Oncospace™

JOHNS HOPKINS MEDICINE

LEARNING HEALTH SYSTEMS FOR RADIATION ONCOLOGY: NEEDS AND CHALLENGES FOR FUTURE SUCCESS

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Disclosures

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Toshiba Medical Systems

as well as
Commonwealth Foundation
Maritz Foundation

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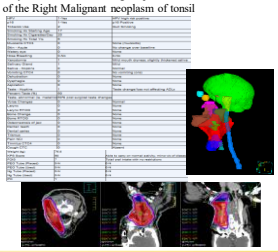
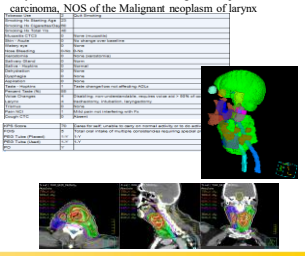
Which patient will do better?

69-year-old man with Stage Squamous cell carcinoma, NOS of the Right Malignant neoplasm of tonsil



63-year-old man with T3 N2b M0 Stage IVA Squamous cell carcinoma, NOS of the Malignant neoplasm of larynx



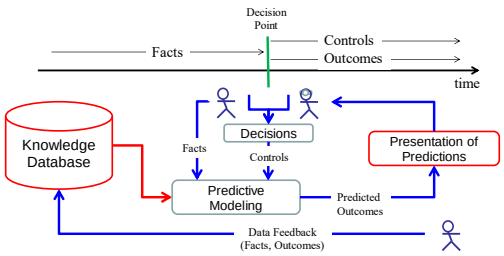
What we need to get there?

- A means of quantifying the patient experience
- A system to capture that knowledge in routine clinical care
- Validated data science models to predict outcomes for the individual patients
- Incorporate models into treatment plan generation **and clinical decisions**

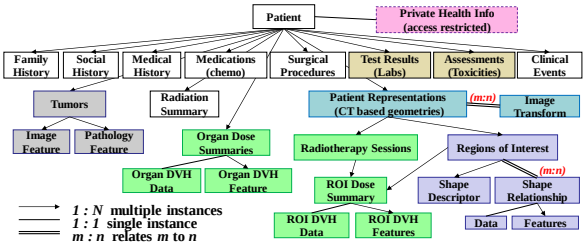
Types of Clinical Data

- Clinician Assessments
- Patient Reported
  - Quality of life
  - Toxicity and complications
- Biospecimen
  - Labs
  - Pathology
- Image derived features (Radiomics)
- Treatment
  - Radiation Dosimetry
  - Surgery
  - Chemotherapy
- Symptom management
  - Nutritional support
  - Pain medications

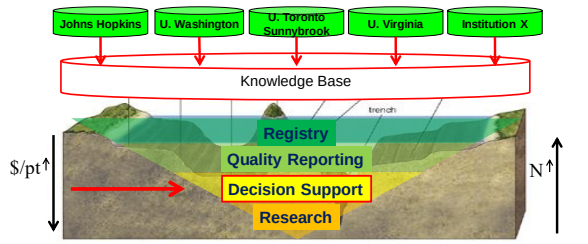
Learning health system



Oncospace tables and schema

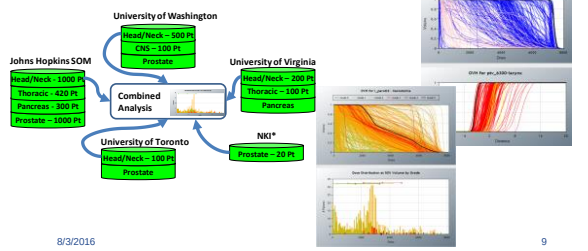


Oncospace Consortium Repository
(It's all about the data)



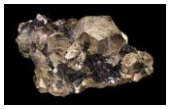
Consortium Status

Michael Bowers MS



Viability and Value

- Predictive factors must be accessible for new patients
- Prediction must be clinically valuable and extend the knowledge of the clinician
- Predictive models must be consistent with existing knowledge



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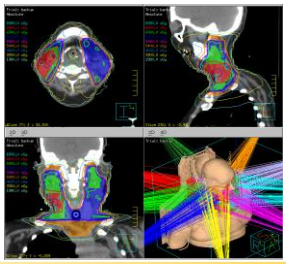
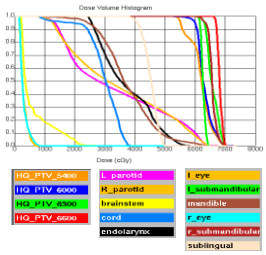
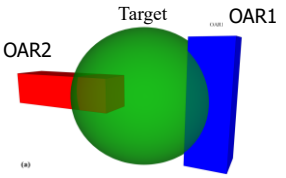
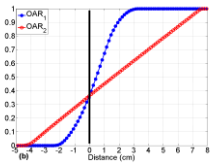
Precision Radiotherapy Treatment





OVH: serial vs parallel



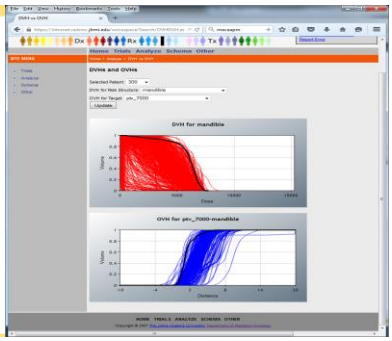


For parallel organs, **OAR2** is more easily spared.
For serial organs, **OAR1** is more easily spared.

Mandible vs PTV_7000

pt: 300

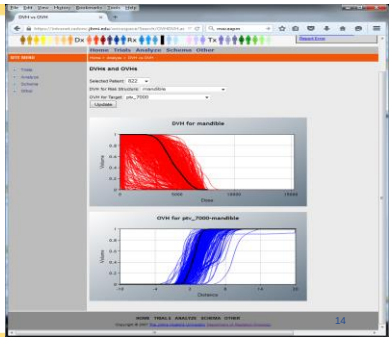
8/3/2016



Mandible vs PTV_7000

pt: 822

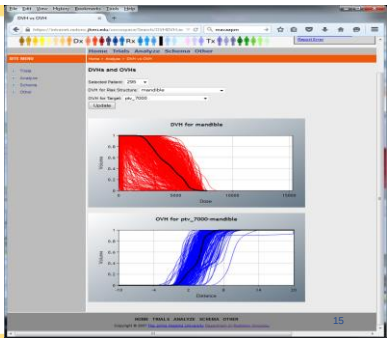
8/3/2016



Mandible vs PTV_7000

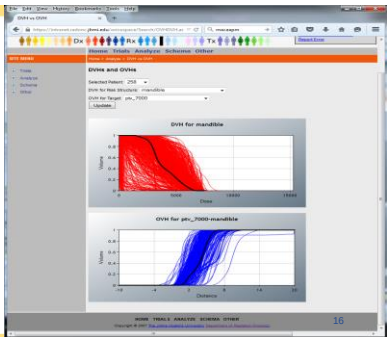
pt: 295

8/3/2016



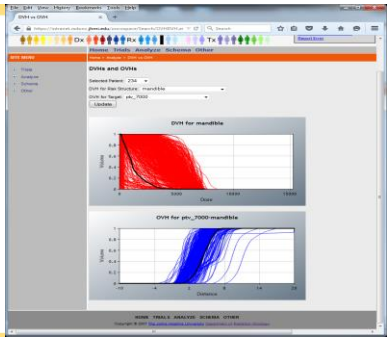
Mandible vs PTV_7000

pt: 258



Mandible vs PTV_7000

pt: 234



Shape-dose relationship for radiation plan quality

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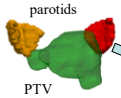
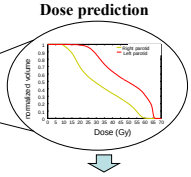
Shape relationship



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:

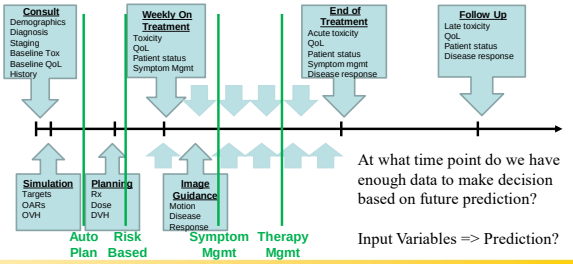
- Plan quality assessment
- Automated planning
  - IMRT objective selection
- Dosimetric trade-offs

Currently, shape (knowledge) based auto-planning…

- has demonstrated improved quality
- removed human variability for standard cases
- can learn as we improve our techniques and change our practices.
- is now advancing commercially

Promote Culture of Data Collection

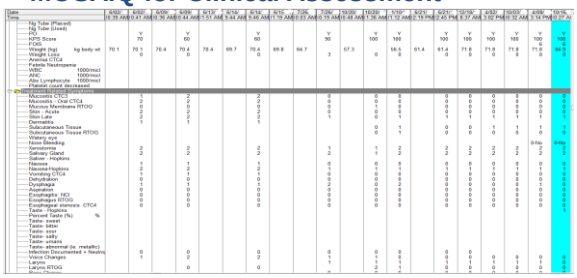
Data collected over entire treatment



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

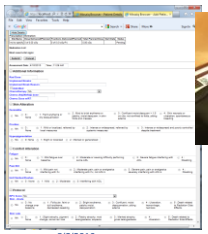
Input Variables => Prediction?

MOSAIQ for Clinical Assessment



Data Collection in Clinic

Clinical Assessment

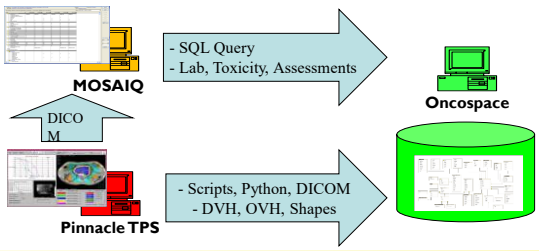


Quality of life

FACT HN
SSQ
SHIM
IPSS
PAN26

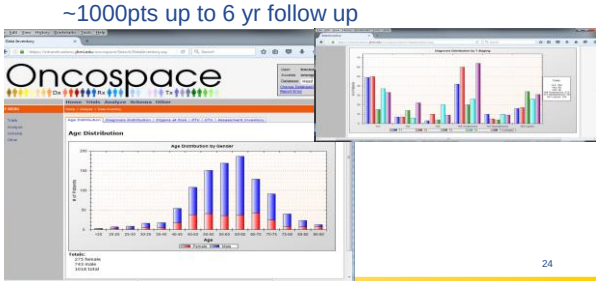
Disease Status

Extract, Transform, Load

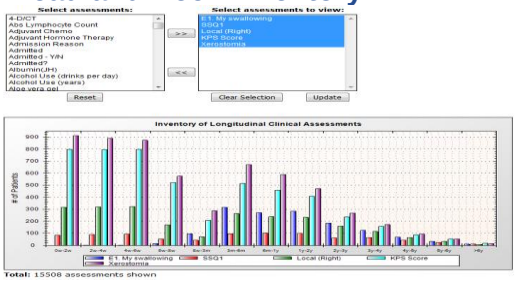


Head and Neck Inventory

~1000pts up to 6 yr follow up

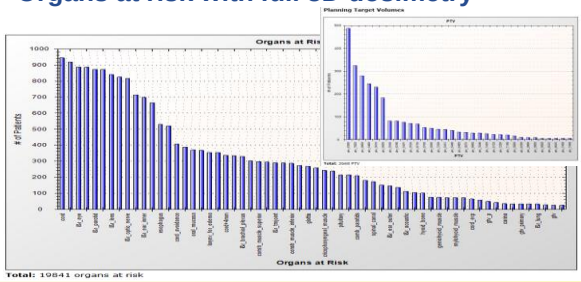


Head and Neck Inventory



Total: 15508 assessments shown

Organs at risk with full 3D dosimetry



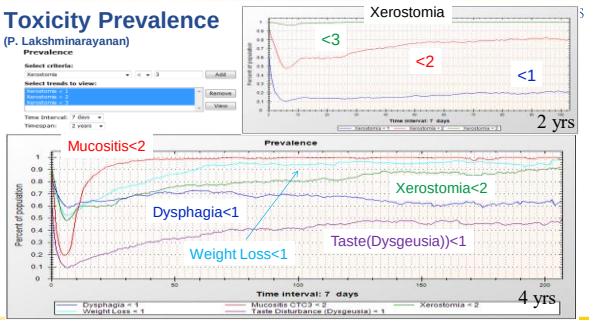
Total: 19841 organs at risk

Prostate Inventory

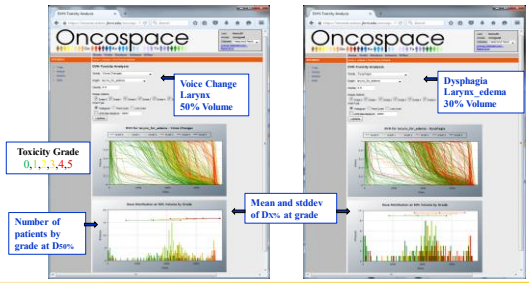
~1800 pts - ~700 with dose

Toxicity Prevalence

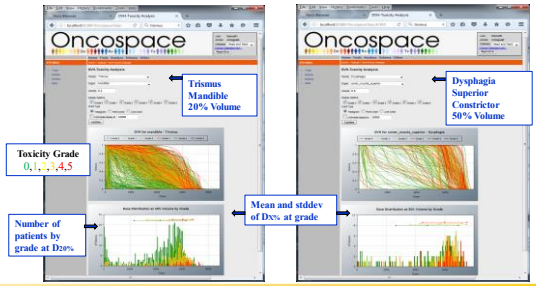
(P. Lakshminarayanan)



DVH, Toxicities and Grade distributions

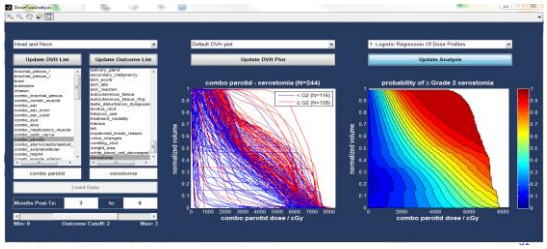


DVH, Toxicities and Grade distributions

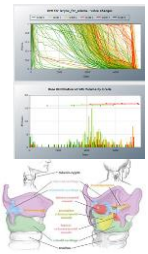


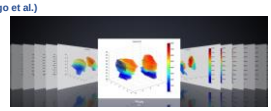
Toxicity and Dose Volume Histogram

(Scott Robertson et al…)



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





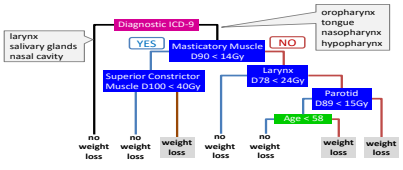
Method	Voice dysfunction n=99, n.=8, n.=91	Xerostomia n=364, n.=275, n.=89
Bagged Naïve Bayes (1000 iterations)	0.915	0.743
Bagged Linear Regression (1000 iterations)	0.905	0.737
Naïve Bayes	0.900	0.734
Linear Regression	0.896	0.731
Random Forest (1000 trees)	0.724	0.683
$NTCP_{LKB}$	0.596	0.700

Results: Weight loss prediction at planning

Endpoint: > 5kg loss at 3 months post RT

Sierra Zhi Cheng MD MS
Minoru Nakatsagawa PhD

- Predictors:
  - **(1: Diagnosis)** ICD-9 code
  - **(2: Dosimetry)** dose to swallowing muscles, larynx, parotid
  - **(3: Patient)** age
- Prediction result: High negative predictive value
  - The model can screen out patient without weight loss
  - Physicians can focus on patients with high probability of weight loss



Prediction result

AUC	0.773
Sensitivity	0.766
PPV	0.426
NPV	0.901

Results: Weight loss prediction during RT

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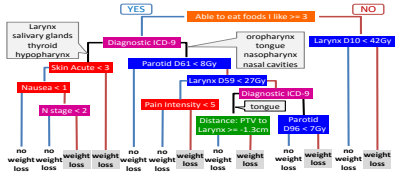
Endpoint: > 5kg loss at 3 months post RT

- Predictors:
  - **(1: QOL)** patient reported oral intake
  - **(2: Diagnosis and staging)** ICD-9, N stage
  - **(3: Dosimetry)** dose to larynx, parotid
  - **(4: Toxicity)** skin toxicity, nausea, pain
  - **(5: Geometry)** minimum distance b/w PTV, larynx

Sierra Zhi Cheng MD MS
Minoru Nakatsagawa PhD



Prediction result

AUC	0.821
Sensitivity	0.977
PPV	0.462
NPV	0.986

Pancreas Resectability

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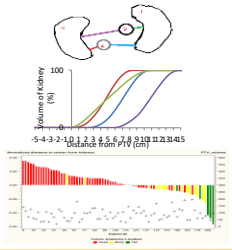
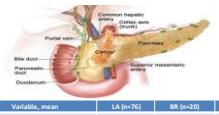
(S. Cheng et al…)





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	86.7585	0.0065*

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Xerostomia Prediction (3-6 Months post RT)

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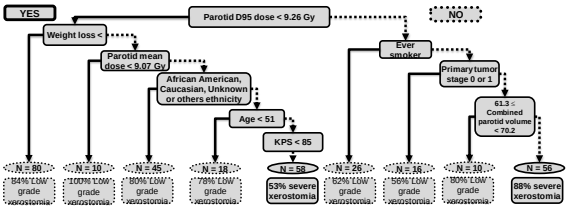
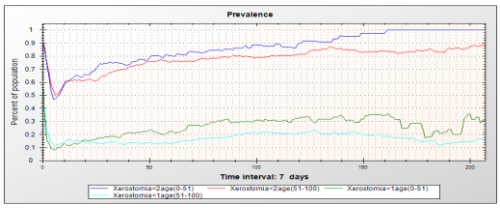
Xuan Hui MD MS



AUC	Accuracy	Sensitivity	Specificity
0.627	0.687	0.536	0.784

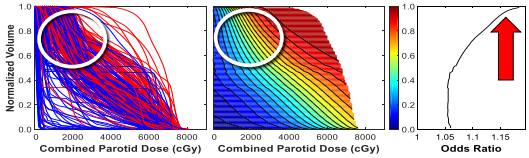
Xerostomia prevalence
separated by age = 51



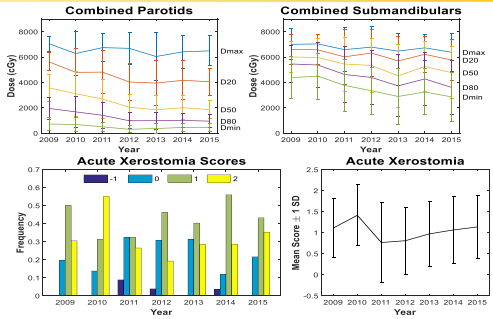
Xerostomia<2age(0-51) :
Initial size: 175
25% lost follow up at time: 26
50% lost follow up at time: 74

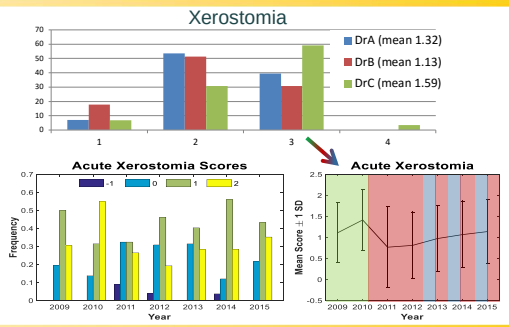
Xerostomia<2age(51-100) :
Initial size: 164
25% lost follow up at time: 27
50% lost follow up at time: 64

Improving Care:
Predicting radiation toxicities (Robertson et al.)



Grades 0-1 xerostomia
Grades 2-3 xerostomia





QUANTEC
Salivary (Deasy et al..)

"To best define xerostomia, we recommend that an observer-based system (*e.g.*, the Common Terminology Criteria for Adverse Events) be supplemented by a validated QOL measurement device (*e.g.*, the XQ (xerostomia questionnaire) [7]) and/or salivary measurements (*e.g.*, whole mouth-stimulated measurements)."

We concur! And will add that CTCAE may not have the necessary resolution at all.

Can't measure – Can't predict

- Can we find viable methods to refine our clinician assessed outcomes **in the clinical setting**?
- What is resolution of the data?
- Patient reported outcomes can validate clinician assessments at somewhat low cost. (SSQ etc…)
- Direct measurements tend to be more costly.
- Can natural language processing of our current documentation achieve the depth and granularity necessary?
- Must our culture change to more quantitative documentation of the patient condition?

Needs…

- For the vision of a learning health system, significantly improved user interfaces are required
- In order to present a prediction, we must first present the "quantitative" patient state
- More continuous assessment of patient condition is needed through mobile devices
- Stronger linkages between genomic, pathology and clinical databases

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 shape-based auto-planning utilizes a learning health system
- Data science models are maturing that can convert the knowledge to clinical predictions
- Sharing data across institutions allows for experience **and expertise** sharing

…we have work to do which requires real partnerships between clinicians and informaticists

Acknowledgments

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- **Toshiba**
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  - Bobby Davey PhD
  - Rachel-Louise Koktava
  - John Haller
- **Elekta**
  - Bob Hubbell
- **University of Washington**
  - Kim Evans MS
  - Mark Philips PhD
  - Kristi Hendrickson PhD

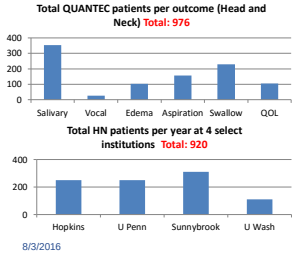
Consent/Ethics

- It is our duty to learn from every patient we treat (experience-wise or electronically)
- Quantifying patient experience provides easier recall and enhances and enables sharing of that experience
- If we are capturing the data on every patient the same way, then isn't it the standard of care for that service?
- Are we doing research or quality management?
- When does it become research?
  - Intent to publish?
  - When a group of patients is separated from standard of care?

Acknowledgements

- Harry Quon MD
- Joseph Herman MD
- Scott Robertson PhD
- Joseph Moore PhD
- Sierra Cheng MD
- Ana Keiss MD
- Minoru Nakatsagawa PhD
- John Wong PhD
- Theodore DeWeese MD

Are current radiobiology models good enough?



Current NTCP models are too simplistic, and based on a small amount of trial data.

…we treat patients every day with radiation, we just fail to capture the impact on all of them…

~60K HN cancer per year in US