CIRMS 2018

Patient Safety in the Age of Big Data

Machine Learning, Measurements, and Standards for Making Radiation Treatments Safer

Christopher Berlind, PhD

Co-founder and Chief Technology Officer, Oncora Medical

April 17th, 2018

0 Introduction

Why?

0 Introduction

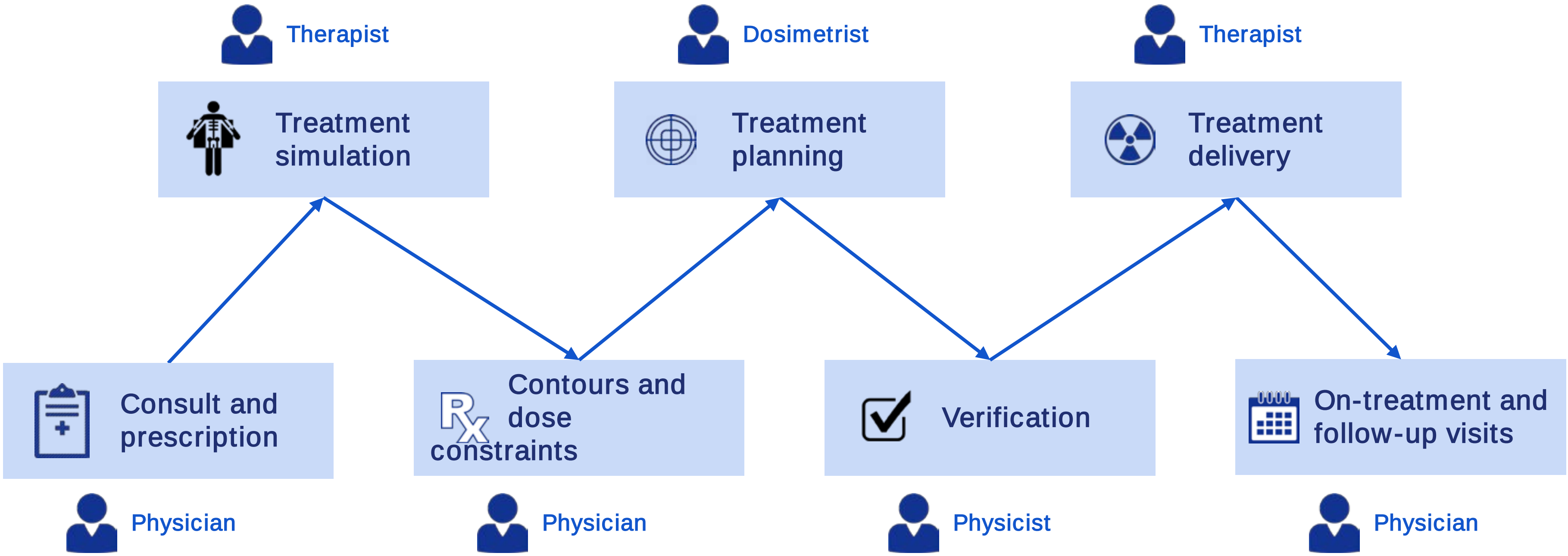
Why?

0 Introduction

Outline

1 Radiation Therapy and Patient Safety

RT Clinical Workflow



1 Radiation Therapy and Patient Safety

Patient Safety

Radiation therapy is a complex **risk-benefit problem.**

Benefit patient

- Shrink or eliminate local tumor
- Prevent recurrence and metastasis
- Prolong patient life

Minimize harm

- Acute toxicities
- Late effects
- Quality of life

Some risk is unavoidable in order to provide sufficient dose.

Any deviation from the optimal risk-benefit tradeoff is an **error** and a **patient safety issue**.

1 Radiation Therapy and Patient Safety

Sources of Error

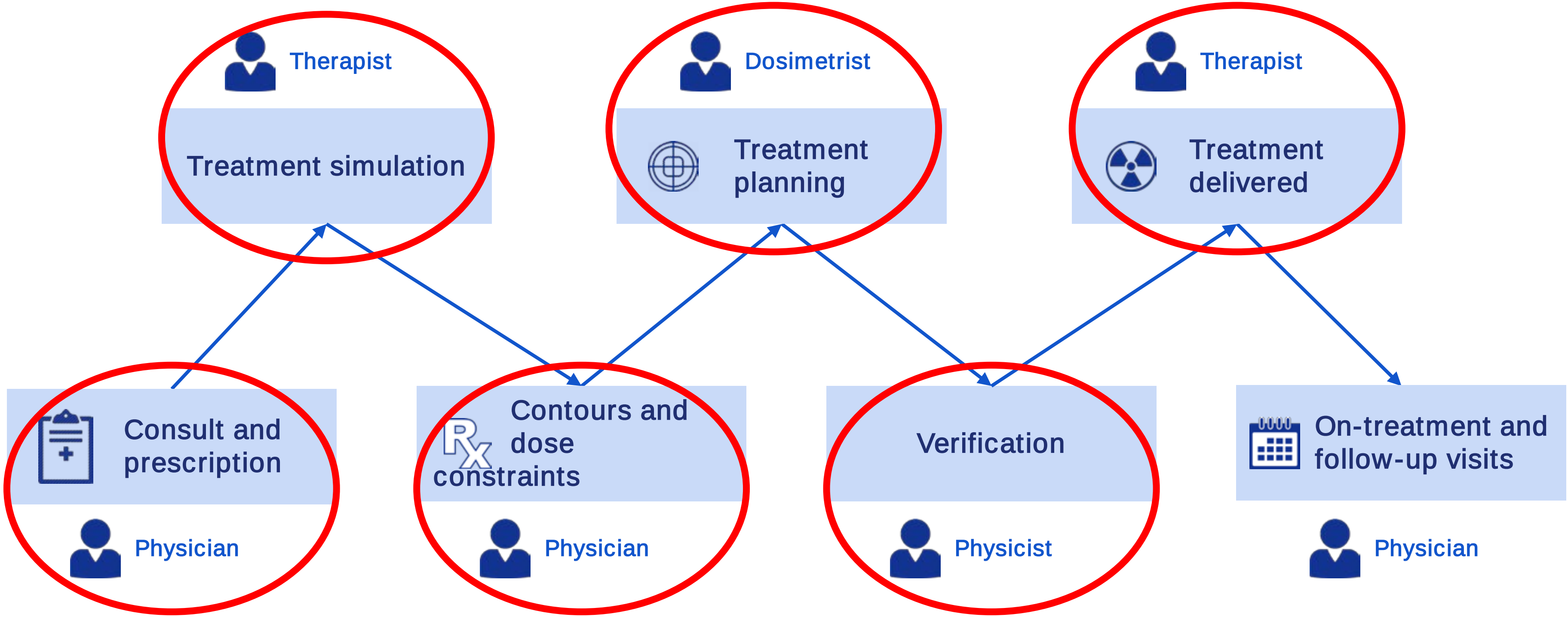
The vast majority of errors in RT
are caused by **human mistakes**.

Where can errors come from?

- Suboptimal clinical decisions
- Suboptimal treatment planning
- Imaging problems
- Machine miscalibration
- Incorrect/inconsistent contours
- Patient positioning errors

1 Radiation Therapy and Patient Safety

Sources of Error



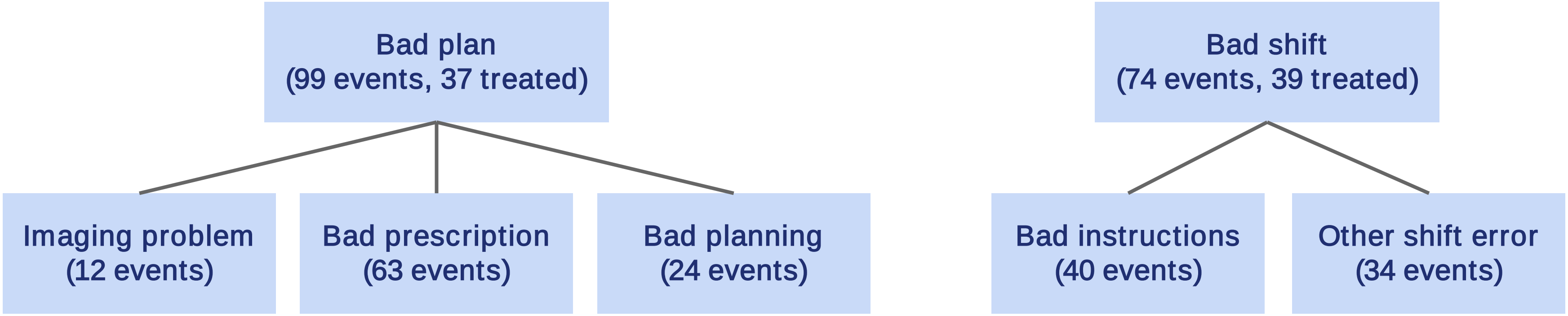
1 Radiation Therapy and Patient Safety

Sources of Error

Common error pathways seen in the RO-ILS data that demonstrate opportunities for improving treatment safety

Ezzell G, Chera B, Dicker A, Ford E, Potters L, Santanam L, Weintraub S

- Radiation Oncology Incident Learning System (RO-ILS)
- Analyzed 396 of the ~2300 events that were considered highest priority
- At least 76 of these (~20%) resulted in incorrectly delivered treatments



1 Radiation Therapy and Patient Safety

Patient Safety Technologies

Provide humans with **tools** to help reduce errors.

Hardware

- Dosimetric measurement (phantoms/arrays)
- Patient immobilization devices
- Innovative couch systems
- Image-guided radiotherapy (IGRT)

Software (plus data from hardware)

- Machine QA
- Plan QA
- Imaging tools
- **Machine learning**

1 Radiation Therapy and Patient Safety

Patient Safety Technologies

Provide humans with **tools** to help reduce errors.

Hardware

- Dosimetric measurement (phantoms/arrays)
- Patient immobilization devices
- Innovative couch systems
- Image-guided radiotherapy (IGRT)

Software (plus data from hardware)

- Machine QA
- Plan QA
- Imaging tools
- **Machine learning**

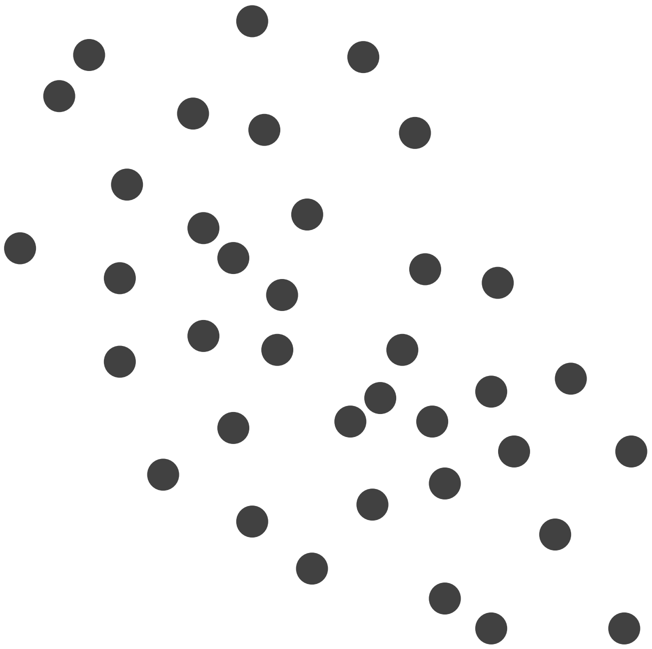
Suboptimal clinical decisions	
Imaging problems	✓
Incorrect/inconsistent contours	✓
Suboptimal treatment planning	✓
Machine miscalibration	✓
Patient positioning errors	✓

2 Machine Learning

Supervised learning (prediction)

Examples

- Images
- Stocks
- Cancer treatments

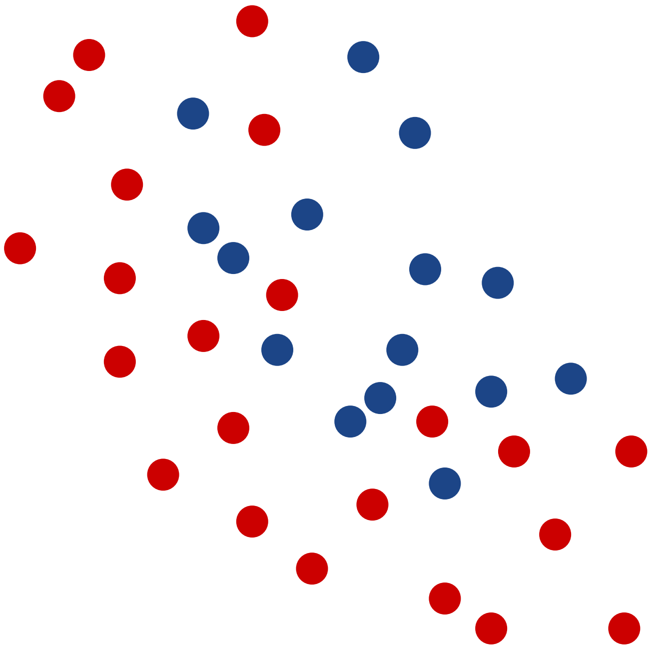


2 Machine Learning

Supervised learning (prediction)

Examples

- Images
  - Cars vs. Trucks
- Stocks
  - Price up vs. Price down
- Cancer treatments
  - Success vs. Failure



2 Machine Learning

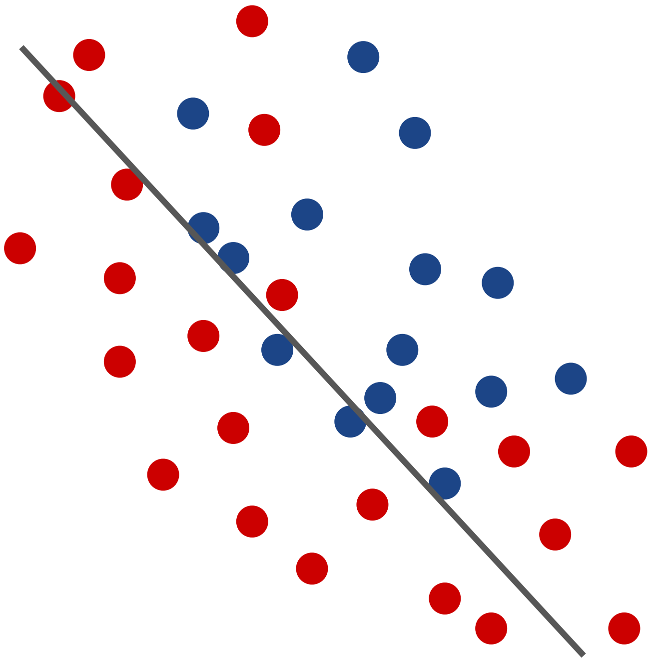
Supervised learning (prediction)

Examples

- Images
  - Cars vs. Trucks
- Stocks
  - Price up vs. Price down
- Cancer treatments
  - Success vs. Failure

Algorithms

- Logistic regression
- Support vector machines
- Random forests
- Neural networks



2 Machine Learning

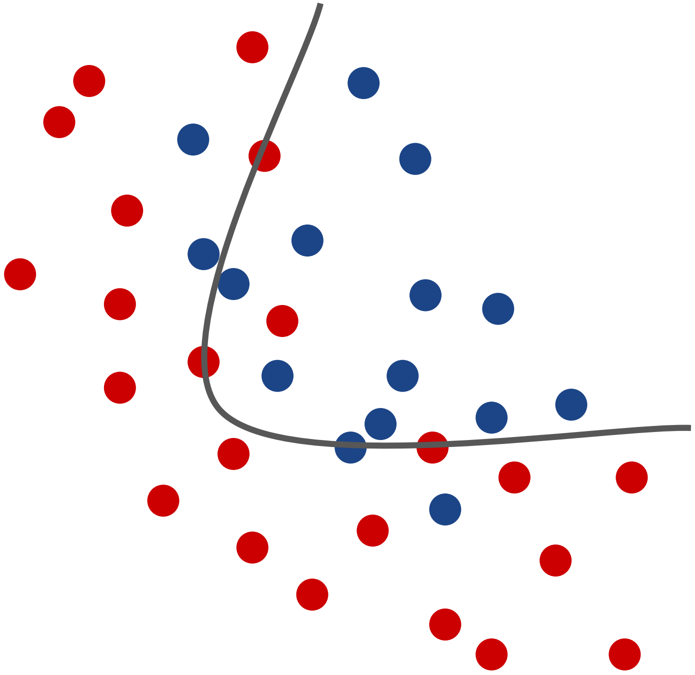
Supervised learning (prediction)

Examples

- Images
  - Cars vs. Trucks
- Stocks
  - Price up vs. Price down
- Cancer treatments
  - Success vs. Failure

Algorithms

- Logistic regression
- Support vector machines
- Random forests
- Neural networks



2 Machine Learning

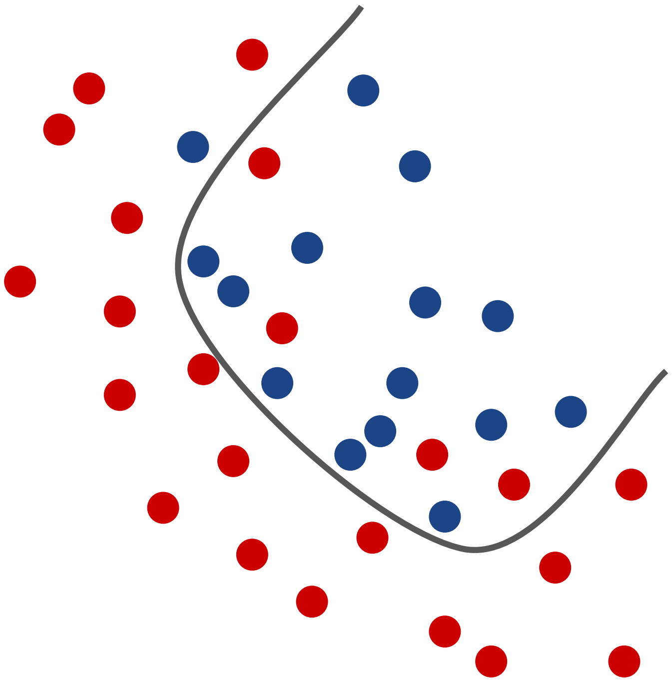
Supervised learning (prediction)

Examples

- Images
  - Cars vs. Trucks
- Stocks
  - Price up vs. Price down
- Cancer treatments
  - Success vs. Failure

Algorithms

- Logistic regression
- Support vector machines
- Random forests
- Neural networks



2 Machine Learning

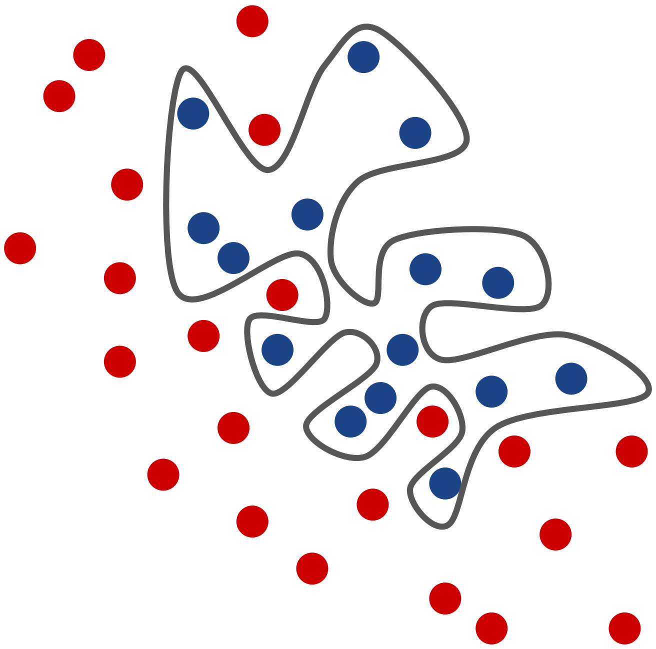
Supervised learning (prediction)

Examples

- Images
  - Cars vs. Trucks
- Stocks
  - Price up vs. Price down
- Cancer treatments
  - Success vs. Failure

Algorithms

- Logistic regression
- Support vector machines
- Random forests
- Neural networks

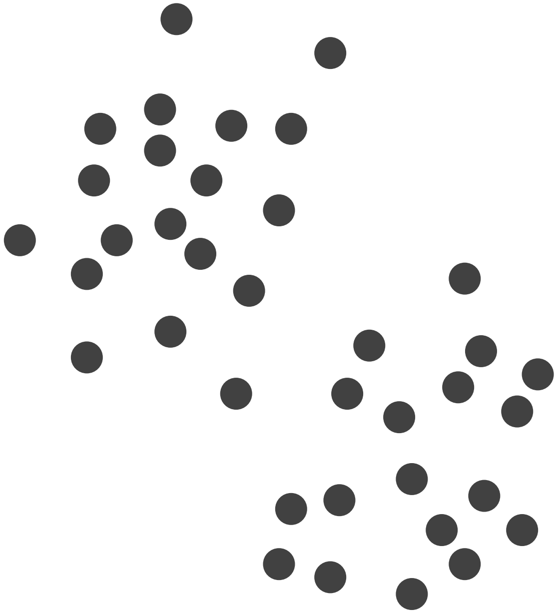


2 Machine Learning

Unsupervised learning (clustering)

Examples

- Images
- Stocks
- Cancer patients
- Cancer treatments



2 Machine Learning

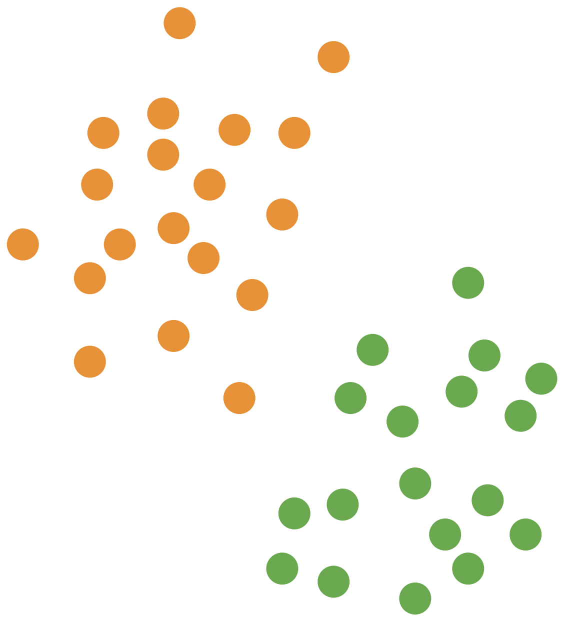
Unsupervised learning (clustering)

Examples

- Images
- Stocks
- Cancer patients
- Cancer treatments

Algorithms

- *k*-Means
- Agglomerative
- Spectral
- DBSCAN



2 Machine Learning

Unsupervised learning (clustering)

Examples

- Images
- Stocks
- Cancer patients
- Cancer treatments

Algorithms

- *k*-Means
- Agglomerative
- Spectral
- DBSCAN

3 Machine Learning for Patient Safety

Predicting outcomes

Patient + Treatment

→ **Predictive Model** →

Efficacy

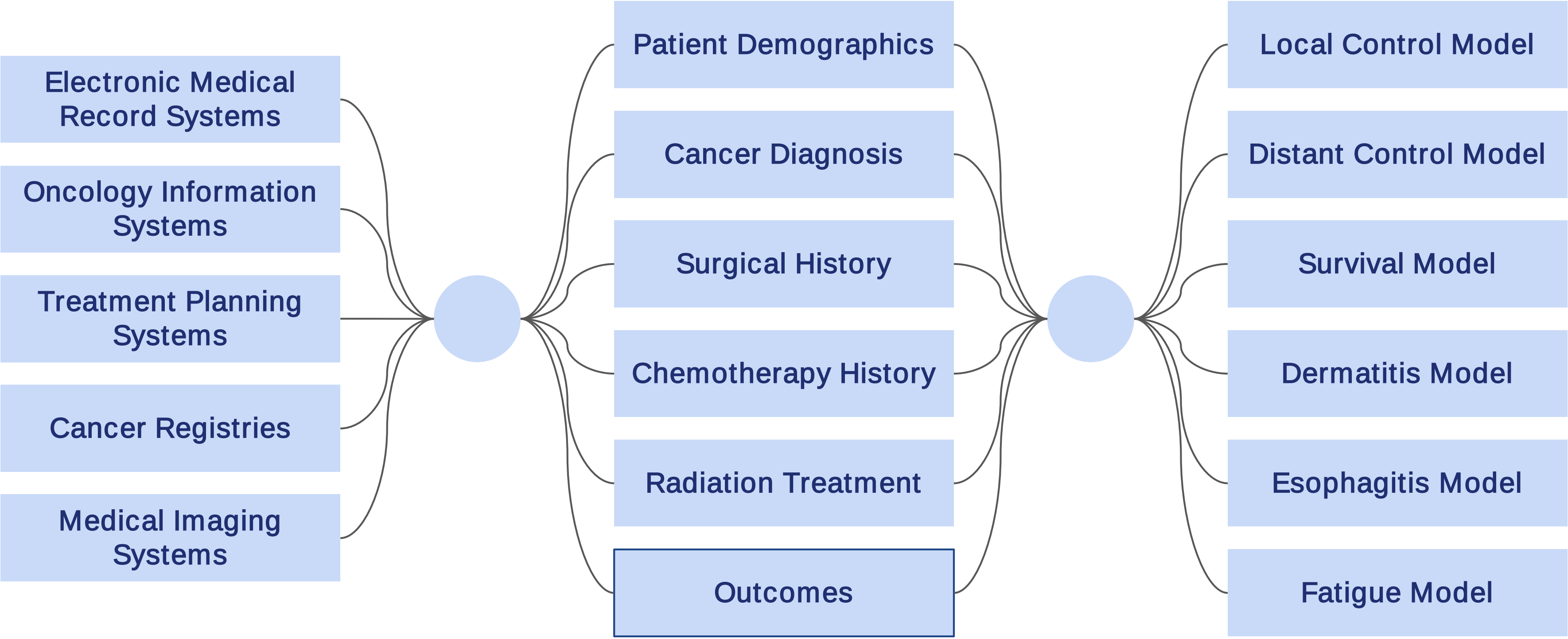
Local control:	95%
Distant control:	97%
3-yr survival:	98%

Toxicities

Dermatitis:	35%
Esophagitis:	3%
Fatigue:	46%

3 Machine Learning for Patient Safety

Predicting outcomes



3 Machine Learning for Patient Safety

Predicting outcomes

Patient demographics

- Age
- Sex
- Height
- Weight
- Race

Diagnosis history

- Smoking history
- Cardiovascular disease
- Endocrine disorders
- Respiratory disease
- CNS disorders

Tumor characteristics

- Primary cancer
- Treatment site
- Tumor size
- TNM staging
- Cancer histology

Surgical history

- Mastectomy
- Prostatectomy
- Pneumonectomy
- Esophagectomy
- Thyroidectomy

Chemotherapy history

- Any chemotherapy agent
- Hormonal therapy
- Alkylating antineoplastics
- Phytogenic antineoplastics
- Myeloablative antineoplastics

Radiation treatment

- Treatment energy
- Treatment modality
- Total dose
- Total fractions
- Cone-down boost

3 Machine Learning for Patient Safety

Predicting outcomes (study 1)

The relative impact of clinical variables on radiotherapy outcome predictions

CA Ahern (Oncora), CG Berlind (Oncora), WD Lindsay (Oncora),
PE Gabriel (Penn), CB Simone II (Maryland)

Presented at AAPM 2017

3 Machine Learning for Patient Safety

Predicting outcomes (study 1)

16,689 RT courses

At **one** institution (Penn)

Across **all disease sites**

From **2008** to **2015**

≥3 months follow-up

230+ predictor variables

76 outcomes

65 adverse events (CTCAE v4.0)

- Radiation dermatitis
- Esophagitis
- Dysphagia
- Fatigue
- *And **many** more*

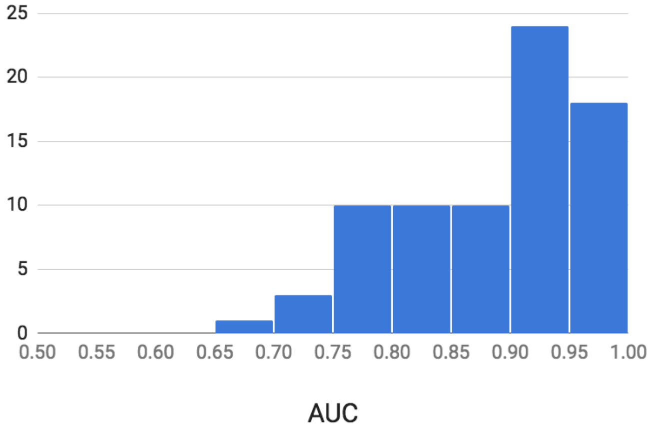
11 treatment efficacy outcomes

- Local, nodal, distant control
- Hospitalization
- Survival

3 Machine Learning for Patient Safety

Predicting outcomes (study 1)

Area under ROC curve across all outcome models



Median AUC: **0.912**

3 Machine Learning for Patient Safety

Predicting outcomes (study 2)

Applying a machine learning approach to predict acute toxicities during radiation for breast cancer patients

J Reddy (MD Anderson), WD Lindsay (Oncora), CG Berlind (Oncora),
CA Ahern (Oncora), and BD Smith (MD Anderson)

Abstract in submission to ASTRO 2018

3 Machine Learning for Patient Safety

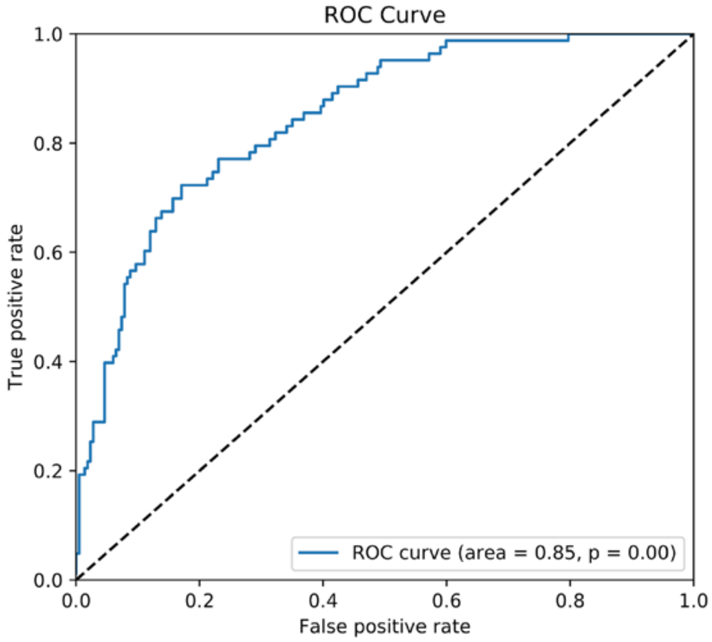
Predicting outcomes (study 2)

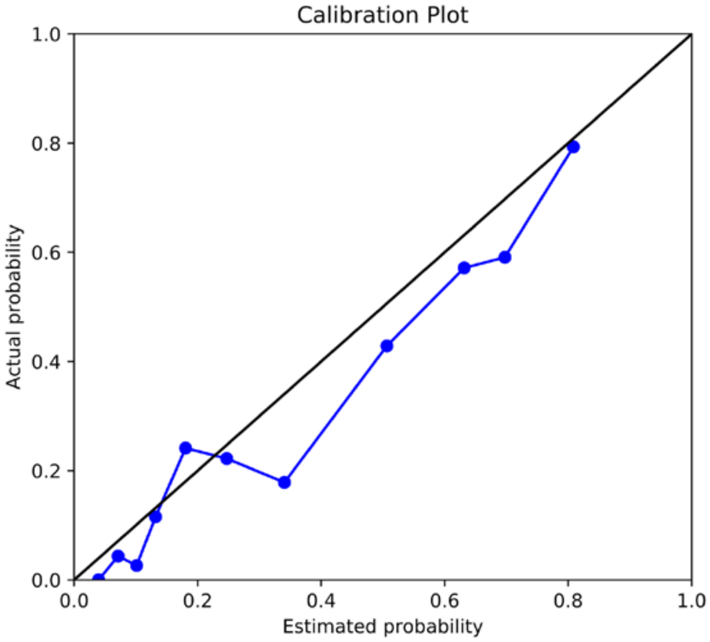
- **4 toxicities:** Dermatitis, moist desquamation, breast pain, fatigue
- **~2,000 breast RT episodes** used for **training** several types of predictive models
  - Logistic regression
  - Random forests
  - Boosted decision trees
- Next **300 episodes** used as **independent validation set**

3 Machine Learning for Patient Safety

Predicting outcomes (study 2)

Performance of predictive model for **radiation dermatitis**:

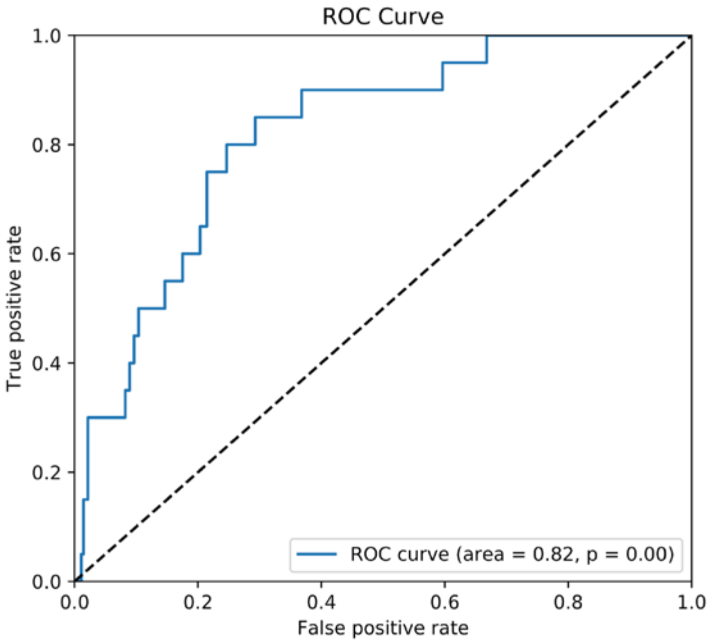


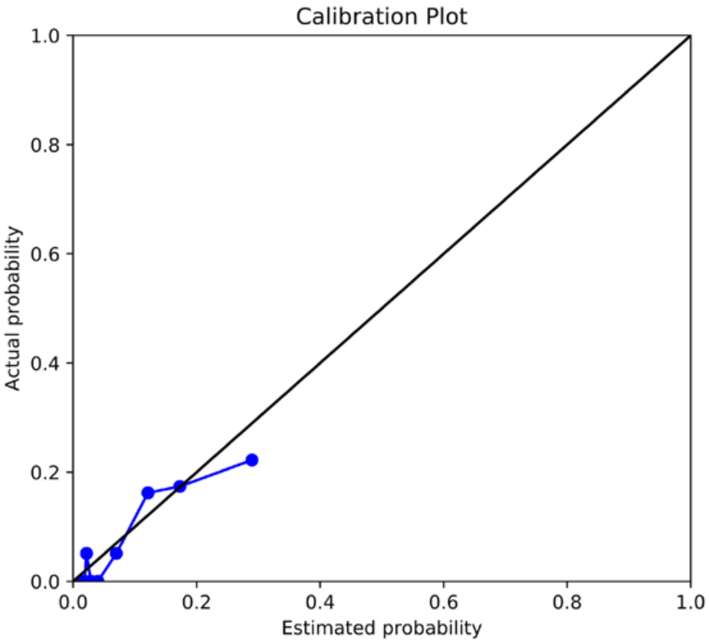


3 Machine Learning for Patient Safety

Predicting outcomes (study 2)

Performance of predictive model for **moist desquamation**:





3 Machine Learning for Patient Safety

Predicting outcomes

How can outcome predictions improve patient safety?

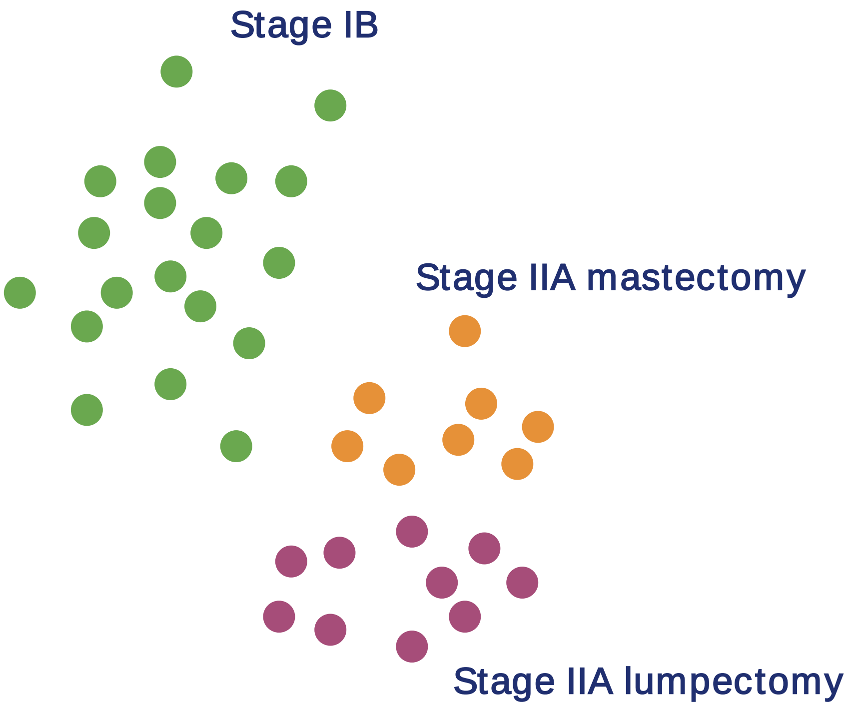
- Improve clinical decision-making by identifying clinical choices resulting in higher than expected risk
- Improve treatment planning by identifying plans resulting in higher than expected risk
- Quantify unavoidable risk to help prepare for likely adverse events
- Predict which patients are most likely to benefit from image guidance

Suboptimal clinical decisions	✔
Imaging problems	
Incorrect/inconsistent contours	
Suboptimal treatment planning	✔
Machine miscalibration	
Patient positioning errors	✔

3 Machine Learning for Patient Safety

Patient clustering

- **Cluster patients** based on
  - Diagnosis
  - Pathology
  - Surgical history
  - Chemotherapy history
- Review prior treatments for similar patients



3 Machine Learning for Patient Safety

Patient clustering

How can patient clustering improve patient safety?

- Improve consistency of clinical decisions and standardize across practice
- Improve clinical decision-making by identifying prescriptions that are unusual for a given patient
- Improve treatment planning by identifying plans that are unusual for a given patient

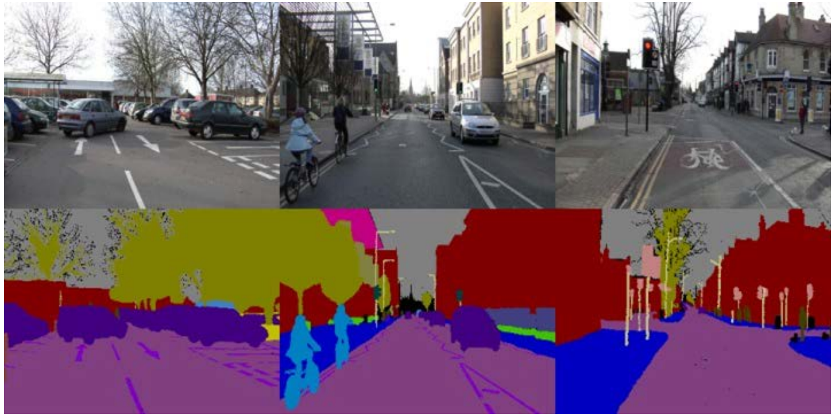
Suboptimal clinical decisions	✓
Imaging problems	
Incorrect/inconsistent contours	
Suboptimal treatment planning	✓
Machine miscalibration	
Patient positioning errors	

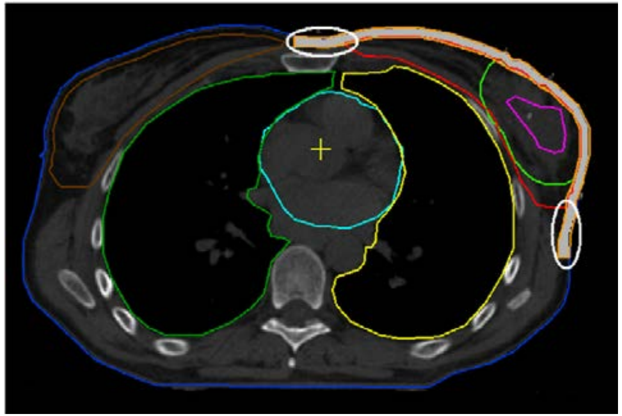
3 Machine Learning for Patient Safety

Imaging analysis and deep learning

Automatic contouring

- Targets and organs at risk
- Improve consistency and efficiency





3 Machine Learning for Patient Safety

Imaging analysis and deep learning

Evaluating the linearity of risk functions across radiotherapy outcomes using deep learning

CA Ahern (Oncora), TS Peiffer (Oncora), CG Berlind (Oncora),
WD Lindsay (Oncora), Y Xiao (Penn), CB Simone II (Maryland)

To be presented at AAPM 2018

3 Machine Learning for Patient Safety

Imaging analysis and deep learning

16,689 RT courses

At **one** institution (Penn)

Across **all disease sites**

From **2008** to **2015**

≥3 months follow-up

230+ predictor variables

68 outcomes

63 adverse events (CTCAE v4.0)

- Radiation dermatitis
- Esophagitis
- Dysphagia
- Fatigue
- *And **many** more*

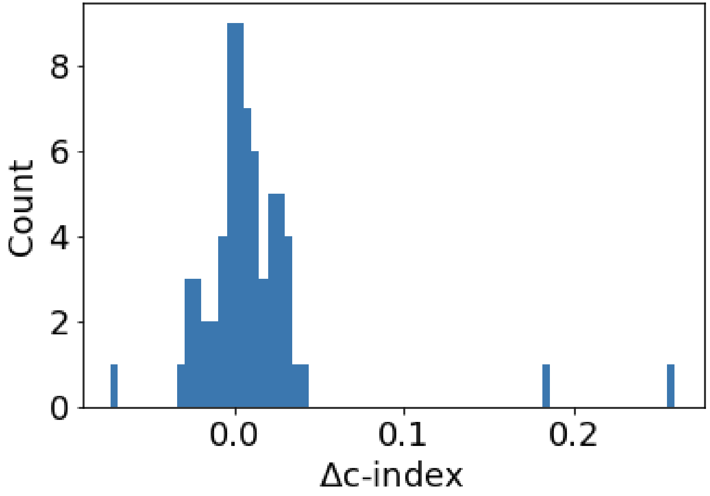
5 treatment efficacy outcomes

- Local, nodal, distant control
- Hospitalization
- Survival

3 Machine Learning for Patient Safety

Imaging analysis and deep learning

- Compared two methods of generating **survival curves** from data
    - Cox proportional hazards model (linear)
    - **Deep survival networks** (non-linear)
- Deep survival networks were **better on average** (average concordance index difference of 0.011)
- Deep survival networks had a big advantage for predicting time until **fatigue** and **depression**



3 Machine Learning for Patient Safety

Imaging analysis and deep learning

How can imaging and deep learning improve safety?

- Auto or assisted contouring to reduce contouring errors and inconsistencies
- Analyze machine QA data to detect machine problems early
- Real-time auto-contouring during IGRT to optimize patient positioning
- Analyze IGRT data for early detection of need for replanning

Suboptimal clinical decisions	✓
Imaging problems	✓
Incorrect/inconsistent contours	✓
Suboptimal treatment planning	✓
Machine miscalibration	✓
Patient positioning errors	✓

4 Standardization to Improve Machine Learning

Data Quality

Better data yields **better models**.

- Accuracy
- Precision
- Completeness
- Feature representation

(Isn’t absolutely necessary though; ML is fairly robust to noisy data.)

4 Standardization to Improve Machine Learning

Standardization Efforts

AAPM Task Group 263

- Units of measure (dose/volume)
- Target structures
- Non-target structures
- Derived and planning structures

Standardizing dose prescriptions: an ASTRO white paper

- Units of measure (dose)
- Data element ordering

Not covered

- Method of delivery (treatment modality)
- **Clinical data**

4 Standardization to Improve Machine Learning

Clinical Data Collection

Electronic data capture

- Data from physicians in *structured* form (not free text)
- Automatically generates free text note for medical records
- Detailed diagnosis, pathological, surgical, chemo history
- Detailed on-treatment visit reports (CTCAE)

Table 3. Mean times to create clinical notes, using dictation versus electronic data capture

Method/Purpose	Estimated No. Notes Per Patient	Dictation: No. Notes Timed	Dictation: Mean Time Per Note	Dictation: Time Per Patient	Electronic data capture: No. Notes Timed	Electronic data capture: Mean Time Per Note	Electronic data capture: Time Per Patient	Difference: Time Per Patient	Difference: P Value
Consult form	1	N/A	N/A	N/A	23	2.5	2.5	−2.5	N/A
Simulation	1.4	20	3.3	4.6	33	0.6	0.9	3.7	<.001
Treatment planning	1	17	2.5	2.5	27	0.7	0.7	1.8	<.001
Quality assurance	1	15	2.1	2.1	N/A	N/A	N/A	2.1	N/A
On treatment visit	5	80	1.8	9.0	39	0.5	2.5	6.5	<.001
Treatment summary	1	13	4.2	4.2	32	0.5	0.5	3.7	<.001
Total				22.4			7.1	15.3	

Note: Times are given in minutes. N/A = not applicable.

~70% reduction in documentation time

Pan et al, J Am Coll Radiol 13:401-407, 2016

5 Conclusion

CIRMS

"RADIATION TECHNOLOGIES FOR THE FUTURE"

5 Conclusion

CIRMS

"Radiation Technologies for the ~~Future~~"

present

6 Acknowledgments

Oncora Medical Team:

David Lindsay

Chris Ahern

Tom Pheiffer

Everyone else (Jacob, Jake, Chris P, Chris H, Alessandra, Angela, Drew, Stephen, Gary)

Research Collaborators:

Chuck Simone

Peter Gabriel

Ben Smith

Jay Reddy

Ying Xiao

CIRMS Organizers