Impact of Artificial Intelligence on Cancer Radiotherapy

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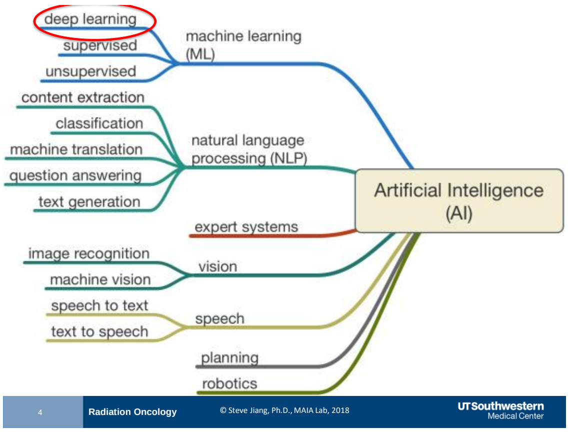
What is Artificial Intelligence (AI)

- Many definitions
- <u>The one I like</u>: AI makes it possible for machines to learn from experience, adjust to new inputs, and perform human-like tasks
  - Learn from human
  - Learn by itself
  - Do human's job

AI Is Changing The World

- Self driving cars
- Computer vision
- Healthcare
- Finance and economics
- … …


deep learning
supervised
unsupervised
machine learning (ML)
content extraction
classification
machine translation
question answering
text generation
natural language processing (NLP)
Artificial Intelligence (AI)
expert systems
image recognition
machine vision
vision
speech to text
text to speech
speech
planning
robotics
4
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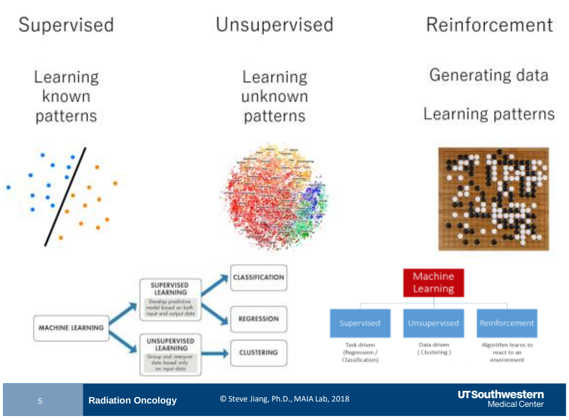
Supervised
Learning known patterns
Unsupervised
Learning unknown patterns
Reinforcement
Generating data
Learning patterns
MACHINE LEARNING
SUPERVISED LEARNING
UNSUPERVISED LEARNING
CLASSIFICATION
REGRESSION
CLUSTERING
Machine Learning
Supervised
Unsupervised
Reinforcement
Task driven (Regression / Classification)
Data driven (Clustering)
Algorithm learns to react to an environment
5
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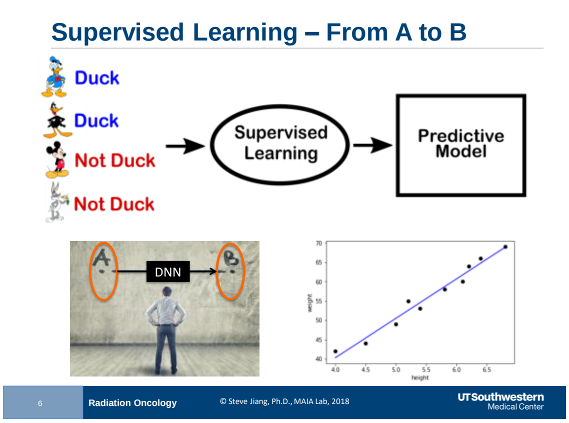
Supervised Learning – From A to B
Duck
Duck
Not Duck
Not Duck
Supervised Learning
Predictive Model
A
DNN
B
height
weight
6
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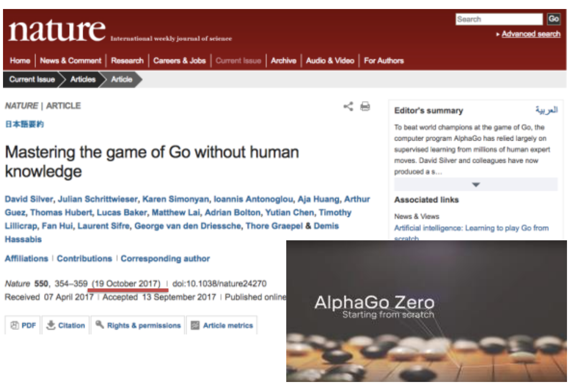
AlphaGo Master

- 5/2017
  - AlphaGo vs Ke Jie 9p (currently No.1 Go player in the world)
  - The final battle between man and machine in the board game
  - Result: 3 to 0
  - AlphaGo: no more competitive Go playing



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NATURE | ARTICLE

日本語要約

Mastering the game of Go without human knowledge

David Silver, Julian Schrittwieser, Karen Simonyan, Ioannis Antonoglou, Aja Huang, Arthur Guez, Thomas Hubert, Lucas Baker, Matthew Lai, Adrian Bolton, Yutian Chen, Timothy Lillicrap, Fan Hui, Laurent Sifre, George van den Driessche, Thore Graepel & Demis Hassabis

Affiliations | Contributions | Corresponding author

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Editor's summary العربية

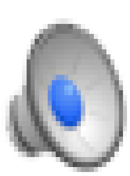
To beat world champions at the game of Go, the computer program AlphaGo has relied largely on supervised learning from millions of human expert moves. David Silver and colleagues have now produced a s…

Associated links

News & Views

Artificial intelligence: Learning to play Go from scratch

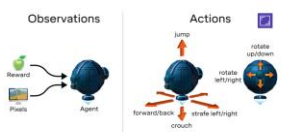
Deep Q-network (DQN) playing Breakout



https://www.youtube.com/watch?v=V1eYniJ0Rnk

Artificial General Intelligence

- Systems that can learn to solve any complex problem without needing to be taught how
- Agents should not be pre-programmed, but rather, able to learn automatically from their raw inputs and reward signals from the environment




NEWS & VIEWS

Learning to see and act

'AI IS THE NEW ELECTRICITY'

"Just as electricity transformed almost everything 100 years ago, today I actually have a hard time thinking of an industry that I don't think AI will transform in the next several years."

Andrew Ng
Former chief scientist at Baidu, Co-founder at Coursera

Narrow AI = Electricity; AGI = nothing we have seen before! - Steve Jiang

Artificial Intelligence in Medicine (AIM)

- Medical imaging and diagnostics
- Clinical decision support
- Treatment outcome prediction
- Precision and individualized medicine
- Prediction of chronic disease trajectories
- Healthcare delivery in resource limited regions
- Care delivery optimization, automation, safety
- Computational drug discovery and development
- Medical error detection and prevention
- Assisted care and chronic disease management with wearable sensors

AI in Radiation Oncology

- AI may greatly improve the treat outcome and reduce toxicity by providing
  - More precise cancer detection, diagnosis, staging etc
  - More personalized and precision treatment strategy
  - More accurate target delineation and organ segmentation
  - Better and faster treatment planning and treatment delivery
  - More convenient, frequent, and accurate patient follow up
- AI may greatly improve patient safety by
  - Automatically detecting and preventing medical errors
  - Using wearable sensors and RTLS technologies
- AI may greatly reduce disparity by
  - Transferring the high quality care from major academic centers to under-served patients via well trained AI software tools

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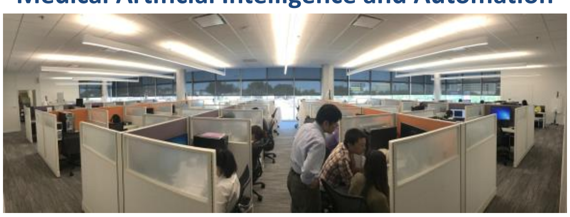
Medical Artificial Intelligence and Automation



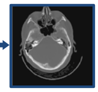
- What we are doing for AI in RO at UTSW MAIA Lab
- AAPM presentations

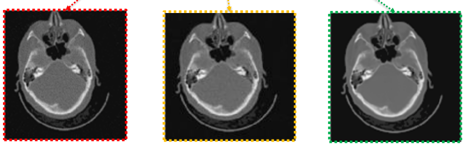
AI for Medical Imaging

CT Recon w/ Human-Like Auto Parameter Adjusting

$$f^* = \arg\min_f \frac{1}{2}|Pf - g|^2 + |\boxed{\lambda} \cdot \nabla f|.$$

pixel-wise parameters





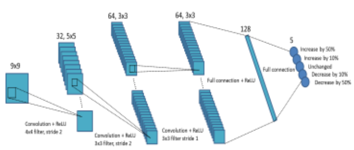
Bad parameters

Manual parameters (image level)

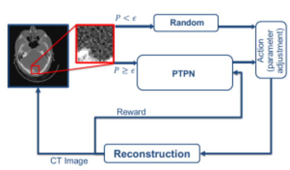
Ideal parameters

Shen, …, Jia, IEEE TMI 37(6):1430–1439, 2018

CT Recon w/ Human-Like Auto Parameter Adjusting

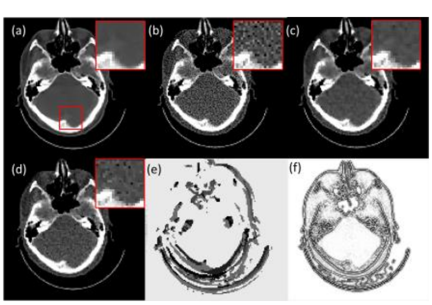


- A parameter tuning policy network (PTPN) is constructed and trained using end-to-end deep reinforcement learning (DRL)



Shen, …, Jia, IEEE TMI 37(6):1430–1439, 2018

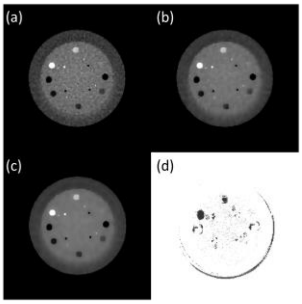
Testing Results on Simulation Data



(a) Ground Truth CT
(b) Reconstructed low-dose CT with random initial parameters
(c) Reconstructed low-dose CT with PTPN tuned parameters (pixel-wise)
(d) Reconstructed low-dose CT with manually tuned parameters (image level)
(e) PTPN tuned parameter map
(f) Optimal parameter map

Shen, …, Jia, IEEE TMI 37(6):1430–1439, 2018

Testing Results on Experimental Data

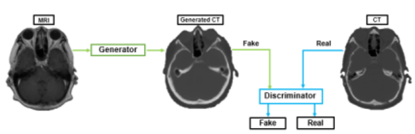


- (a) Reconstructed low-dose CT with random initial parameters
- (b) Reconstructed low-dose CT with manually tuned parameters (image level)
- (c) Reconstructed low-dose CT with PTPN tuned parameters (pixel-wise)
- (d) PTPN tuned parameter map

Shen, …, Jia, IEEE TMI 37(6):1430–1439, 2018

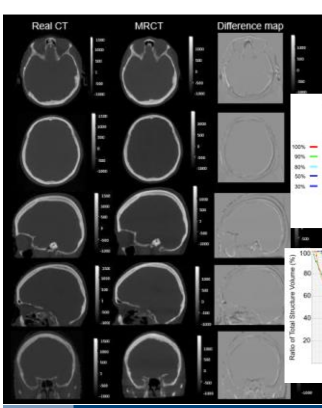
CT Synthetization from MRI

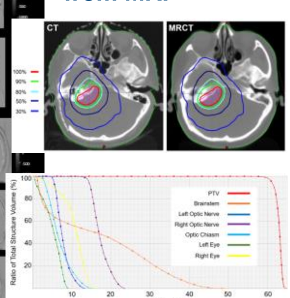
- Unpaired CT and MR images from 77 brain patients who underwent brain tumor radiotherapy
- CT images were acquired with a 512x512 matrix and voxel size 0.68mm×0.68mm×1.50mm
- MR images were acquired at 1.5T using a post-gadolinium 2D T1-weighted spin echo sequence with TE/TR = 15/3500 ms



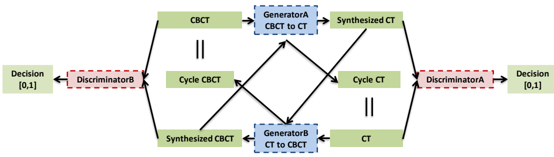
DCGAN - Deep convolutional generative adversarial network

CT Synthetization from MRI





CBCT to CT Translation using CycleGAN



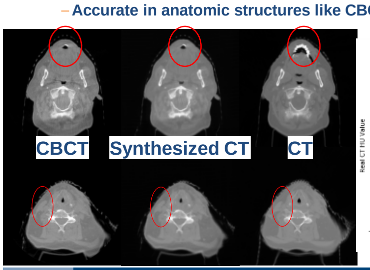
- **Generator**
  - 21 layers U-Net architecture
- **Discriminator**
  - 142×142 patch GAN
- **Loss function**
  - Adversarial loss
  - Cycle consistency loss
  - Identity mapping loss

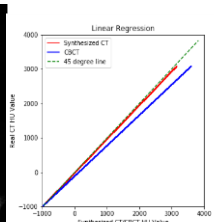
CBCT to CT Translation using CycleGAN

- **Training and validation data**
  - 13 H&N patients with **unpaired** CBCT and CT images
  - 80 slices/patient, totally 1360 slices
  - 960 slices for training, 80 slices for validation
- **Testing data**
  - 4 patients with CBCT and **deformed** CT images
  - Totally 320 slices

CBCT to CT Translation using CycleGAN

- **SCT is accurate in both spatial and intensity domains**
  - **Accurate in CT numbers like CT**
  - **Accurate in anatomic structures like CBCT**



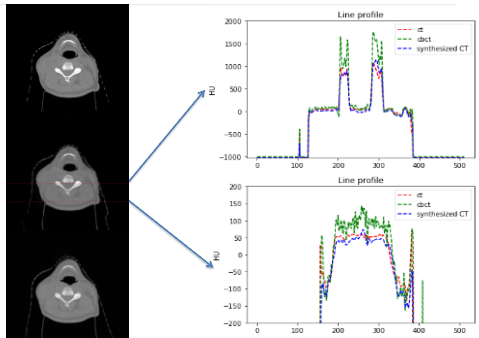


Results: Line Profiles

CBCT

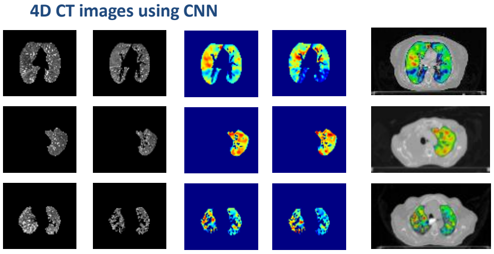
SCT

CT



From 4DCT Image to Ventilation Image

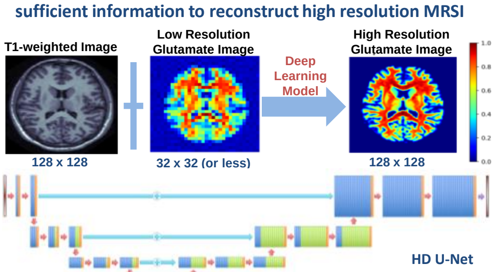
- Generating functional lung ventilation image from anatomical 4D CT images using CNN



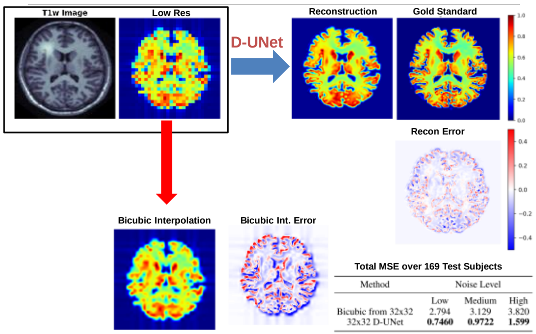
Input Predicted Truth Predicted on CT

Super-Resolution of MR Spectroscopic Imaging (MRSI)

<u>Hypothesis</u>:
Low resolution MRSI plus T1 weighted MRI should have sufficient information to reconstruct high resolution MRSI



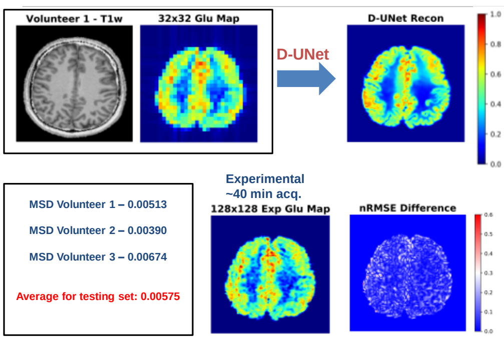
Super-Resolution MRSI: Testing Results (Simulation)



Total MSE over 169 Test Subjects

Method	Noise Level		
	Low	Medium	High
Bicubic from 32x32	2.794	3.129	3.820
32x32 D-UNet	**0.7460**	**0.9722**	**1.599**

Super-Resolution MRSI: Testing Results (In Vivo)



MSD Volunteer 1 – 0.00513

MSD Volunteer 2 – 0.00390

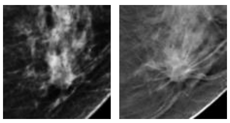
MSD Volunteer 3 – 0.00674

Average for testing set: 0.00575

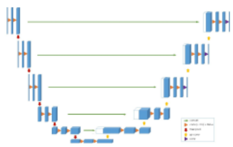
AI for Diagnosis and Prognosis

Breast Cancer Screening w/ DL and DBT

- Digital Breast Tomosynthesis (DBT): better accuracy than mammography especially for dense breasts
- 496 cases with mass-like lesions
- Ground truth for mass detection/segmentation
  - 3 radiologists, each with > 5 years experience in breast screening
- Ground truth for mass classification
  - Malignant cases were confirmed by biopsy surgical pathology

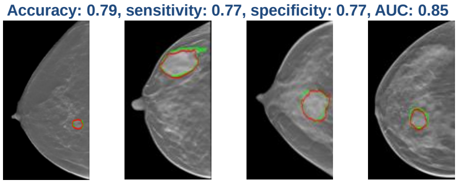


Mammography DBT



Mass Detection, Segmentation, and Classification

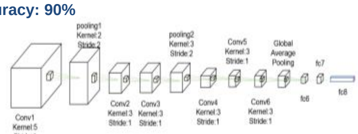
- Detection
  - Detection rate: 93%
- Segmentation
  - Average Dice Coefficient : 81%
- Classification
  - Accuracy: 0.79, sensitivity: 0.77, specificity: 0.77, AUC: 0.85



Green: Ground truth, Red: Model Output

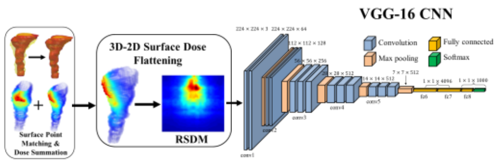
Cervical Lymph Node Malignancy Identification

- Large uncertainty in delineation of malignant lymph nodes in head and neck cancer
- AI-based clinical decision support tool for physicians to identify malignant lymph nodes using PET/CT
- Accuracy: 90%



CNN with Transfer Learning for Rectum Toxicity Prediction

- The VGG-16 convolutional neural network (CNN) is used as the prediction model
- Pre-trained the VGG-16 CNN with a large natural image dataset ImageNet (1.2 million)
- 42 cervical cancer patients treated with combined brachytherapy and external beam radiotherapy, including 12 patients w/ ≥Grade 2 rectal proctitis (bleeding)
- 58% accuracy for current clinical practice using logistic regression on D0.1/1/2cc rectal doses
- 88% accuracy for this work



Zhen, ..., Gu, *Phys Med Biol*. 2;62(21):8246-8263, 2017.

Stratify high-risk NSCLC patients after SBRT

- SBRT (Stereotactic Body Radiation Therapy) is the standard of care for local control in medically inoperable NSCLC patients:
  - High local control rate (>95% in three yeas)
  - Relatively high distant failure rate (31% in five years, RTOG 0236)
- Stratify patients with high risk of distant failure
  - Additional systemic therapy may reduce the risk and improve overall survival
  - Predict patients with distant failure using machine learning methods
  - Accuracy: 88%, Sensitivity: 83%, Specificity: 94%

Zhou, ..., Wang, *Phys Med Biol*. 62(11):4460-4478, 2017.

Prediction of Local Persistence/Recurrence after RT

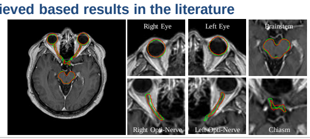
- 100 H/N cancer patients with definitive RT
- Post-treatment PET/CT images with FDG

Imaging	Accuracy	AUC	Sensitivity	Specificity
CT	72.0%	64.0%	70.0%	73.3%
PET	64.0%	62.7%	60.0%	67.7%
PET&CT	80.0%	72.7%	70.0%	86.6%

AI for Treatment Planning

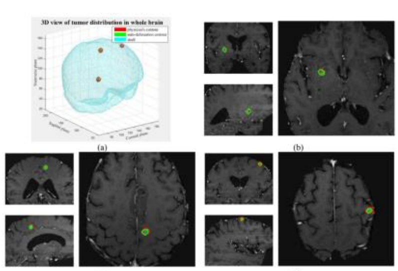
Brain Organ Segmentation in MRI

- Developed a recursive ensample deep neural network (Unet)
  - Organs are segmented recursively based on the difficulty level
  - Ensemble of local and global features is used
  - Achieved based results in the literature



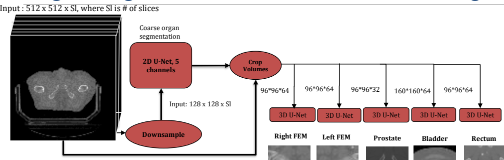
Metrics	Methods	R_Eye	L_Eye	BS	R_ON	L_ON	Chiasm
DSC(%)	Rough	89.4±3.1	86.4±3.9	83.2±4.7	71.4±15.0	69.3±15.5	54.8±11.6
	Fine	94.3±2.0	94.3±1.3	90.1±3.4	76.5±11.1	72.5±12.6	58.8±12.3
	Ensemble	**94.9±1.6**	**94.9±1.3**	**90.3±3.2**	**79.6±9.0**	**76.9±11.4**	**68.3±8.0**
HD(mm)	Rough	1.8±0.4	2.1±0.4	4.0±1.2	2.7±1.4	3.5±2.7	4.0±1.5
	Fine	1.3±0.4	1.3±0.4	3.0±1.2	3.1±3.2	3.2±2.1	3.4±1.3
	Ensemble	1.2±0.2	1.2±0.3	3.0±1.2	2.1±0.9	3.2±2.5	3.9±3.0

Brain Mets Segmentation

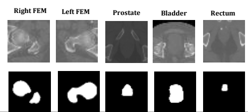


Liu, …, Gu, PLoS One. 2017 Oct 6;12(10):e0185844. doi: 10.1371

Organ Segmentation in Male Pelvis CT Images

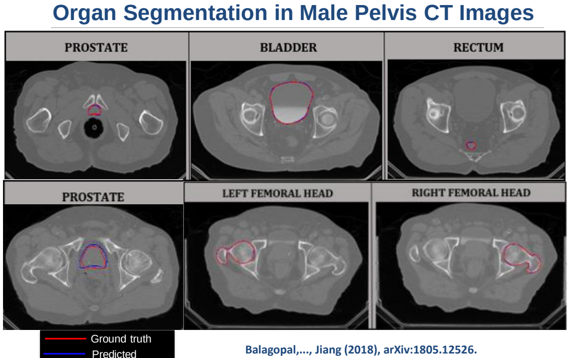


- 2D Unet for organ localization
- 3D Unet for refined organ segmentation
- Best results in literature



	Shao Y et al. (2014)	Gao Y et al. (2012)	Gao Y et al. (2016)	Feng Q et al. (2010)	Martinez et al. (2014)	Ma L et al. (2017)	Our method
Method	Regression forest	Deformable model	Multi-task random forest	Population-patient based learning	Geometrical shape model	Deep learning	Deep learning
Prostate	88%	86%	87%	89%	87%	86.8%	90%
Bladder	86%	91%	92%	-	89%	-	95%
Rectum	85%	79%	88%	-	82%	-	84%

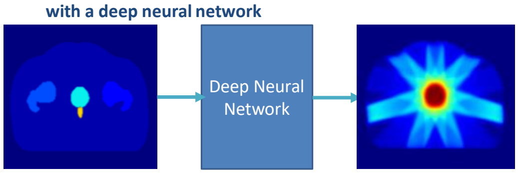
Organ Segmentation in Male Pelvis CT Images



Balagopal,..., Jiang (2018), arXiv:1805.12526.

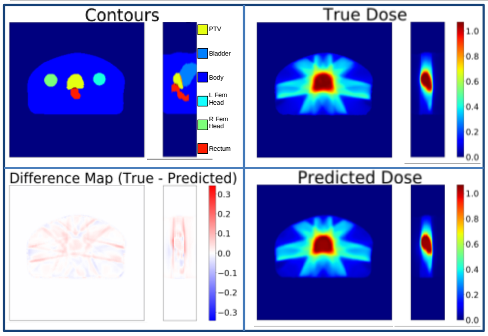
3D Dose Prediction Using Deep Learning

- Predict 3D radiation dose distribution based on
  - Patient's anatomy and physician's prescription
- <u>Hypothesis</u>: Patients of similar medical conditions should have a similar relationship between optimal radiation dose and patient anatomy and this relationship can be learned with a deep neural network

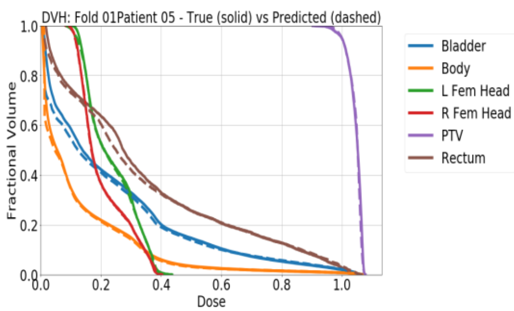


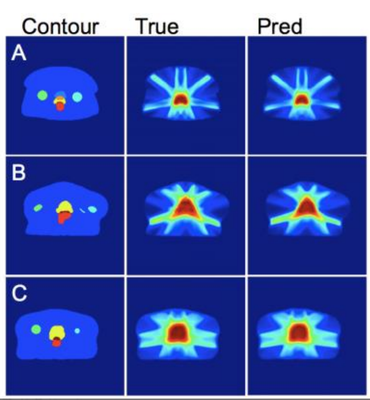
Nguyen, ..., Jiang, (2017) arXiv:1709.09233.

Test Results for A Prostate Case (IMRT)



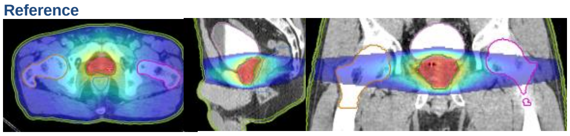
Test Results for A Prostate Case (IMRT)



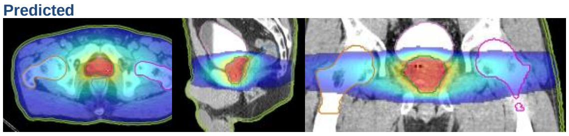


Prostate VMAT Dose Prediction w/ HD U-Net

Reference

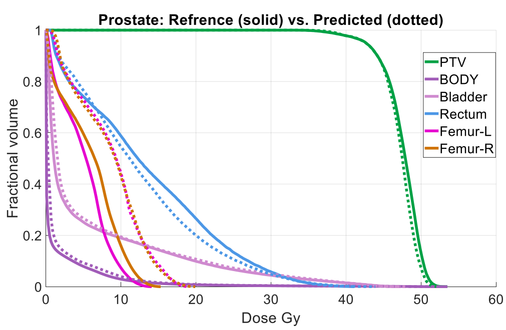


Predicted

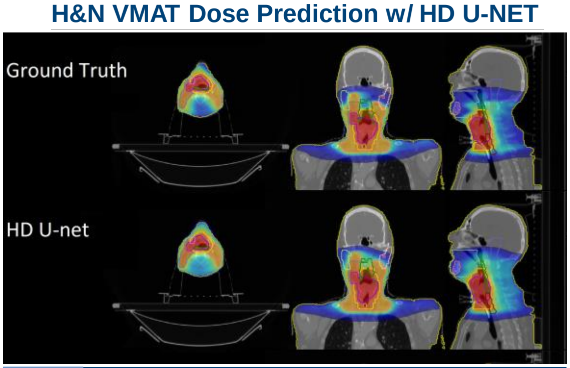


- 83 prostate VMAT patients
- 53 for training, 13 for validation, 17 for testing

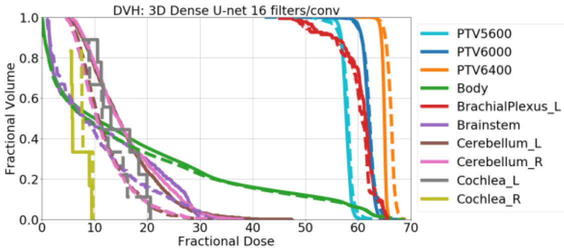
Prostate VMAT Dose Prediction w/ HD U-Net



H&N VMAT Dose Prediction w/ HD U-NET

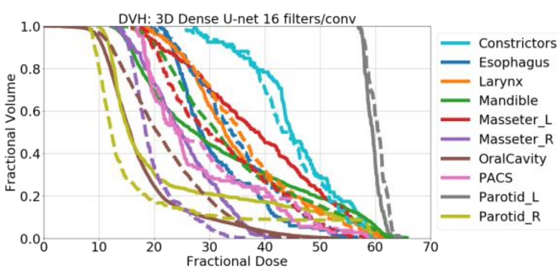


H&N VMAT Dose Prediction w/ HD U-NET

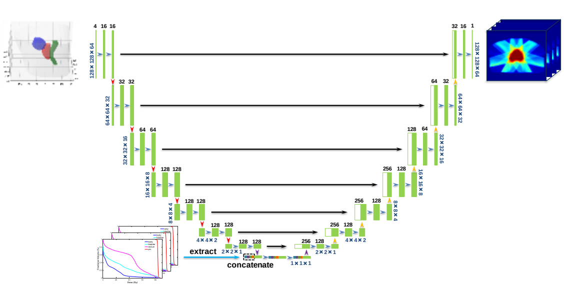


Nguyen, …, Jiang, (2017) arXiv:1805.10397

H&N VMAT Dose Prediction w/ HD U-NET



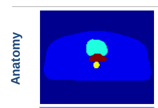
Individualized 3D Dose Distribution Prediction



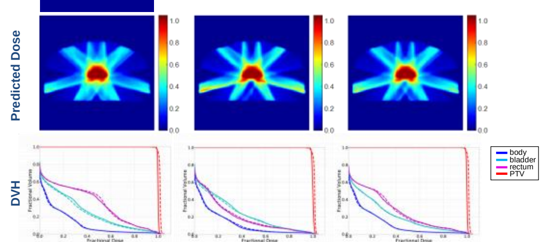
Individualized 3D Dose Distribution Prediction

- Prostate IMRT Patient
  - 97 patients with 10 different plans for each patient
  - 77 patients for training while 20 patients for testing
- Data preprocessing
  - Input 1: PTV, rectum, bladder, body contours
  - Input 2: DVH vector for each contour
  - Output: 3D dose distribution

Same Patient with Different Input DVH's

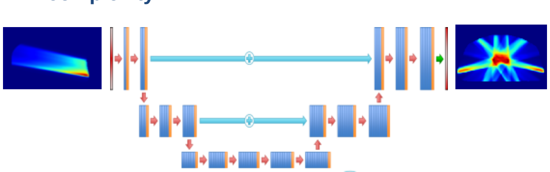


- Solid lines - desired DVH curves
- Dashed lines - DVH curves of the predicted dose distributions



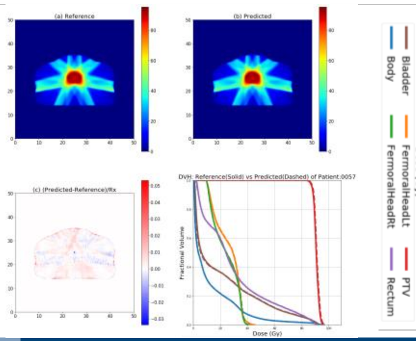
Dose Calculation using Deep Learning

- Dose calculation using deep learning directly from fluence maps is a complex system
- Combining 1st order approximation (ray tracing) with deep learning can greatly reduce the complexity



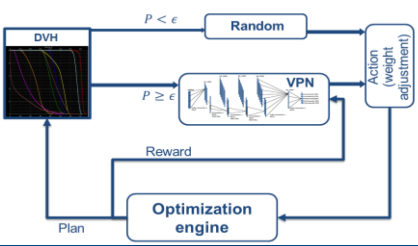
HD Unet

Dose Calculation using Deep Learning



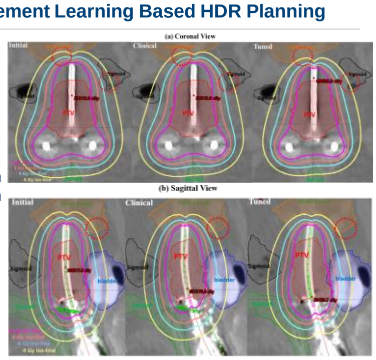
Deep Reinforcement Learning Based HDR Planning

- We train a virtual planner network (VPN) to automatically adjust weights for optimal HDR plan quality
- Use Deep reinforcement learning (DRL) to teach the network to tune weights



Deep Reinforcement Learning Based HDR Planning

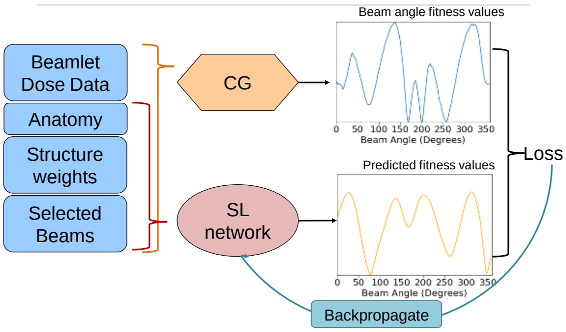
- Testing case 4
- Same PTV coverage
- OARs are spared better in auto-tuned plan



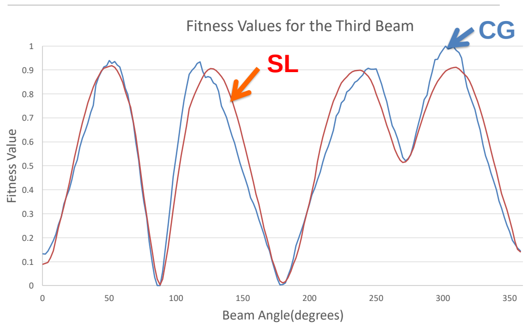
Beam Orientation Optimization (BOO) w/ DL

- BOO is important for 4Pi RT and CyberKnife
- Traditional BOO algorithms
  - requires pre-dose calculation for a large number of candidate beams
  - Difficulty to explore the huge solution space
- Goal: develop an AlphaGo type of DL algorithm
  - reinforcement learning (RL) policy network
  - Monte Carlo Tree Search (MCTS)
- 1st step: train a supervised learning (SL) policy network as a good starting point for RL policy network, using column generation (CG)

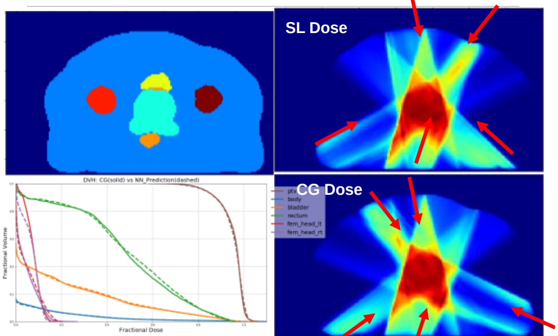
Training a SL Network using CG



SL Policy Network vs Column Generation



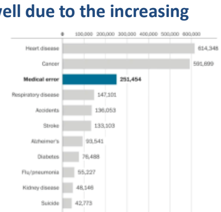
SL Policy Network vs Column Generation



AI for QA and Error Detection

Medical Error Detection and Prevention

- After heart disease and cancer, medical errors are the third leading cause of death in US
- Many quality assurance and error detection processes are still done manually by humans
- Rule based methods don't work well due to the increasing complexity in patient treatment
- *SafetyNet*
  - Run quietly in the background in patient electronic medical records and treatment management systems
  - Automatically detect and highlight any anomalies
  - Serve as an assistant to clinicians



Automated Patient Data Cleaning: Organ Labeling

- About 80% efforts for clinical data analysis are spent on data cleaning
- One typical problem in radiation oncology: inconsistent organ labeling
- 17% of misadministration caused by modifying and/or renaming organs

Patient 1	Patient 2	Patient 3
GTV-P 70	PTV HN 66 Gy	Old ptv
GTV-N 70	Brainstem	Brainstem
CTV-P 59.4	Squeeze	Esophagus
R Neck 1b RP 56	TMJR	Spinal_cord
R Parotid 56 (11)	Parotid SUP R	ParotidGland_R
RT PAROTID	R66	PTV600_NEW
LT PAROTID	Parotid L	ParotidGland_L
L Parotid	Warm	Normal
Larynx	Coverage	P5940
RT Brachial Plexus	SMG L	BrachialPlexus_R
LT Brachial Plexus	SMG R	BrachialPlexus_L
RT Cochlea	Cochlea R	C5
LT Cochlea	Cochlea L	T2
PTV 56 L Neck wo 1b	ICAL	r66
PTV 56 L Neck w 1b	NT	r1(167)
RT MASSETER	Masseter R	r2(163)
LT MASSETER	Masseter L	r3(157)

Authority, P P S Errors in radiation therapy Pennsylvania Patient Safety Advisory 6 3 87-92

Three Patient Data Sets

- 100 prostate patients w/ 5 organs
- 54 H&N patients w/ 9 organs
- 218 H&N patients w/ 29 organs

Organ ID	Organ Name	Organ count
0	BrachialPlexus_L	63
1	BrachialPlexus_R	61
2	Brain	51
3	Brainstem	189
4	Cerebellum_L	113
5	Cerebellum_R	105
6	Chiasm	33
7	Cochlea_L	158
8	Cochlea_R	156
9	Constrictors	149
10	Epiglottis	33
11	Esophagus	143
12	Eye_L	34
13	Eye_R	34
14	Larynx	166

Organ ID	Organ Name	Organ count
15	Lens_L	22
16	Lens_R	24
17	Lips	24
18	Mandible	160
19	Masseter_L	108
20	Masseter_R	106
21	OralCavity	167
22	Parotid_L	180
23	Parotid_R	129
24	Skin	26
25	SMG_L	92
26	SMG_R	101
27	SpinalCord	205

Model: Deep 3D ResNeXt-44

Stage	Output	ResNeXt-44
conv1	96X96X48	32, 5X5X5, 2
conv2	48X48X24	3X3X3 max pool, 2 1X1X1, 64 3X3X3, 64, C=32 X3 1X1X1, 128
conv3	24X24X12	1X1X1, 128 3X3X3, 128, C=32 X4 1X1X1, 256
conv4	12X12X6	1X1X1, 256 3X3X3, 256, C=32 X4 1X1X1, 512
conv5	6X6X3	1X1X1, 512 3X3X3, 512, C=32 X3 1X1X1, 1024
fc	1X1X1	global average pool 29-d , softmax

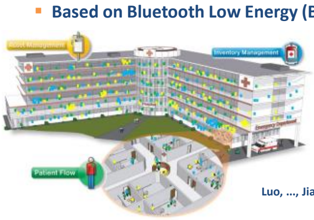
Testing Results

- 100 prostate patients w/ 5 organs
  - 80% for training and 20% for testing
  - 100% accuracy
- 54 H&N patients w/ 9 organs
  - 80% for training and 20% for testing
  - 100% accuracy
- 218 H&N patients w/ 29 organs
  - 80% for training and 20% for testing
  - 97% accuracy

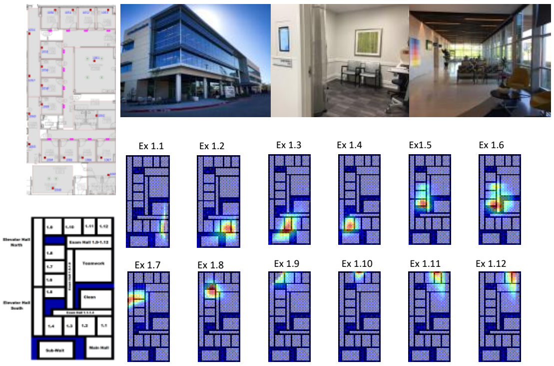
Wearable Sensors and Smart Clinic

Wearable Sensors and Smart Clinic

- Tracking patients, clinical staff, and assets to improve efficiency and safety
- Measuring patient vital signs etc
- Based on Bluetooth Low Energy (BLE)



Luo, ..., Jiang, Work in progress, 2018. (MAIA Lab)

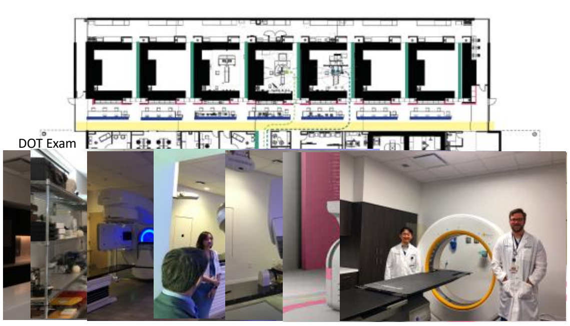


70 Radiation Oncology UTSouthwestern Medical Center

Moved in New Rad Onc Building in April 2017

71 Radiation Oncology UTSouthwestern Medical Center

First Floor



72 Radiation Oncology UTSouthwestern Medical Center

Second Floor

Moving Forward

- We are designing a new building
  - Another 7 vaults
  - The whole building will be an AI laboratory
- We are hiring
  - Director of clinical physics
  - Junior clinical faculty (assistant professor level)
  - Junior research faculty (instructor level)
  - Postdoctoral fellows
  - Residents

Acknowledgement