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
Introduction

Why?

Google  Amazon

facebook  NETFLIX
Introduction

Why?
0 Introduction

Outline

1 Radiation Therapy and Patient Safety
2 Machine Learning and Big Data
3 Machine Learning for Patient Safety
4 Standardization to Improve Machine Learning
1 Radiation Therapy and Patient Safety

RT Clinical Workflow

- **Consult and prescription** (Physician)
- **Treatment simulation** (Therapist)
- **Contours and dose constraints** (Physician)
- **Treatment planning** (Dosimetrist)
- **Verification** (Physicist)
- **Treatment delivery** (Therapist)
- **On-treatment and follow-up visits** (Physician)
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**.
The vast majority of errors in RT are caused by human mistakes.

Where can errors come from?

- Suboptimal clinical decisions
- Imaging problems
- Incorrect/inconsistent contours
- Suboptimal treatment planning
- Machine miscalibration
- Patient positioning errors
1 Radiation Therapy and Patient Safety

Sources of Error

- Treatment simulation
  - Therapist
  - Consult and prescription
    - Physician

- Treatment planning
  - Dosimetrist
  - Contours and dose constraints
    - Physician

- Treatment delivered
  - Therapist
  - Verification
    - Physicist

- On-treatment and follow-up visits
  - Physician
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
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**
Patient Safety Technologies

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</tr>
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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

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Algorithms
- Logistic regression
- Support vector machines
- Random forests
- Neural networks
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Algorithms
- $k$-Means
- Agglomerative
- Spectral
- DBSCAN
2 Machine Learning

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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

- Electronic Medical Record Systems
- Oncology Information Systems
- Treatment Planning Systems
- Cancer Registries
- Medical Imaging Systems

Patient Demographics
- Cancer Diagnosis
- Surgical History
- Chemotherapy History
- Radiation Treatment

Outcomes

- Local Control Model
- Distant Control Model
- Survival Model
- Dermatitis Model
- Esophagitis Model
- Fatigue Model
# Machine Learning for Patient Safety

## Predicting outcomes

<table>
<thead>
<tr>
<th>Patient demographics</th>
<th>Diagnosis history</th>
<th>Tumor characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Sex, Height, Weight, Race</td>
<td>Smoking history, Cardiovascular disease, Endocrine disorders, Respiratory disease, CNS disorders</td>
<td>Primary cancer, Treatment site, Tumor size, TNM staging, Cancer histology</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Surgical history</th>
<th>Chemotherapy history</th>
<th>Radiation treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mastectomy, Prostatectomy, Pneumonectomy, Esophagectomy, Thyroidectomy</td>
<td>Any chemotherapy agent, Hormonal therapy, Alkylating antineoplastics, Phytogenic antineoplastics, Myeloablative antineoplastics</td>
<td>Treatment energy, Treatment modality, Total dose, Total fractions, Cone-down boost</td>
</tr>
</tbody>
</table>
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
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
Machine Learning for Patient Safety

Predicting outcomes (study 1)

Area under ROC curve across all outcome models

Median AUC: **0.912**
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
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
Performance of predictive model for radiation dermatitis:
3 Machine Learning for Patient Safety

Predicting outcomes (study 2)

Performance of predictive model for moist desquamation:
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

3 Machine Learning for Patient Safety

Predicting outcomes

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<tr>
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Machine Learning for Patient Safety

Patient clustering

- **Cluster patients** based on
  - Diagnosis
  - Pathology
  - Surgical history
  - Chemotherapy history

- Review prior treatments for similar patients

- Stage IB
- Stage IIA mastectomy
- Stage IIA lumpectomy
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
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Machine Learning for Patient Safety

Imaging analysis and deep learning

Automatic contouring

- Targets and organs at risk
- Improve consistency and efficiency
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
• 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**
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
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)

~70% reduction in documentation time

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

<table>
<thead>
<tr>
<th>Method/Purpose</th>
<th>Estimated No. Notes Per Patient Timed</th>
<th>Dictation</th>
<th>No. Notes Mean Time Per Note</th>
<th>Electronic data capture</th>
<th>No. Notes Mean Time Per Patient Timed</th>
<th>Difference</th>
<th>Time Difference Per Patient</th>
<th>P Value</th>
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</thead>
<tbody>
<tr>
<td>Consult form</td>
<td>1</td>
<td>N/A</td>
<td>N/A</td>
<td>23</td>
<td>2.5</td>
<td>2.5</td>
<td>-2.5</td>
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<tr>
<td>Simulation</td>
<td>1.4</td>
<td>20</td>
<td>3.3</td>
<td>33</td>
<td>0.6</td>
<td>0.9</td>
<td>3.7</td>
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<tr>
<td>Treatment planning</td>
<td>1</td>
<td>17</td>
<td>2.5</td>
<td>27</td>
<td>0.7</td>
<td>0.7</td>
<td>1.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Quality assurance</td>
<td>1</td>
<td>15</td>
<td>2.1</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>2.1</td>
<td>N/A</td>
</tr>
<tr>
<td>On treatment visit</td>
<td>5</td>
<td>80</td>
<td>1.8</td>
<td>39</td>
<td>0.5</td>
<td>2.5</td>
<td>6.5</td>
<td>&lt;.001</td>
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<tr>
<td>Treatment summary</td>
<td>1</td>
<td>13</td>
<td>4.2</td>
<td>32</td>
<td>0.5</td>
<td>0.5</td>
<td>3.7</td>
<td>&lt;.001</td>
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<tr>
<td>Total</td>
<td>22.4</td>
<td>71</td>
<td>15.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

5 Conclusion

“Radiation Technologies for the Future”
5 Conclusion

“Radiation Technologies for the Future”

present
6 Acknowledgments

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CIRMS Organizers