PIONEERING BIG DATA IN RADIATION ONCOLOGY

Todd McNutt PhD
Associate Professor
Radiation Oncology
Johns Hopkins University

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Problem

Ability to advance radiotherapy is limited by our knowledge of which patients are at risk of high grade toxicity or of limited ability to cure.

Knowledge from clinical trials is quite coarse and fails to consider all of the aspects of the individual patient.

‘Big Data’ offers an opportunity to better predict treatment outcome and provide improved clinical decisions for individual patients.
Personalized care using database of prior patients

- How to best treat individual patient?
- Prediction of complications for early intervention?
- Diagnosis
- Performance Status
- Comorbidities
- Patient History
- Pathology
- Surgery
- Radiotherapy
- Chemotherapy
- Clinical assessments
- Lab Values
- Toxicities
- Disease Status
- Quality of Life
- Survival
- Follow-up
- Consult

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Precision Radiotherapy
Treatment Planning
Mucositis data collected at JHU

GRADE 1

GRADE 2

GRADE 3

GRADE 4

# patients

Toxicity grade

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Promote Culture of Data Collection

Data collected over entire treatment

At what time point do we have enough data to make decision based on future prediction?

Input Variables => Prediction?
MOSAIQ Browser

Departmental Analytics

Mobile Solutions

Framework

Multi-Disciplinary Clinics

Clinical Analytics

MOSAIQ Browser

- IIS
- ASP.NET
- C#
- SQL

IDE
- Visual Studio
- SVN repository

Security Certificate

Johns Hopkins Enterprise Login
SiteMinder Access Management

RadOnC Users

Data Access Layer

SQL

Query Log

SQL

MOSAIQ DB

MOSAIQ Browser

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Data Collection in Clinic

Clinical Assessment

Quality of life

Disease Status
Head and Neck Oncospace Landscape

- Home-based Assessment (FitNinja)
- Head and Neck Tissue Bank (Chung)
- SNP Genotyping
- Pre-Treatment Imaging (Kiess/Hobbs/Shen)
- On-Treatment Imaging (Lee/Shekhar, Toshiba)

**Oncospace**
- On-Treatment Evaluation
- RT dosimetry

**Oncologic Outcome**
- Neck Function (Sweet)
- Ocular Function (Subramanian)
- Post-Treatment Oncologic and Toxicity (Ding/Fakhry/Murano/Prince/Wasserman)
- Ecological Momentary Assessments (EMAs)

**PROs**

**Toxicity**

Swallow Function (Starmer et al)
Extract, Transform, Load

- MOSAIQ
- DICO M
- Pinnacle TPS

- Scripts, Python, DICOM
- DVH, OVH, Shapes

- SQL Query
- Lab, Toxicity, Assessments

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Oncospace tables and schema

Family History  Social History  Medical History  Medications (chemo)  Surgical Procedures  Test Results (Labs)  Assessments (Toxicities)  Clinical Events

Patient

Private Health Info (access restricted)

1 : N  multiple instances
1 : 1  single instance
m : n  relates m to n

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Data inventory

- Toxicities (24var/pt)
- Quality of Life (64var/pt)
- Measured data (6 var/pt)
- Disease response (8var/pt)
Organs at risk with full dose
Learning health system can’t exist without data

Knowledge Database

Predictive Modeling

Decisions

Presentation of Predictions

Facts

Controls

Outcomes

Decision Point

Predicted Outcomes

Data Feedback (Facts, Outcomes)
Oncospace Consortium Repository
(It’s all about the data)


Knowledge Base

Registry  Quality Reporting  Decision Support  Research

$/pt↑  N↑
Toxicity trends during and after treatment – detect outliers

**Dysphagia**
Swallowing

- Worsens after Tx for many patients then improves long term

**Mucositis**
Inflammation

- Heals after Tx for most patients

**Xerostomia**
Dry Mouth

- Tends to be permanent

During Treatment

Follow up
Toxicity trends during and after treatment – detect outliers

Dysgeusia
Taste disturbance

Voice Change

Worsens through Tx then improves long term

Worsens through Tx

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DVH, Toxicities and Grade distributions

- Voice Change Larynx 50% Volume
- Dysphagia Larynx swelling 30% Volume

Toxicity Grade 0, 1, 2, 3, 4, 5

Mean and stddev of Dx% at grade

Number of patients by grade at D50%
For parallel organs, OAR2 is more easily spared.
For serial organs, OAR1 is more easily spared.
Shape-dose relationship for radiation plan quality

**Decisions:**
- Plan quality assessment
- Automated planning
  - IMRT objective selection
- Dosimetric trade-offs

For a selected Organ at Risk and %V, find the lowest dose achieved from all patients whose %V is closer to the selected target volume?

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Sample automated radiation planning result

Original plan

Automated plan

30% reduction in dose to parotids

<table>
<thead>
<tr>
<th></th>
<th>brain (Gy) (max)</th>
<th>Brainstem (Gy) (max)</th>
<th>Cord4mm (Gy) (max)</th>
<th>L inner ear (Gy)(mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>original</td>
<td>61.25</td>
<td>54.58</td>
<td>41.75</td>
<td>57.18</td>
</tr>
<tr>
<td>re-plan</td>
<td>56.33</td>
<td>46.48</td>
<td>37.89</td>
<td>43.72</td>
</tr>
<tr>
<td>R inner ear (Gy) (mean)</td>
<td>40.57</td>
<td>66.58</td>
<td>61%</td>
<td>63.74</td>
</tr>
<tr>
<td>re-plan</td>
<td>38.38</td>
<td>63.78</td>
<td>59%</td>
<td>61</td>
</tr>
</tbody>
</table>
Toxicity and Dose Volume Histogram

Scott Robertson PhD

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Prevalence and prediction of treatment-related complications

TOXICITIES / OUTCOMES

RISK STRUCTURES

MODELLED RISK

5% / Gy

10% / Gy
Voice Change
**Bad DVH!**

- DVH assumes that every sub-region of an OAR has the same radiosensitivity and functional importance to the related toxicity.
- DVH assumes that each OAR is uniquely responsible for the overall human function related to the toxicity.
Spatial dose analysis

<table>
<thead>
<tr>
<th>Method</th>
<th>Voice dysfunction (n=99), (n_{+}=8), (n_{-}=91)</th>
<th>Xerostomia (n=364), (n_{+}=275), (n_{-}=89)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bagged Naïve Bayes (1000 iterations)</td>
<td>0.915</td>
<td>0.743</td>
</tr>
<tr>
<td>Bagged Linear Regression (1000 iterations)</td>
<td>0.905</td>
<td>0.737</td>
</tr>
<tr>
<td>Naïve Bayes</td>
<td>0.900</td>
<td>0.734</td>
</tr>
<tr>
<td>Linear Regression</td>
<td>0.896</td>
<td>0.731</td>
</tr>
<tr>
<td>Random Forest (1000 trees)</td>
<td>0.724</td>
<td>0.683</td>
</tr>
<tr>
<td>NTCPLKB</td>
<td>0.596</td>
<td>0.700</td>
</tr>
</tbody>
</table>
Classification with correlated features: unreliability of feature ranking and solutions

\[ V(Y^i) = \frac{1}{n_{tree}} \sum_t (\text{errOOB}_t^j - \text{errOOB}_t) \]

Simulation of 1, 10 and 20 variables with a correlation of 0.9 with variable 3

Genuer et al.

http://www.cedars-sinai.edu/
Weight loss prediction

Endpoint: > 5kg loss at 3 months post RT

At planning

At end of RT
What can we do with the data?

- **Shape based auto-planning**
  - Clinical (prostate, pancreas)
  - Efficient high quality plan

- **Weight loss prediction**
  - Improved symptom management

- **Toxicity Risk**
  - DVH based
  - Spatial dose based

- **Disease response prediction**
  - Pancreas resectability
  - Head and neck HPV dose de-escalation
Summary

• The Oncospace model can house RT data effectively and provides a model for sharing

• Data collection in the clinical environment has been demonstrated
  – All patient on trial

• Data exploration and analysis across multiple institutions is possible

• Exploring models to stratify patients to improve the predictive power of the data

• Decision support to improve quality and safety has been demonstrated

• Personalized medicine has not been fully demonstrated, but remains a tenable goal
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