Knowledge-based Treatment Planning in Radiotherapy

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Learning Objectives

1. KBP background
2. Clinical indication for KBP
3. Importance of KBP model training and validation
Clinical Experience with Knowledge-Based Planning

Lindsey Olsen, M.S.
Washington University in St. Louis
Learning Objectives

1. **KBP background**

2. **Clinical indication for KBP**

3. **Importance of KBP model training and validation**
Motivation

• IMRT treatment planning relies on user expertise to consistently achieve optimal results

• Evaluation of IMRT plans is based on subjective judgment and population based guidelines rather than knowledge from previous radiotherapy treatment data
Motivation

Variation in external beam treatment plan quality: An inter-institutional study of planners and planning systems

Benjamin E. Nelms PhD, Greg Robinson CMD, Jay Markham CMD, Kyle Velasco CMD, Steve Boyd CMD, Sharath Narayan CMD, James Wheeler MD, PhD, Mark L. Sobczak MD

Conclusions

There is a large inter-planner variation in plan quality as defined by a quantitative PQM score that measures the ability of the planner to meet very specific plan objectives. Plan quality was not statistically different between different TPS or delivery techniques and was not correlated to metrics of plan complexity. Certification and education demographics, experience, and confidence level of the planner were not good predictors of plan quality.
Motivation

$\delta \text{ (prior)} = 0.28 \pm 0.24$

$\delta \text{ (after)} = 0.12 \pm 0.13$

KBP Process Overview

**Step 1**
- Identify a set of site similar training patients

**Step 2**
- Generate model from training cohort

**Step 3**
- Utilize model to obtain DVH estimation for new patient

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Appenzoller et al, “Predicting DVHs for OARs in IMRT planning” Med Phys 39, 7446 (2012)
In general…

- **Significance of Knowledge-Based Planning**

Prior Experience
- Training Plan 1
- Training Plan 2
- Training Plan 3
- Training Plan 4
- Training Plan...

Knowledge-Based Model

Improves Plan:
- Quality
- Standardization
- Efficiency
- Automation
Knowledge-based Planning Models

- A model-based method for estimating DVHs
  - Based on patient geometry and prior knowledge from a set of training plans

- Automated planning
  - IMRT objectives based on the estimated DVH, prescription dose, and prior planning experience

- Treatment plan quality control
  - Ability to identify sub-optimal plans
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KBP experience at WashU

Table 3. Average Reduction in V65 and V40 for Rectum and Bladder

<table>
<thead>
<tr>
<th>Organ</th>
<th>V65(orig)-V65(replan)</th>
<th>dV65</th>
<th>V40(orig)-V40(replan)</th>
<th>dV40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectum</td>
<td>4.8%±2.3%</td>
<td>0.9%±1.1%</td>
<td>17.9%±10.3%</td>
<td>0.7%±1.4%</td>
</tr>
<tr>
<td>Bladder</td>
<td>3.4%±2.1%</td>
<td>0.4%±0.5%</td>
<td>6.0%±2.8%</td>
<td>0.6%±0.9%</td>
</tr>
</tbody>
</table>

Appenzoller L.M., et. al. Predictive DVH models developed at a large institution impact clinically relevant DVH parameters in IMRT plans at an unrelated radiotherapy facility, Oral presentation AAPM 2013.
KBP experience at IOSI

Luca Cozzi
Antonella Fogliata

IOSI, Bellinzona, Switzerland

RapidPlan model for SIB Head and Neck

- Very inhomogenous dataset
- SIB head and neck with different dose prescriptions and different number of PTVs (2 or 3)
  - 16 pts with 3 PTVs: H) 65.4-71.9Gy; M) 64-54Gy; L) 50-59Gy
  - 24 pts with 2 PTVs: H) 63.6-69.6Gy; L) 52-62Gy
- 40 patients included in the model
- Almost all plans to configure the model were IMRT
- Structures in the model: 2 or 3 PTVs, spinal cord, parotid left, parotid right
- All organs at risk had generated priorities: line and mean dose for parotids, max dose for spinal cord
KBP experience at IOSI

**Model based vs. original plan**

- Model based RapidArc (69.96Gy)
- Original IMRT plan (66.6Gy)

**Model based plan better than original**

- Mean right parotid: 25.2 Gy
- Mean left parotid: 17.4 Gy
- Max spinal cord: 34.1 Gy

- Mean right parotid: 41.7 Gy
- Mean left parotid: 23.8 Gy
- Max spinal cord: 34.1 Gy
**KBP experience at MSKCC**

Sean L Barry  
Amanda Boczkowski  
Rongtao Ma  
Penpeng Zhang  
Margie Hunt

Memorial Sloan-Kettering  
Cancer Center
KBP experience at MSKCC

Building the model

Data Source:
- Retrospective selection of main campus IMRT esophagus plans created b/w 2009-2014.
- Started w/ 64 candidate plans
  - Extracted dosimetric details and reviewed/excluded:

- Non-standard anatomy
- Non-standard clinical trade-offs
- Ultimately, 58 patients were available for the RapidPlan Model Configuration
KBP experience at MSKCC

KBP can be used as a tool to retrospectively analyze patient data in order to identify sources of variability in plan consistency within a multi-campus institution.

Future studies will investigate whether the variation observed for esophageal IMRT can be diminished with the prospective use of a KBP model during planning.
Learning Objectives

1. KBP background
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3. Importance of KBP model training and validation
Training and Validation Process

- Patient selection
- Model training evaluation
- Model validation
- Clinical use of model
Training and Validation Process

- Patient selection
- Model training and evaluation
- Model validation
- Clinical use of model
Patient Selection: Geometry

- PTV / OAR Geometry
  - Similar target shape
  - Similar target location
  - Similar relative position of OARs to PTV

- CCMB ex.

Courtesy of J. Alpuche
Patient Selection: Guidelines

- Similar Clinical Objectives
  - Same PTV coverage/OAR sparing criteria
- Similar Clinical Trade-Offs
  - Importance of PTV coverage / OAR sparing
- PTV prescription dose can vary
  - Estimated DVHs will be scaled as a percentage of Rx dose

<table>
<thead>
<tr>
<th>H&amp;N</th>
<th>Bilateral Neck Treatment</th>
<th>Ipsilateral Neck Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV</td>
<td>95% of PTV &gt; 95% of Rx; Max dose &lt; 110% of Rx  Max dose 40 Gy</td>
<td>95% of PTV &gt; 95% of Rx  Max dose &lt; 110% of Rx  Max dose 40 Gy</td>
</tr>
<tr>
<td>Spinal Cord</td>
<td></td>
<td>Max dose 52 Gy; &lt; 1% (or 1 cc) exceeds 50 Gy  Max dose 54 Gy</td>
</tr>
<tr>
<td>Spinal Cord + Margin</td>
<td></td>
<td>Max dose 54 Gy; &lt; 1% exceeds 60 Gy</td>
</tr>
<tr>
<td>Optic Nerves, Optic Chiasm</td>
<td></td>
<td>Max dose 50 Gy; &lt; 1% exceeds 45 Gy</td>
</tr>
<tr>
<td>Brainstem</td>
<td></td>
<td>As low as possible; mean dose &lt; 45 Gy</td>
</tr>
<tr>
<td>Brain</td>
<td></td>
<td>As low as possible; mean dose &lt; 45 Gy</td>
</tr>
<tr>
<td>Retina</td>
<td></td>
<td>As low as possible; mean dose &lt; 26 Gy</td>
</tr>
<tr>
<td>Larynx</td>
<td></td>
<td>As low as possible; mean dose &lt; 26 Gy</td>
</tr>
<tr>
<td>Upper Esophagus</td>
<td></td>
<td>As low as possible; mean dose &lt; 26 Gy</td>
</tr>
<tr>
<td>Parotid</td>
<td></td>
<td>As low as possible; mean dose &lt; 26 Gy</td>
</tr>
<tr>
<td>Pharyngeal Constrictors</td>
<td></td>
<td>As low as possible; mean dose &lt; 39 Gy</td>
</tr>
<tr>
<td>Submandibular</td>
<td></td>
<td>As low as possible; mean dose &lt; 39 Gy</td>
</tr>
<tr>
<td>Oral Cavity</td>
<td></td>
<td>As low as possible; mean dose &lt; 35 Gy</td>
</tr>
<tr>
<td>Mandible</td>
<td></td>
<td>Max 70 Gy; &lt; 5% exceeds PTV Rx</td>
</tr>
<tr>
<td>Unspecified Tissue</td>
<td>Less than PTV Rx; &lt; 5% exceeds PTV Rx</td>
<td>Less than PTV Rx; &lt; 5% exceeds PTV Rx</td>
</tr>
</tbody>
</table>
Patient Selection: Patient Numbers

- Number of training patients increases as the model complexity increases.
- Model validation process is used to ensure the number of training patients is sufficient.
Patient Selection: Plan Quality

- Training set plan quality
  - Output of KBP model directly correlated to input
  - Statistical noise present in KBP training set can impact model behavior

- QA of training set
  - Clinically approved, safe treatment
  - Consider iterative process in model training to obtain adequate model
Plan Quality Considerations

- Ex. Prostate and Node model: OAR = Rectum
  - Poor correlation between actual and estimated DVH principal components for model trained with 70 mixed quality treatment plans
Plan Quality Considerations

- Ex. Prostate and Node model: OAR = Rectum
  - Good correlation between actual and estimated DVH principal components for model trained with 48 good quality treatment plans
Training and Validation Process

- Patient selection
- Model training and evaluation
- Model validation
- Clinical use of model
Model Training and Evaluation

- Review the model statistical results
- Review the clinical vs. estimated DVHs
- Review model outliers
  - Geometric and dosimetric
Review Model Statistics

- Assess model over-fitting
- Assess predictive ability of the model
Review Clinical vs. Estimated DVHs

- Model properly identifies variation in training set DVHs
Review Clinical vs. Estimated DVHs

- Clinical DVH > estimate \(\rightarrow\) Outlier
  - Clinically relevant parameter
Identify and Remove Outliers

• **Geometric outlier**
  - PTV volume/shape substantially differs from the majority of the training set
  - Structure volume/shape substantially differs from the majority of the training set
  - Positional relationship between structure and PTV substantially differs from the majority of the training set

• **Dosimetric outlier**
  - Clinical DVH substantially differs from estimated DVH based on a clinically significant parameter
Steps to Improve Model Quality

1. Add patients to address over-fitting
2. Remove geometric outliers or add similar patients
3. Remove or re-plan dosimetric outliers
Steps to Improve Model Quality

1. Add patients to address over-fitting
2. Remove geometric and/or dosimetric outliers or add similar patients
3. Re-plan possible dosimetric outliers

Iterative process
Training and Validation Process

- Patient selection
- Model training and evaluation
- Model validation
- Clinical use of model
Validation Patients

- Independent from patients used to train model
- Represent the range of patient geometries, plan geometries, and plan prescriptions for which the model will be clinically used
- Good plan quality
  - PTV coverage
  - OAR sparing
Clinical vs. Estimated DVHs

- Review that clinically approved plan is within DVH estimation range
- If it is not, it is possible that plan can be improved
Create Validation Plan w/ Model
Objective Selection

- IMRT objective selection
  - Ensures clinically acceptable plan that achieves model estimate
  - Based on prior clinical experience
  - Priorities and objectives tuned during model validation
Assess Clinical Acceptability

- Review validation plans as per normal institution clinical standards
- Isodose distribution
- Clinical guidelines (scorecard)
  - PTV coverage
  - Hotspots
  - Population-based OAR DVH cut-points
- Plan technical integrity
Training and Validation Process

- Patient selection
- Model training and evaluation
- Model validation
- Clinical use of model
Clinical Use of Model

- Do not venture far from your validation set
- Consider automation/standardized protocols
  - Beam arrangement
  - Contouring guidelines
  - Plan quality reports (scorecards)
- Develop guidelines for clinical use
  - When should I use the model?
  - When should I plan manually?
Final Thoughts

• Proper model training and validation is necessary for the clinical use of knowledge-based planning models
  • Possibility for systematic errors

• KBP is an exciting advancement
  • Potential to improve quality, efficiency, and standardization
  • Does not replace human/clinician judgment
KBP experience at UCSD

To study effects on a large scale, one needs a multi-institutional study...

**RTOG 0126 Protocol Information**

A Phase III Randomized Study of High Dose 3D-CRT/IMRT versus Standard Dose 3D-CRT/IMRT in Patients Treated for Localized Prostate Cancer

- **Protocol Documents**
  - Protocol
  - Informed Consent
  - Summary of Changes

- **Principal Investigator:** Jeff Michalski, M.D., M.B.A.

- **Primary Objective:**
  - Determine whether 3D-CRT/IMRT to 79.2 Gy in 44 fractions will lead to improved overall survival in patients treated for prostate cancer compared to a group of patients treated with 3D-CRT/IMRT to 76.2 Gy in 39 fractions.

- **Patient Population:**
  - Histologically confirmed prostate adenocarcinoma within 180 days of randomization
  - Zubrod Performance Scale 0-1
  - Prostatic biopsy tumor grading by the Gleason Score Classification
  - One of the following combinations of factors:
    - Clinical stage T1b-T2b, Gleason score 2-6, and prostate-specific antigen $> 10$ but $< 20$
    - Clinical stage T1b-T2b, Gleason score 7, and prostate-specific antigen $< 15$
    - Clinically negative lymph nodes or histologically negative by nodal sampling or dissection
    - No distant metastases (M0)
    - No previous or concurrent invasive cancers, other than localized basal cell or squamous cell skin carcinoma, unless continually disease free for at least 5 years
    - No prior pelvic irradiation, prostate brachytherapy, or bilateral orchidectomy
    - No previous or concurrent cytotoxic chemotherapy for this cancer
    - No previous hormonal treatment (no minoxidil or phytoestrogen preparation within 3 months prior to registration)
    - No radical surgery or cryosurgery for prostate cancer
    - Pretreatment evaluations must be completed as specified in Section 4.1

- **Target Accrual:** 1520
- **Current Accrual:** 1532

**University of California, San Diego Medical Center, Moores Cancer Center**


PMID: 25847605
KBP experience at UCSD

Bladder and rectum DVH comparisons
KBP experience at UCSD
KBP experience at UCSD

Conclusions

• This KBP-driven study on RTOG 0126 demonstrates that poor planning can expose patients to significant and unnecessary risk of normal tissue complications

• Toxicity data are consistent with poor planning leading to worse outcome, though this study was not powered to reach statistical significance
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- Sasa Mutic, Ph.D.
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Thank you