

Implementation of Automated Planning in Clinical Trials and Multi-Institutional Environments

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Automated Planning Methods

- Automation is possible through:
 - Prediction models trained on prior cases
 - Atlas or library based planning
 - Treatment planning goal evaluation and automated cost function adjustment
 - Standardized navigation of pre-computed multi-criteria plans based on a standard initial template

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Automated/Knowledge Based Planning Roles

- Treatment Planning Aid:
 - Learn what is achievable in a new patient
 - Increased
 - Reduced
 - Reduced
 - Equivalent
- Treatment
 - Determin
 - Identify plan quality outliers
 - Provide feedback to planners on potential plan quality

Caution is warranted when case geometry, planning goals, and technique are not in the same ballpark as cases used to evaluate the tools



Where do automated planning tools fit into clinical trials?

1. Retrospective Protocol Evaluation
 - Determine if suboptimal treatment planning may have played a role in study outcomes or results
2. Initial Protocol Development
 - Test if protocol objectives are achievable in a similar cohort of patients
3. Prospective Protocol Planning & Feedback
 - Provide rapid planning and/or feedback and quality control for ongoing trials
4. Model Creation & Validation
 - Clinical trial cases can serve as a standardized training and/or validation set for new or existing models



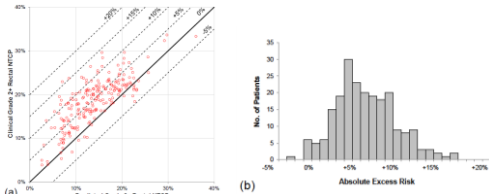
Examples of Automated/Knowledge Based Planning in Clinical Trials

- Retrospective Evaluation of the impact of suboptimal planning in RTOG0126 (Prostate 3D vs IMRT)
- Model Creation and Retrospective plan quality evaluation for RTOG 0631 (Spine SBRT)
- *Prospective* Plan Quality Control with NRG GY006 (Gyn IMRT)



Retrospective Knowledge-Based Protocol Evaluation: RTOG 0126

(A Phase III Randomized Study of High Dose 3DCRT/IMRT versus Standard Dose 3DCRT/IMRT
In Patients Treated for Localized Prostate Cancer)



Moore *et al*, IJROBP, **92**, 228-235 (2015)

Courtesy of KL Moore,
UC San Diego

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Spine Radiosurgery RTOG 0631

- Examine effects of applying in-house KBP model for cases submitted to a multi-institutional trial
- Collaboration with NRG to test KBP model on cases from other institutions submitted to 0631
- 22 cases with 16 Gy VMAT / single target
- Generate fully automatic KBP plan for each case
 - Compare scores, plan quality metrics

Younge *et al*, IJROBP, **100**, 1067-1074(2018)

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Automated KBP for Spine SBRT (RTOG 0631)

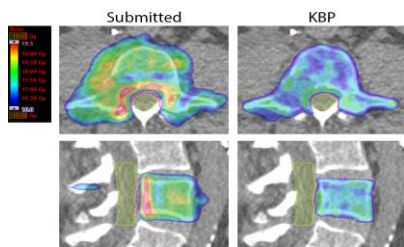
- In 22 cases, a KBP model automatically generated protocol compliant plans
 - 2 of the submitted cases were originally deviation unacceptable in the protocol
- No statistically significant differences in spinal cord metrics between submitted plans vs. model, but PTV coverage was significantly better VRx went from **93.3 +/- 3.2% to 98.3 +/- 1.5% (p=0.01)**
- Poor dosimetric outliers were identified and may have been prevented had the model been applied clinically

Younge *et al*, IJROBP, **100**, 1067-1074(2018)

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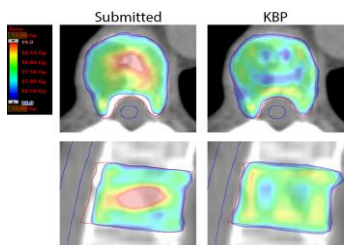
**Outlier Quality Control Example:
Submitted RTOG 0631 Protocol Patient vs. KBP Model**



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**Example of Differing Planning Strategy:
Submitted RTOG 0631 Protocol Patient vs. KBP Model**

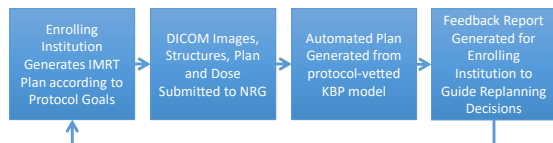


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**Example of *Prospective* Use of Automated KBP in
Clinical Trials: NRG GY006**

- **NRG GY006:** Radiation Therapy and Cisplatin With or Without Triapine in Treating Patients With Newly Diagnosed Stage IB2, II, or IIIB-IVA Cervical Cancer or Stage II-IVA Vaginal Cancer



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Sample of Knowledge Based Quality Control Report for GY006

Submitting Institution:
Patient Identifier:
Report prepared on:

Diagnostic Analysis Summary:

| Structure | NRG GY006 dose criteria | KBP feedback statement |
|-----------------|---|---|
| CTV Boost | All metrics meet practical specifications | Dose metrics are unlikely to be improved |
| CTV Boost | All metrics meet practical specifications | Dose metrics are unlikely to be improved |
| PTV Boost | All metrics meet practical specifications | Dose metrics are unlikely to be improved |
| Bone Marrow All | Some acceptable deviations | Plan could be improved to meet specifications |
| Bone Marrow All | All metrics meet practical specifications | Some dose metrics could likely be improved |
| Bowel | Some acceptable deviations | Plan could be improved to meet specifications |
| Rectum | Some acceptable deviations | Some dose metrics could likely be improved |
| Bladder | Some acceptable deviations | Dose metrics are unlikely to be improved further |
| Femurs | Some acceptable deviations | Plan could be improved to meet practical specifications |

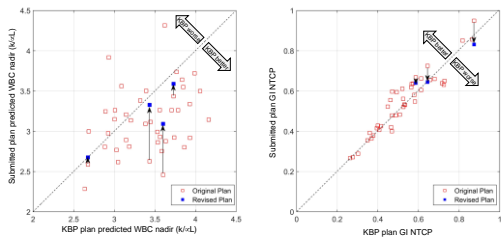
| Structure | Mean Dose | Metric | | Knowledge based plan quality check |
|-----------|-----------|--------|-----------|------------------------------------|
| | | For | Structure | |
| Bladder | 30.48 | For | Structure | 33.11 |
| Bladder | 30.48 | For | Structure | 34.84 |
| Bladder | 30.48 | For | Structure | 38.16 |

Courtesy of KL Moore, UC San Diego

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Preliminary Mid-Trial Quality Control Data from NRG GY006



Courtesy KL Moore UC San Diego

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Where do automated planning tools fit into multi-institutional environments?

1. Retrospective Independent Plan Evaluation
 - Determine if suboptimal or non-standardized treatment planning may have played a role in clinical outcomes or increased variation between sites
2. Initial Planning Technique Deployment
 - Aid in rolling out new planning techniques at new sites
3. Prospective Planning & Feedback
 - Provide rapid planning and/or feedback and quality control for ongoing patients without real-time interaction with other sites
4. Ongoing Quality Control and Improvement
 - Monitor performance and conformance with standardized planning goals

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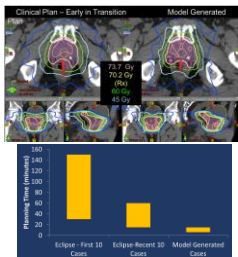


Examples of Multi-Institutional use of Automated KBP

- Prostate KBP model evaluated across a network of 4 affiliated departments for quality evaluation, improvement, and technique rollout
- Statewide consortium generated model for lung KBP and subsequent quality evaluation

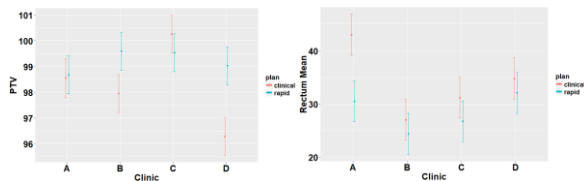
Multi-Institutional Prostate Model Evaluation

- Initial model generated with 60 plans, prostate and prostate bed
 - Prescription range: 68.4-79.2 Gy
 - All plans had been generated from an in-house optimization system and clinically delivered
 - Model validated in 20 cases (early and late in a new treatment planning system transition)
- Automated plans generated on 10 cases each from 4 affiliated departments with the same treatment planning directives

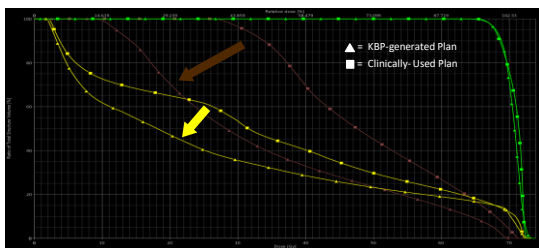


Masi et al. Med Dos 2017

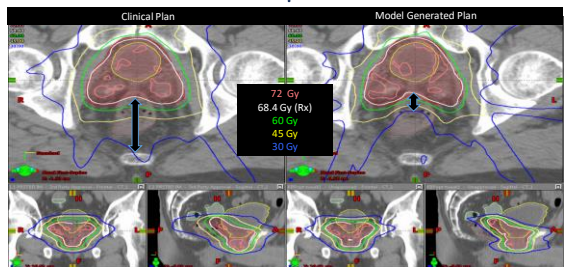
Model Plan QA Across 4 Centers



Outlier Example – Clinic A



Outlier Example – Clinic A



Multi-institutional Plan Quality Evaluation and Improvement in a Statewide Quality Consortium

- Goal: Use high quality lung treatment plans from sites participating in a statewide quality consortium (MROQC = Michigan Radiation Oncology Quality Consortium) to train a knowledge based planning model to use as a quality assurance and quality improvement tool within the consortium



Project Details

- Collection of high quality lung plans from consortium sites
 - 56 cases collected from 9 institutions
- Multidisciplinary case reviews done to score all cases
- Model creation and refinement
 - 43 cases in model
 - 3 complete plans excluded
- Model validation
 - 10 independent (scored) cases used for model testing and validation
- Quality Check Clinical Cases evaluated to determine potential for model as a QC tool
 - 32 cases from 7 institutions

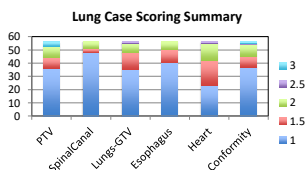


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Multi-Disciplinary Case Reviews

- Reviewed 56 Cases with Physicians, Physicists, and Dosimetrists from MROQC sites
- Scoring Schema
 1. Excellent - Any possible improvements would be very small
 2. Good – Clinically acceptable, but improvement is possible
 3. Unacceptable – Should be improved



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Model Validation & Confirmation

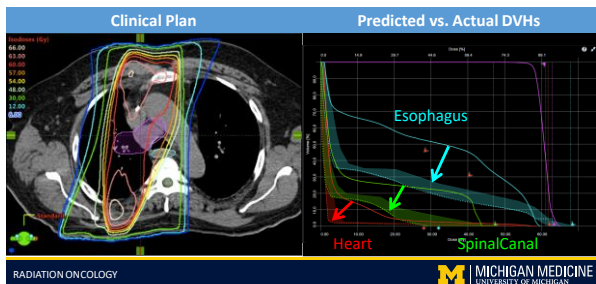
- 43 cases included in initial model
- In the 10 high quality cases set aside for validation, there were **no significant differences** in any of the target and normal tissue metrics for **automated KBP plans vs. high quality manual plans**
- This validated that the KBP model was able to predict and confirm high quality treatment plans in MROQC lung cases



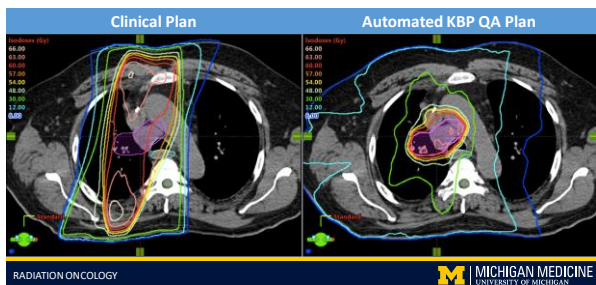
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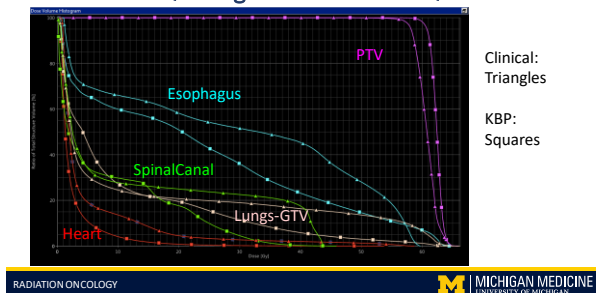
MROQC Lung KBP Model as a QA Tool



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MROQC Lung KBP Model as a QA Tool

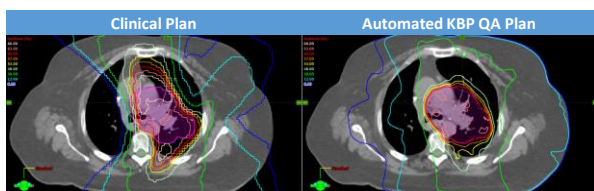
- In 25/32 clinical MROQC cases, the KBP model suggested that PTV coverage may be improved
- In 13/32 clinical MROQC cases, the KBP model suggested that 5 or more OAR metrics may be simultaneously improved



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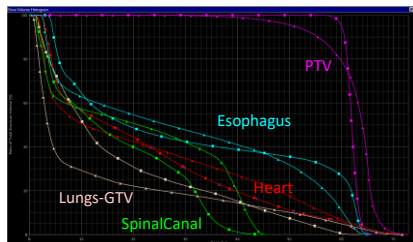
Differences Highlight Model Tradeoffs Compared to Individual Practices



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Differences Highlight Model Tradeoffs Compared to Individual Practices



Clinical: Triangles

KBP: Squares



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Next Steps for Rollout

- Hold multi-disciplinary site review with QA cases to score the utility of the model as a decision making QA tool
- Devise a vendor neutral online tool for dissemination to all sites



Summary/Take-Home Points

- Knowledge based planning concepts and tools have and can continue to play a role in clinical trial development, prospective plan evaluation, and retrospective plan quality analysis
- The use of KBP tools within clinical trials may help to identify outliers and standardize plans – reducing the risk that clinical trials are undermined by plan quality issues
- Automated knowledge based planning methods can play a variety of roles in multi-institutional settings such as quality control, training, and standardization.

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