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INCLUSION OF DATA-DRIVEN RISK PREDICTIONS IN RADIATION TREATMENT PLANNING IN THE CONTEXT OF A LOCAL LEVEL LEARNING HEALTH SYSTEM

Todd McNutt PhD
Associate Professor
Radiation Oncology
Johns Hopkins University

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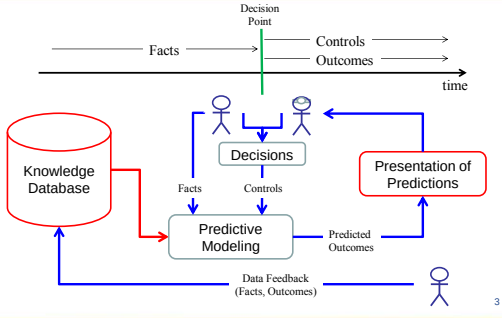
Learning health system



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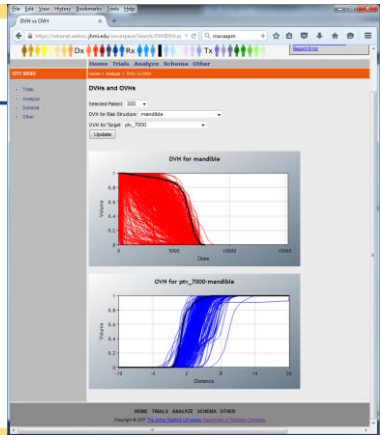
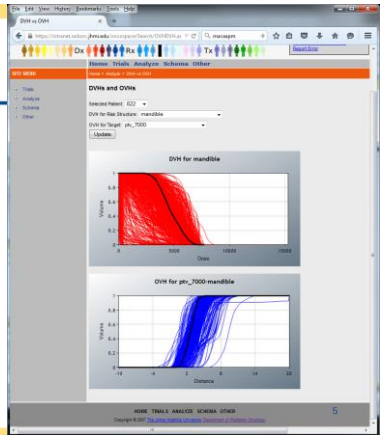
Mandible vs PTV_7000

pt: 300



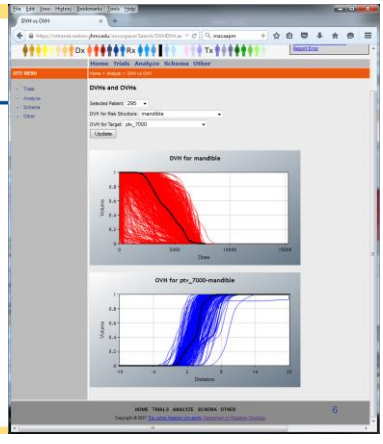
Mandible vs PTV_7000

pt: 822



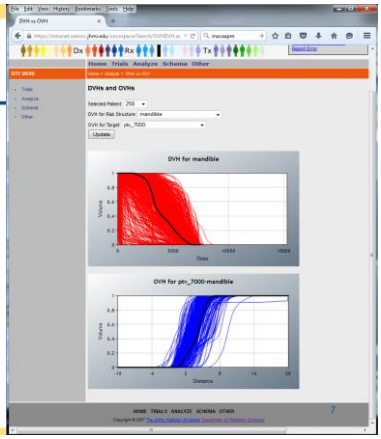
Mandible vs PTV_7000

pt: 295



Mandible vs PTV_7000

pt: 258



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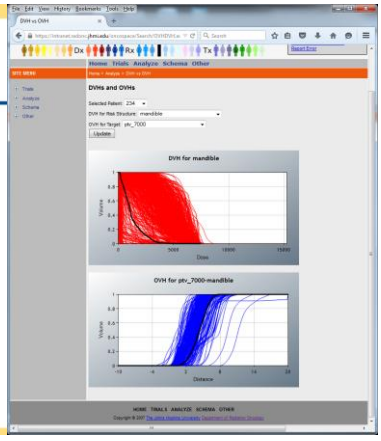
Mandible vs PTV_7000

pt: 234



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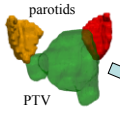
Shape-dose relationship for radiation plan quality

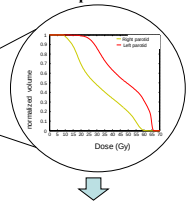
JOHNS HOPKINS MEDICINE

Shape relationship



DB of prior patients

Dose prediction

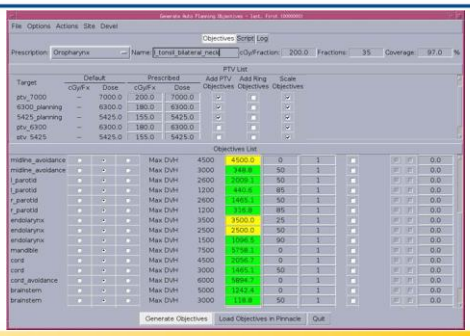


For a selected Organ at Risk and %V, find the lowest dose achieved from all patients whose %V is closer to the selected target volume?

Decisions:

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

Interface



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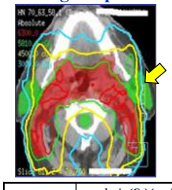
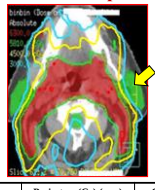
Sample automated radiation planning result

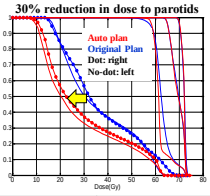
Original plan



Automated plan



30% reduction in dose to parotids



	brain (Gy) (max)	Brainstem (Gy) (max)	Cord4mm (Gy) (max)	L inner ear (Gy)(mean)
original	61.25	54.58	41.75	57.18
re-plan	56.33	46.48	37.89	43.72
	R inner ear (Gy) (mean)	**mandible (Gy) (max)**	**larynx for edema (V50)**	**esophagus (Gy)(max)**
original	40.57	66.58	61%	63.74
re-plan	38.38	63.78	59%	61

Current dose based auto-planning

- Has demonstrated improved quality
- Removed human variability for standard cases
- Now advancing commercially

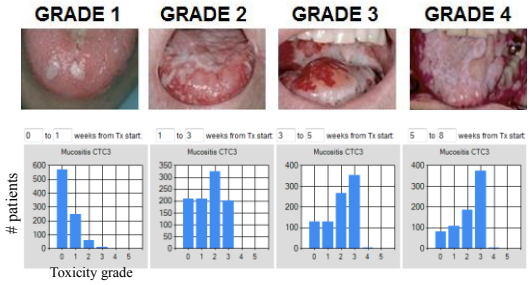
That was all DVH based

- Dose is not what matters to the patient
- Quantify the patient experience?

Should we just apply existing NTCP and TCP models to dose predictions?

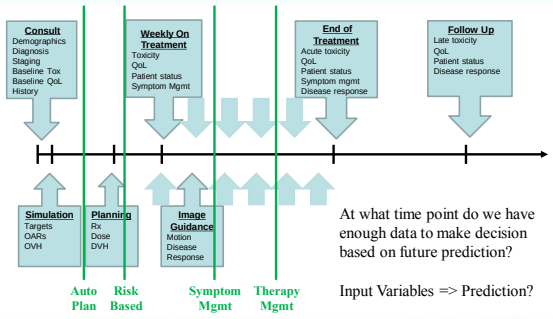
…or should we try to expand the knowledge based approach using clinical data?

Mucositis data collected at JHU



Promote Culture of Data Collection

Data collected over entire treatment

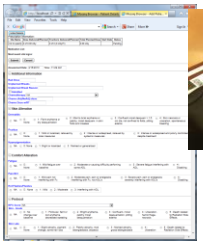


At what time point do we have enough data to make decision based on future prediction?

Input Variables => Prediction?

Data Collection in Clinic

Clinical Assessment



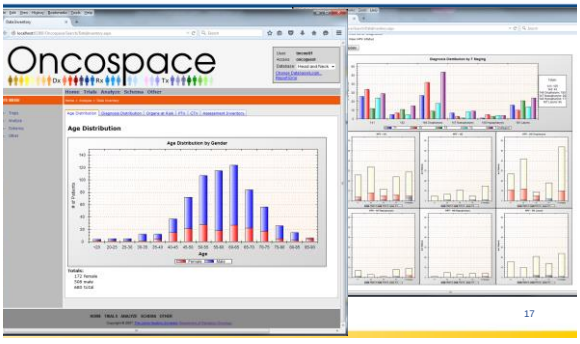
Quality of life

FACT HN
SSQ
SHIM
IPSS
PAN26

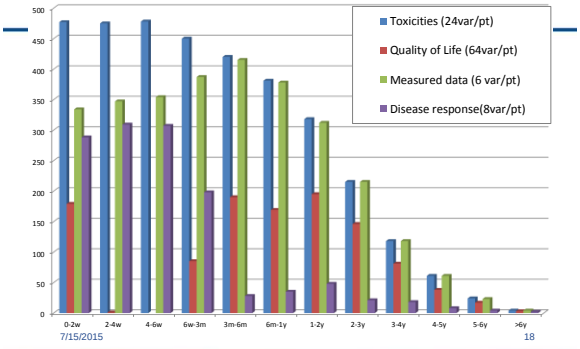
Disease Status

Head and Neck Inventory

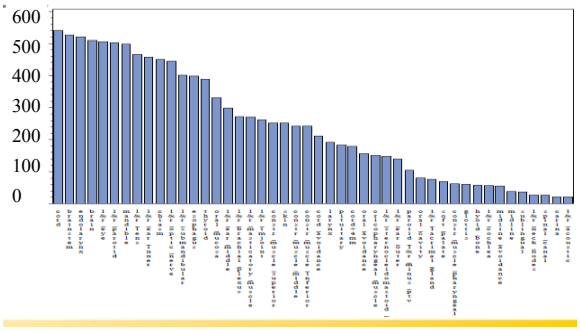
~800 pts up to 6 yr follow up



Head and Neck Inventory

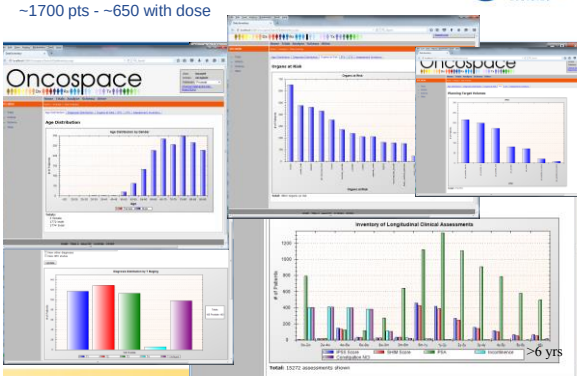


Organs at risk with full 3D dosimetry

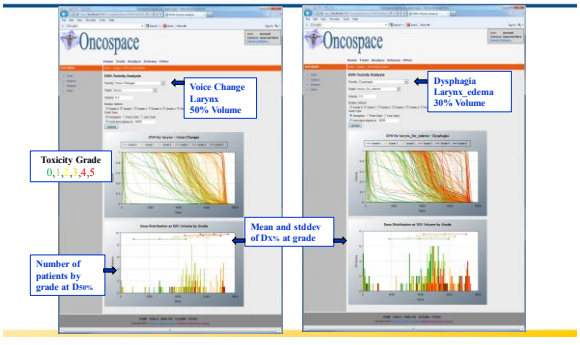


Prostate Inventory

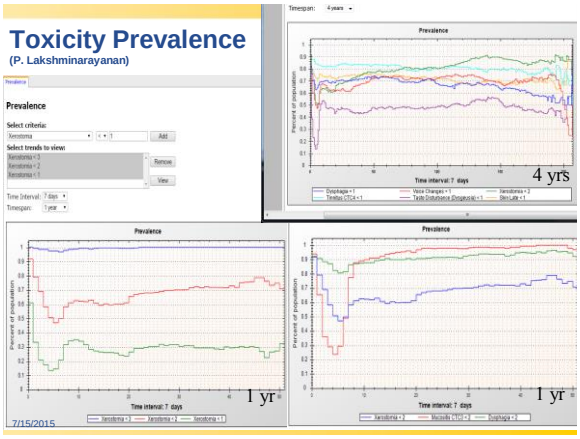
~1700 pts - ~650 with dose



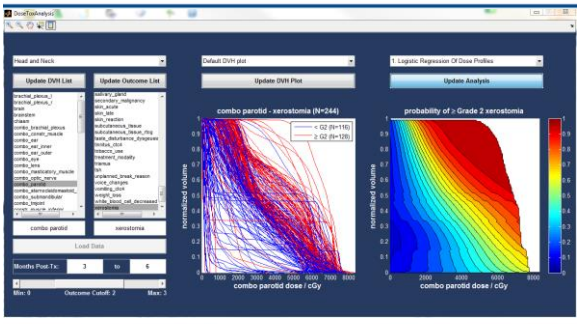
DVH, Toxicities and Grade distributions



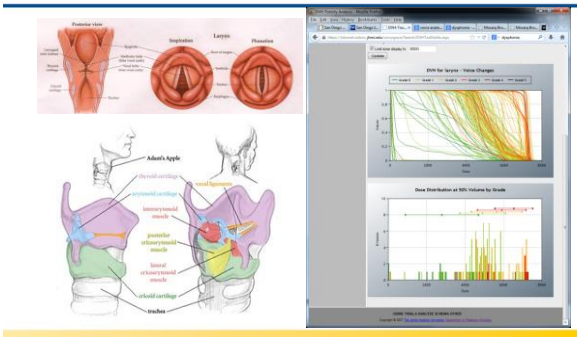
Toxicity Prevalence
(P. Lakshminarayanan)



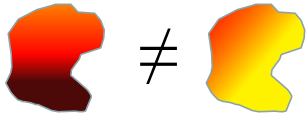
Toxicity and Dose Volume Histogram
(Scott Robertson et al…)



Voice Change

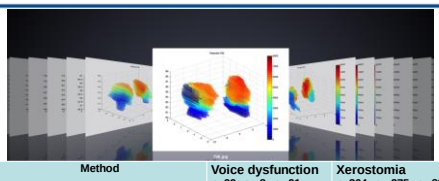


Bad DVH!



- 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

Spatially dependent features of dose in the structures (F. Marungo et al.)



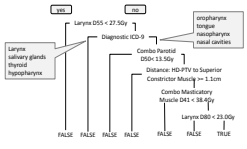
Method	Voice dysfunction n=99, n_+=8, n_-=91	Xerostomia n=364, n_+=275, n_-=89
Bagged Naïve Bayes (1000 iterations)	0.915	0.743
Bagged Linear Regression (1000 iterations)	0.905	0.737
Naïve Bayes	0.900	0.734
Linear Regression	0.896	0.731
Random Forest (1000 trees)	0.724	0.683
$NTCP_{LKB}$	0.596	0.700

Weight loss prediction

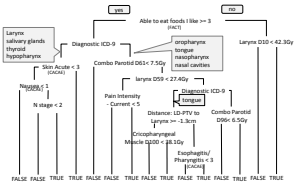
(N. Minoru, S. Cheng et al…)

Endpoint: > 5kg loss at 3 months post RT

At planning

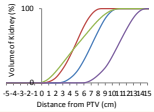


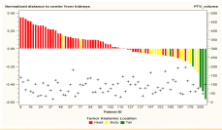
At end of RT

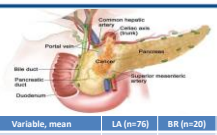


Pancreas Resectability

(S. Cheng et al…)







Variable, mean	LA (n=76)	BR (n=20)	P-value
Distantce_SMA_0%	-0.8302	-0.3216	0.0764
Distantce_SMA_25%	-0.3739	0.1231	0.0922
Distance_SMA_50%	-0.0362	0.4849	0.0882
Distance_SMA_75%	0.4101	0.9975	0.0805
Distance_ClosestVessel_0%	-1.0421	-0.4121	0.0361*
Distance_ClosestVessel_25%	-0.6513	-0.0427	0.0454*
Distance_ClosestVessel_50%	-0.3894	0.2739	0.0373*
Distance_ClosestVessel_75%	-0.08	0.5603	0.0238*
PTV volume	89.2791	66.7585	0.0065*

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Summary

- We can quantify the patient experience and are improving our capabilities rapidly
- It is possible to collect and house RT data/knowledge in a clinical setting
- Current dose based auto-planning utilizes a learning health system
- Data science models are maturing that can convert the knowledge to clinical predictions
- Incorporation of these predictions into the planning process would make Leonard “Bones” McCoy proud
- The potential to have clinical impact is evident…

…we have work to do which requires real partnership with our clinicians

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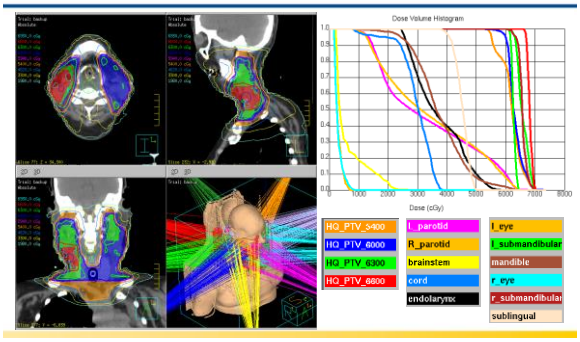
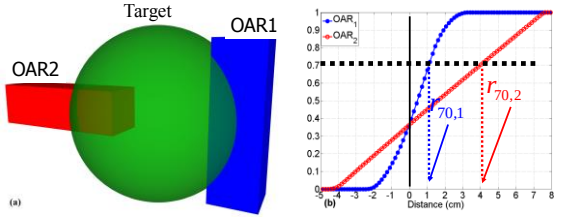
Precision Radiotherapy Treatment Planning



OVH: serial vs parallel



For parallel organs, **OAR2** is more easily spared.
For serial organs, **OAR1** is more easily spared.

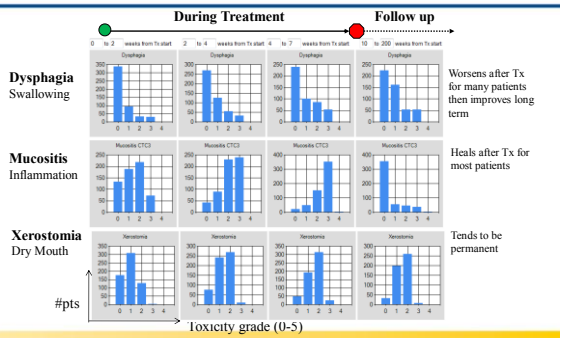
Problem

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.

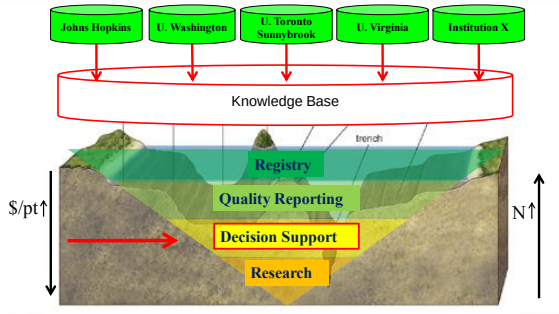
Knowledge from clinical trials is quite coarse and fails to consider **all of the aspects** of the individual patient.

'Big Data' offers an opportunity to **better predict treatment outcome** and provide improved clinical decisions for individual patients.

Toxicity trends during and after treatment – detect outliers



Oncospace Consortium Repository (It's all about the data)



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**