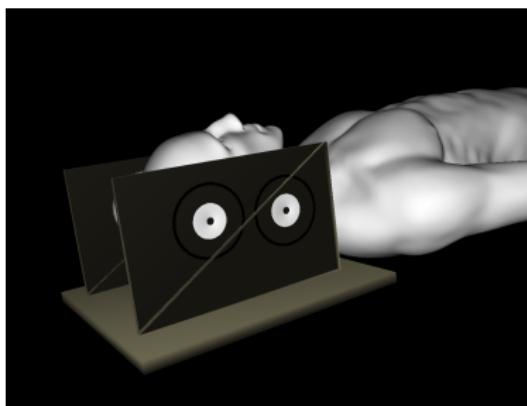
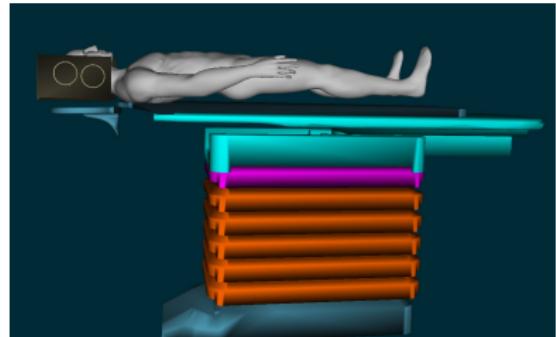
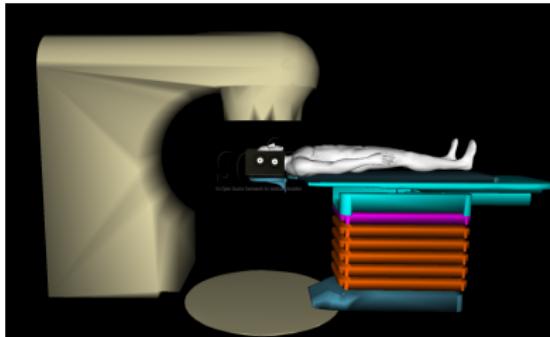
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IMRT
MRI-LINAC

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Robustness issues
Approach
iDG Results

Future Work
Publications
References



Cephalopods-inspired CCOARSE Actuator Design

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Radiation
Therapy

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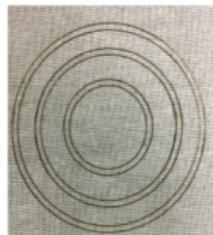
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Approach

Head
Stabilization
IMRT
MRI-LINAC

iDG
Robustness issues
Approach
iDG Results

Future Work
Publications
References

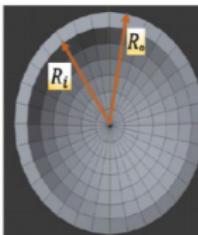
Circumferentially Constrained And Radially Symmetric Elastomers [Pikul et al. (2019)].



(a) Laser-Cut Fiber



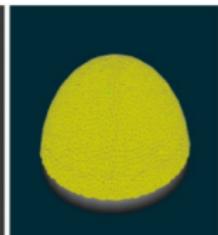
(b) Fiber+Rubber



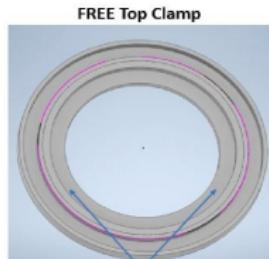
(c) Deformation Model



(d) Actuator+PVC Base



(e) Finite Element Model



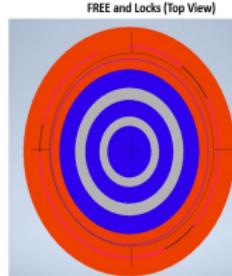
FREE Holder

FREE Top Clamp

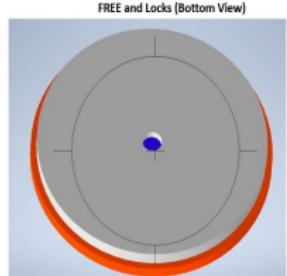


Push-to-Connect Fitting Hole

(f,g)



FREE and Locks (Top View)



FREE and Locks (Bottom View)

(h)

CCOARSE Actuator Schematic

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Approach

Head
Stabilization
IMRT

MRI-LINAC

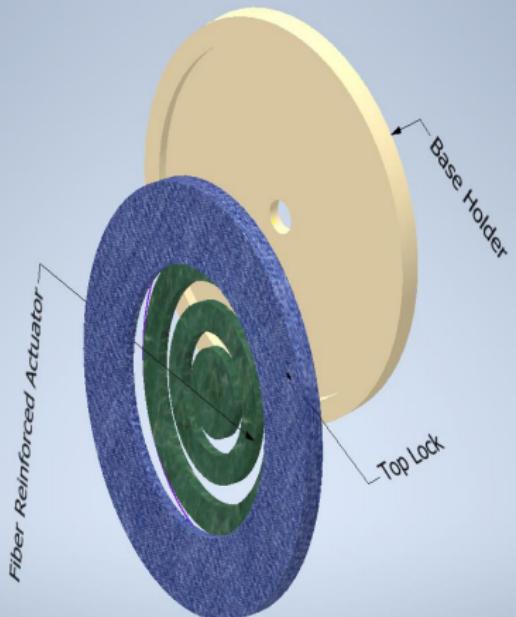
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Robustness issues
Approach
iDG Results

Future Work

Publications

References



Nonlinear Elastic Deformation Analysis

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Treatment
Planning in
Radiation
Therapy

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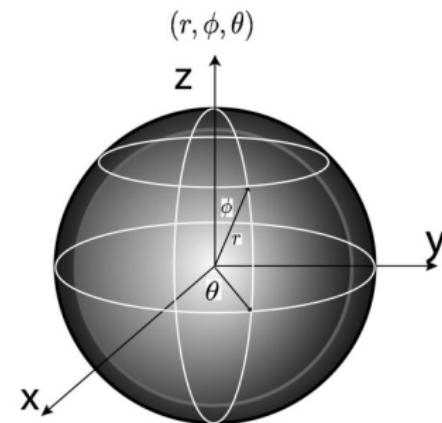
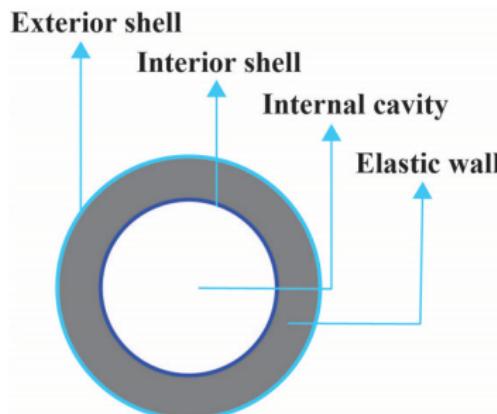
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Approach

Head
Stabilization
IMRT
MRI-LINAC

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Robustness issues
Approach
iDG Results

Future Work
Publications
References

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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Therapy

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Approach
Head
Stabilization
IMRT
MRI-LINAC

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Robustness issues
Approach
iDG Results
Future Work
Publications
References

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

Volumetric Deformation Results (Simulation)

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Planning in
Radiation
Therapy

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Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

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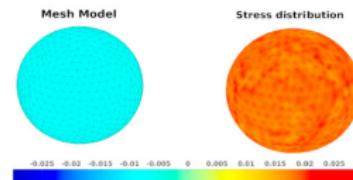
Approach

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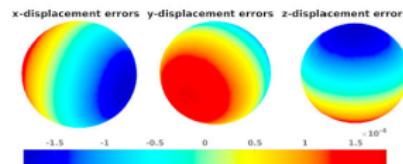
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Publications

References



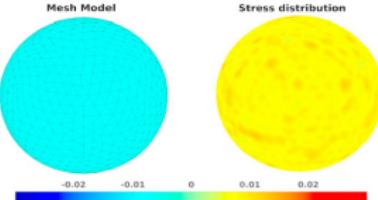
(a) Left: Mesh model. Right: Stress distribution on outer skin.



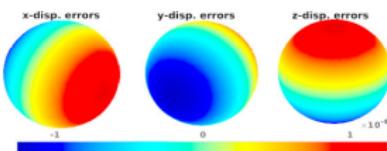
(b) Displacement errors along x, y, z coordinates.

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.

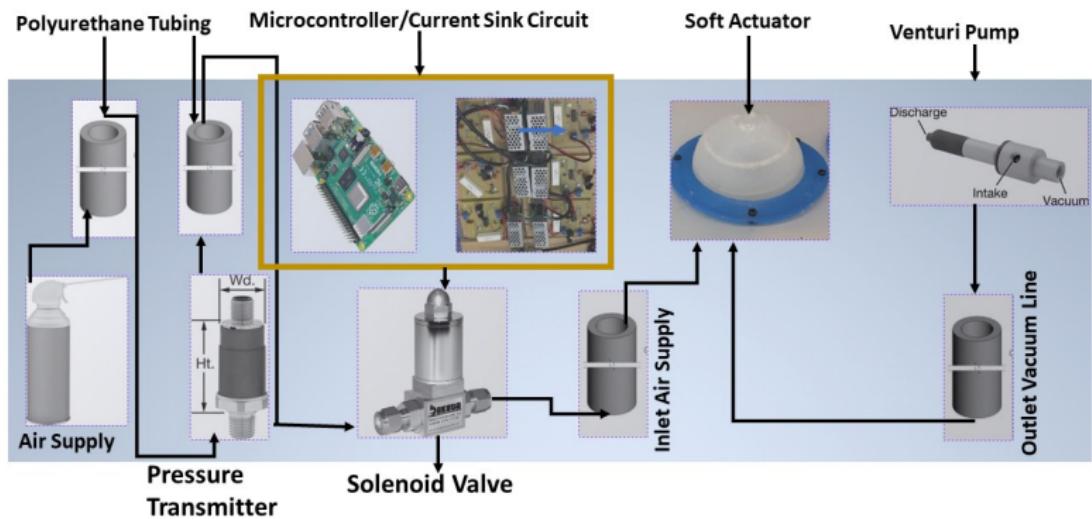


(b) Displacement errors along x, y, z coordinates.

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



Volumetric Deformation Results (Actual)

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Therapy

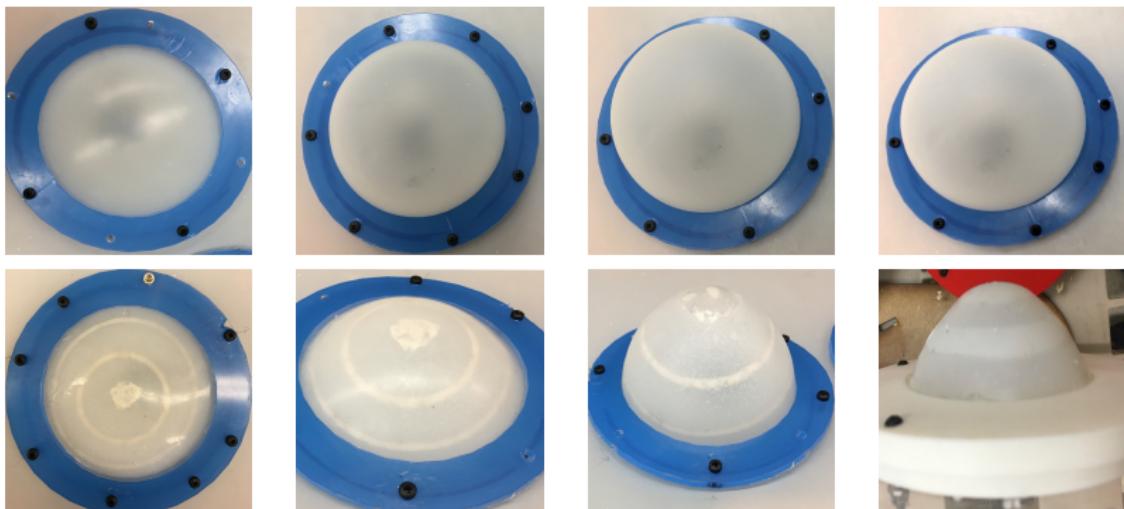
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Approach

Head
Stabilization
IMRT
MRI-LINAC

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Robustness issues
Approach
iDG Results

Future Work
Publications
References



Mechanism Setup

Automating
Treatment
Planning in
Radiation
Therapy

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Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG

Robustness issues
Approach
iDG Results

Future Work

Publications

References



Mechanism Setup with Phantom

Automating
Treatment
Planning in
Radiation
Therapy

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Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG

Robustness issues
Approach
iDG Results

Future Work

Publications

References



Head Motion Control (Independent Actuation)

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MRI-LINAC

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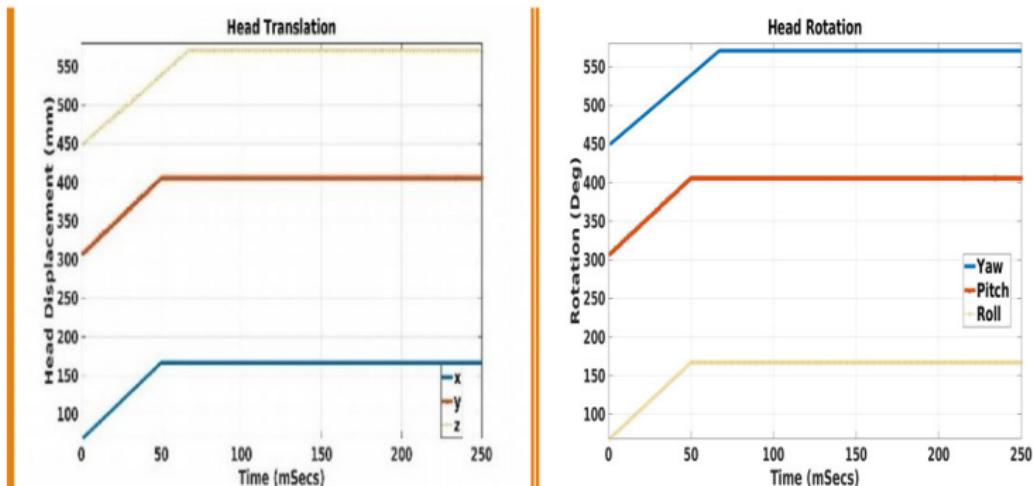
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iDG Results

Future Work

Publications

References



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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Treatment
Planning in
Radiation
Therapy

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Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues

Approach

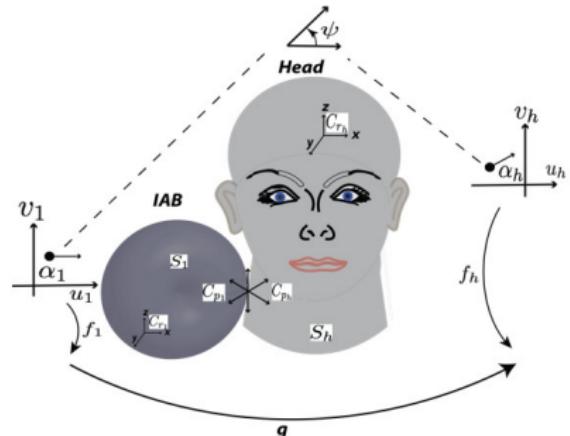
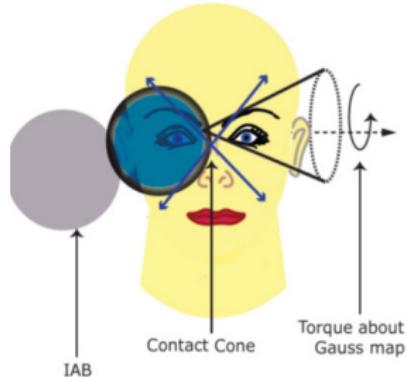
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Future Work

Publications

References

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



Pneumatic Actuated Soft Robots for Head Motion Compensation

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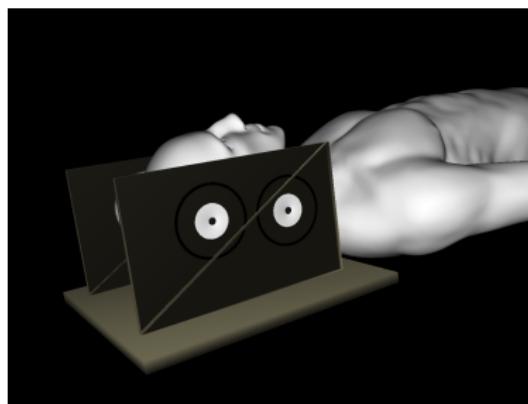
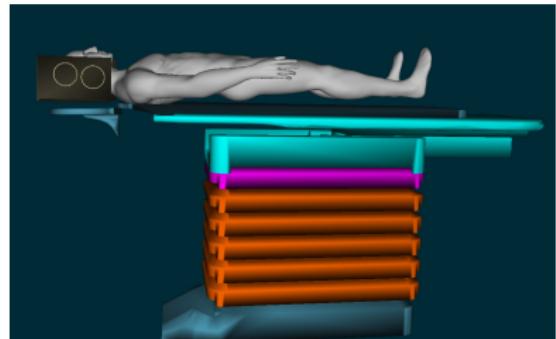
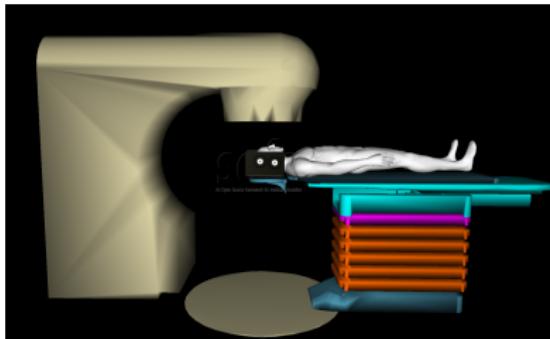
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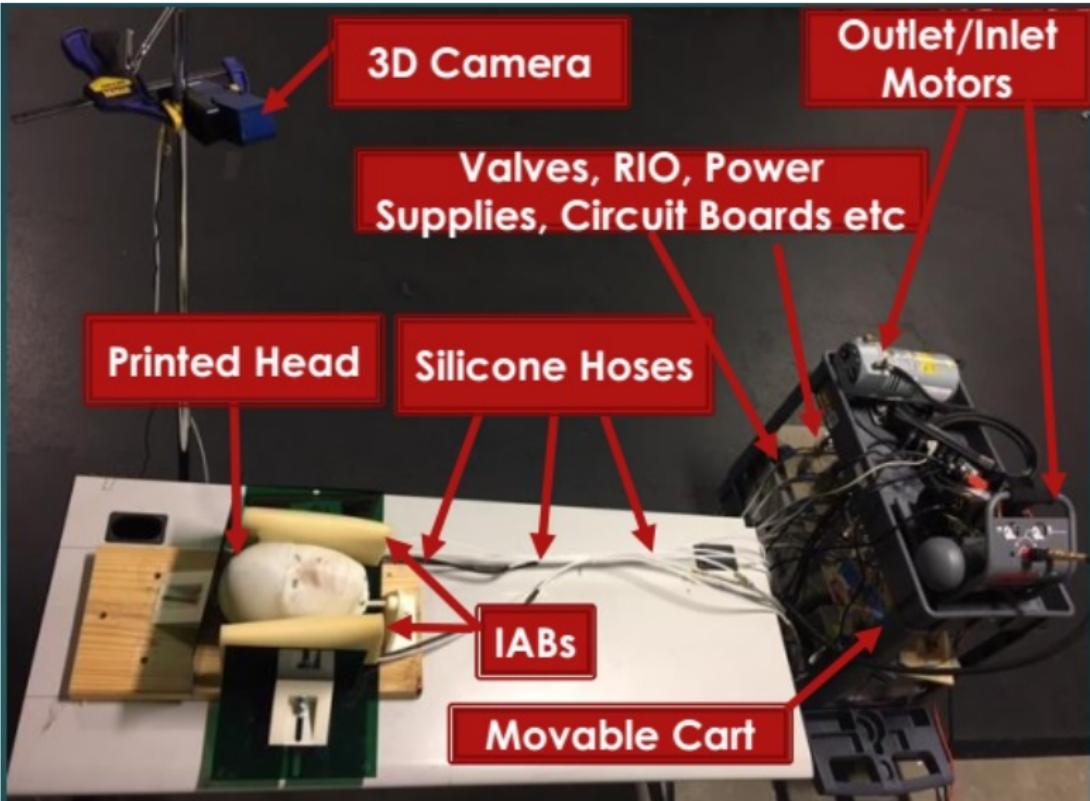
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IMRT
MRI-LINAC

iDG
Robustness issues
Approach
iDG Results

Future Work
Publications
References



3-DOF Simulation Testbed



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Head Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues

Approach

iDG Results

Future Work

Publications

References

Control Design Goals

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Treatment
Planning in
Radiation
Therapy

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Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues
Approach

iDG Results

Future Work

Publications

References

- 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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Therapy

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Approach

Head
Stabilization

IMRT

MRI-LINAC

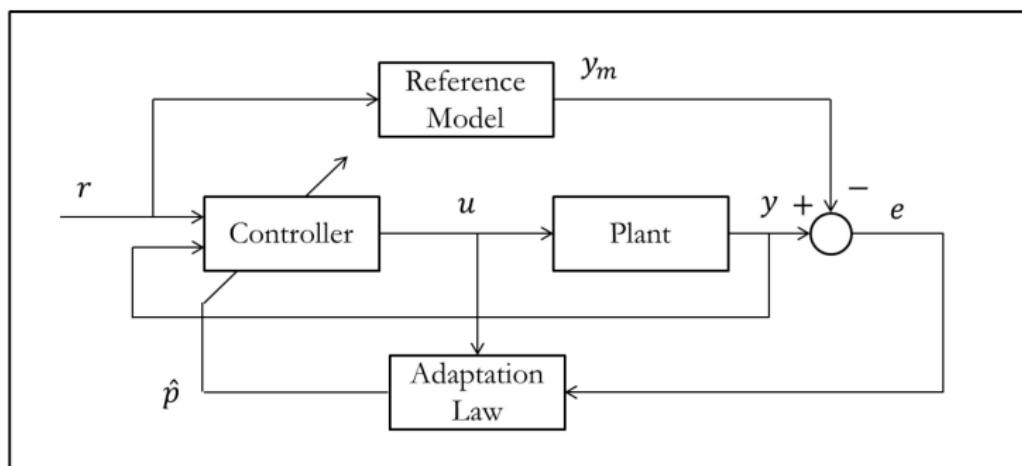
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Publications

References

- 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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Radiation
Therapy

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Head
Stabilization
IMRT
MRI-LINAC

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Robustness issues
Approach
iDG Results

Future Work
Publications
References

- 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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Therapy

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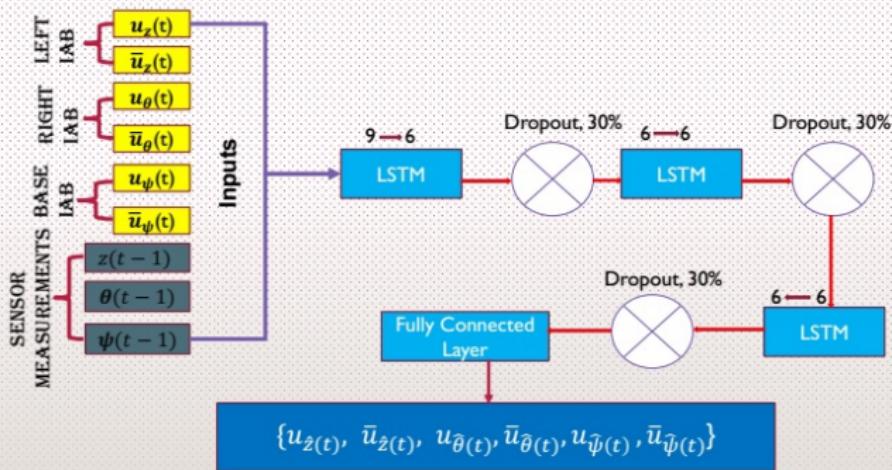
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Approach

Head
Stabilization
IMRT
MRI-LINAC

iDG
Robustness issues
Approach
iDG Results

Future Work
Publications
References

Neural Net Architecture



Lyapunov Redesign: Theorem

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Treatment
Planning in
Radiation
Therapy

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Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues

Approach

iDG Results

Future Work

Publications

References

- 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

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

Stability Results: Ogunmolu et al. (2017)

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Radiation
Therapy

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Approach

Head
Stabilization

IMRT
MRI-LINAC

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Robustness issues
Approach

iDG Results

Future Work

Publications

References

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

- $\{\lambda_{low}, \lambda_{high}\} \equiv \min/\max \text{ eigenvalues of } Q \text{ and } \boldsymbol{\Lambda}$.
- $\dot{\mathbf{V}}(\cdot)$ is thus negative definite outside the compact set:
$$\chi = \left(\mathbf{e} : \|\mathbf{e}\| \leq \frac{2\|\mathbf{P} \mathbf{B}\| \lambda_{high}(\boldsymbol{\Lambda}) \varepsilon_{max}(\mathbf{y})}{\lambda_{low}(Q)} \right)$$
 - 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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Therapy

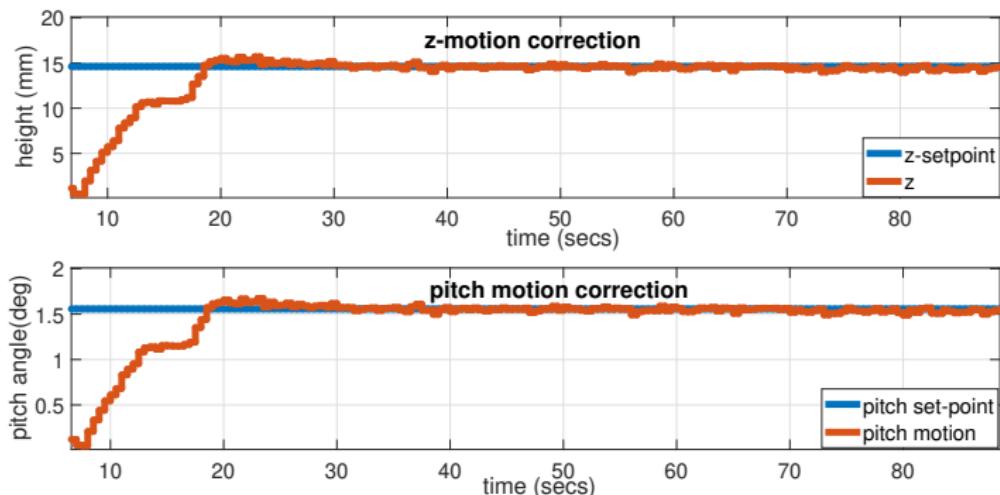
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Head
Stabilization
IMRT
MRI-LINAC

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Robustness issues
Approach
iDG Results

Future Work
Publications
References



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

Results: Roll Motion

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Planning in
Radiation
Therapy

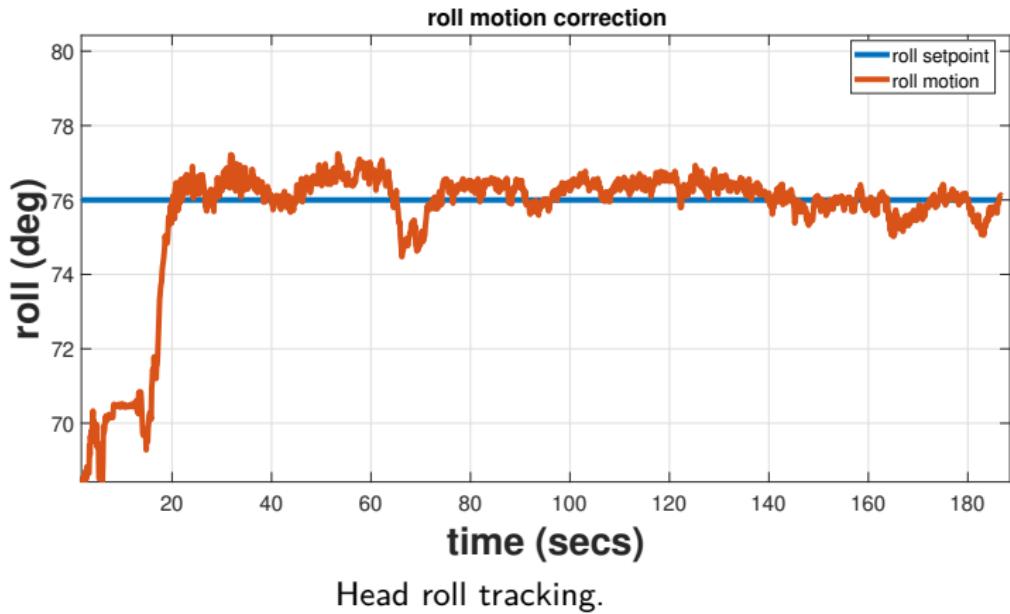
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Head
Stabilization
IMRT
MRI-LINAC

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Robustness issues
Approach
iDG Results

Future Work
Publications
References



Conclusions

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Treatment
Planning in
Radiation
Therapy

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Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues

Approach

iDG Results

Future Work

Publications

References

- 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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Approach

Head Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues

Approach

iDG Results

Future Work

Publications

References

- Robustness Margins and Robust Deep Policies for Nonlinear Control

The robustness conundrum

Automating
Treatment
Planning in
Radiation
Therapy

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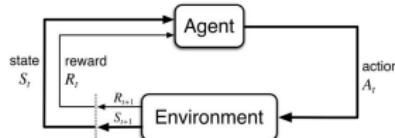
BOO
MCTS
BOO Motivation
Approach

Head
Stabilization
IMRT
MRI-LINAC

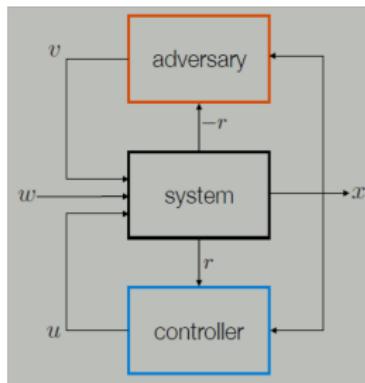
iDG
Robustness issues
Approach
iDG Results

Future Work
Publications
References

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



- How to inculcate robustness into multistage decision policies?



Problem Setup

Automating
Treatment
Planning in
Radiation
Therapy

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BOO
MCTS
BOO Motivation
Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG

Robustness issues

Approach
iDG Results

Future Work

Publications

References

- 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

Automating
Treatment
Planning in
Radiation
Therapy

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MCTS
BOO Motivation

Approach

Head
Stabilization
IMRT

MRI-LINAC

iDG

Robustness issues

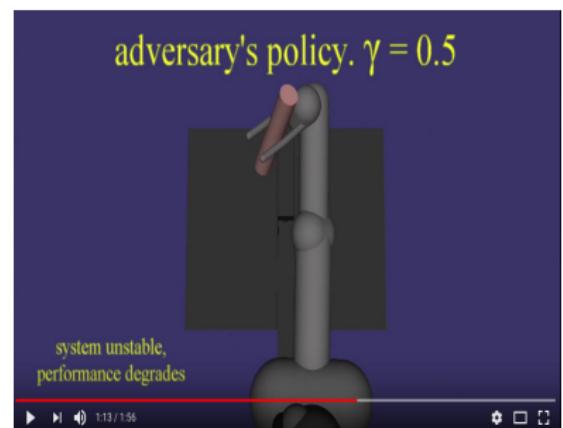
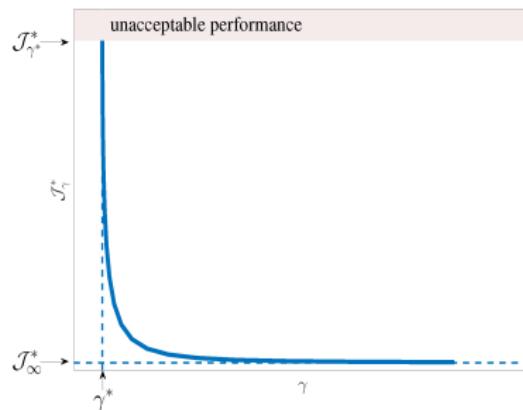
Approach

iDG Results

Future Work

Publications

References



Results: Iterative Dynamic Game

Automating
Treatment
Planning in
Radiation
Therapy

Lekan
Ogunmolu

BOO

MCTS
BOO Motivation

Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues

Approach

iDG Results

Future Work

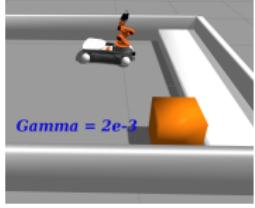
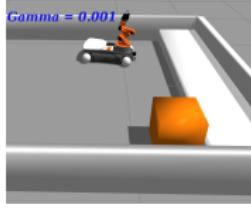
Publications

References

y_1^*



y_2^*



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

Future Work: MRI/RT Immobilization

Automating
Treatment
Planning in
Radiation
Therapy

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Ogunmolu

BOO
MCTS
BOO Motivation
Approach

Head
Stabilization
IMRT
MRI-LINAC

iDG
Robustness issues
Approach
iDG Results

Future Work
Publications
References

- 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

Automating
Treatment
Planning in
Radiation
Therapy

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Ogunmolu

BOO

MCTS
BOO Motivation
Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG

Robustness issues
Approach
iDG Results

Future Work

Publications

References

- 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. ✓

Publications

Automating
Treatment
Planning in
Radiation
Therapy

Lekan
Ogunmolu

BOO

MCTS
BOO Motivation
Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG

Robustness issues
Approach
iDG Results

Future Work

Publications

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Publications

Automating
Treatment
Planning in
Radiation
Therapy

Lekan
Ogunmolu

BOO

MCTS
BOO Motivation
Approach

Head
Stabilization

IMRT
MRI-LINAC

iDG

Robustness issues
Approach
iDG Results

Future Work

Publications

References

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Publications

Automating
Treatment
Planning in
Radiation
Therapy

Lekan
Ogunmolu

BOO

MCTS

BOO Motivation
Approach

Head
Stabilization

IMRT

MRI-LINAC

iDG

Robustness issues
Approach

iDG Results

Future Work
Publications

References

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