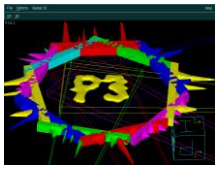
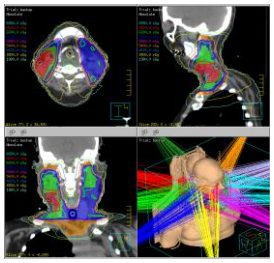
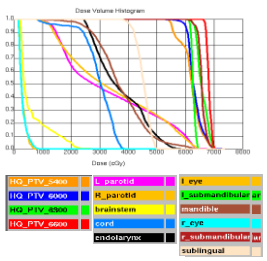
IMRT OPTIMIZATION: FROM THE ORIGINS AND DELIVERY TO ROBUSTNESS, AUTOMATION AND BIG DATA

Todd McNutt PhD
Johns Hopkins University

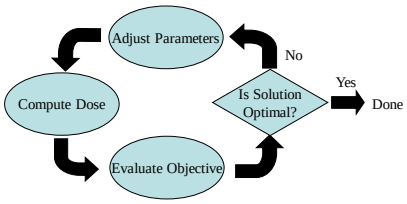


Intensity Modulated Radiotherapy





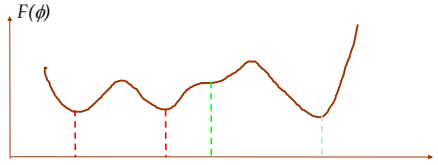
Iterative Optimization



Gradient or Stochastic

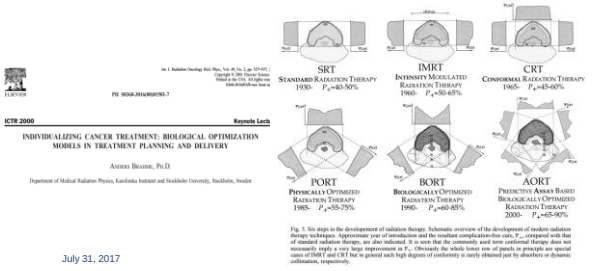
JOHNS HOPKINS MEDICINE

How do we know we found the global minimum? ... not sure we ever did.



Biological or Physical Objectives

JOHNS HOPKINS MEDICINE



ICTR 2000 Keynote Lecture

INDIVIDUALIZING CANCER TREATMENT: BIOLOGICAL OPTIMIZATION MODELS IN TREATMENT PLANNING AND DELIVERY

ANDERS BRAHME, PH.D.

Department of Medical Radiation Physics, Karolinska Institutet and Stockholm University, Stockholm, Sweden

Fig. 3. Six steps in the development of radiation therapy. Schematic overview of the development of modern radiation therapy techniques. Approximate year of introduction and the resultant complication-free cure, P_{cure}, compared with that of standard radiation therapy, are also indicated. It is seen that the commonly used term conformal therapy does not necessarily imply a very large improvement in P_{cure}. Obviously the whole lower row of panels in principle are special cases of IMRT and CRT but in general such high degrees of conformity is rarely obtained just by absorbers or dynamic collimation, respectively.

In the beginning…

JOHNS HOPKINS MEDICINE

- Planning would be easier and automatic
- Planning became a process of manipulating regions of interest and objectives to get what you wanted

doi:10.1016/j.ijrobp.2010.11.016

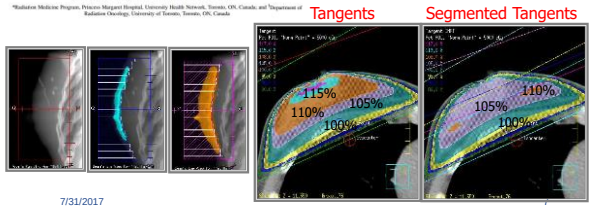
JOHNS HOPKINS MEDICINE

PHYSICS CONTRIBUTION

AUTOMATED PLANNING OF TANGENTIAL BREAST INTENSITY-MODULATED RADIOTHERAPY USING HEURISTIC OPTIMIZATION

Thomas G. Purdie, Ph.D.,*† Robert E. Dinniwell, M.D.,*‡ Daniel Letourneau, Ph.D.,*† Christine Hill, B.Sc.,* and Michael B. Sharpe, Ph.D.*†

Tangents | Segmented Tangents



Beam orientation

JOHNS HOPKINS MEDICINE

European Journal of Operational Research 205 (2010) 522–527

Contents lists available at ScienceDirect

European Journal of Operational Research

journal homepage: www.elsevier.com/locate/ejor

Continuous Optimization

Neighborhood search approaches to non-coplanar beam orientation optimization for total marrow irradiation using IMRT

V.V. Mišić [a], D.M. Aleman [a,*], M.B. Sharpe [b]

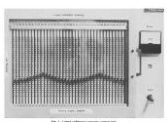
[a] Department of Mechanical and Industrial Engineering, University of Toronto, 5 King's College Road, Toronto, Canada, ON M5S 3G8
[b] Princess Margaret Hospital, Department of Radiation Oncology, University of Toronto, 610 University of Avenue, Toronto, Canada, ON M5G 2M9

Int. J. Radiation Oncology Biol. Phys., 1977, Vol. 2, pp. 697–704. Pergamon Press. Printed in the U.S.A.

JOHNS HOPKINS MEDICINE

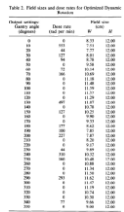
AUTOMATIC VARIATION OF FIELD SIZE AND DOSE RATE IN ROTATION THERAPY†

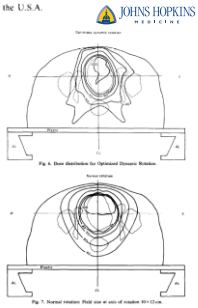
Joseph Mantel, Ph.D. and Harold Perry, M.D.
Abraham and Anna Srere Radiation Therapy Center, Department of Radiology, Sinai Hospital of Detroit, Detroit, MI 48235, U.S.A.
and
James J. Weinkam, D.Sc.
Computing Science Program, Simon Fraser University, Burnaby B.C., Canada V5A 1S6



Optimization method

The search for a plan which is optimum with respect to a reasonably chosen set of objective functions provides a well defined problem for computer solution.[1,2,3,4,5,6] Finding a plan that is "good enough" generally requires realistic trials and human judgment, both of which are costly and slow. An optimization technique has been developed in order to obtain further improvement in the dose distribution.





Nomos MIMiC (Serial Tomotherapy)

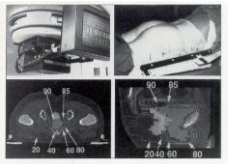
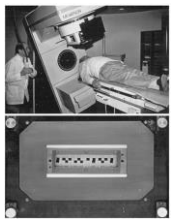
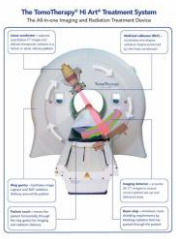
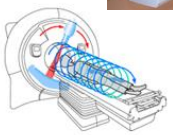


Figure 7: Axial tomotherapy approach to intensity-modulated radiation therapy. Nomos Peacock system uses a mini-multileaf collimator system (MIMiC) that is mounted to a conventional low-energy megavoltage medical linear accelerator, and treatment is delivered to a narrow slice of the patient using arc rotation. The radiation beam is turned on and off by driving the MIMiC leaves in and out of the beam path, thus creating the optimized nonuniform beam intensity. A transverse and sagittal dose distribution for a prostate cancer patient treated with this form of intensity-modulated radiation therapy is shown.

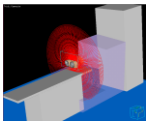


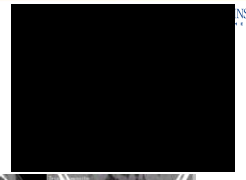
Helical Tomotherapy

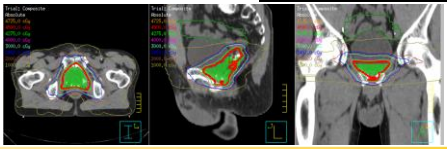




VMAT - RapidArc





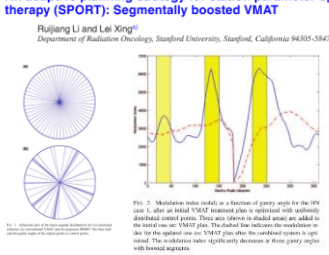


Medical Physics Letter

JOHNS HOPKINS MEDICINE

An adaptive planning strategy for station parameter optimized radiation therapy (SPORT): Segmentally boosted VMAT

Ruijiang Li and Lei Xing[a)]
Department of Radiation Oncology, Stanford University, Stanford, California 94305-5847



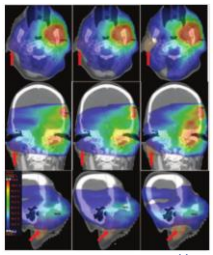
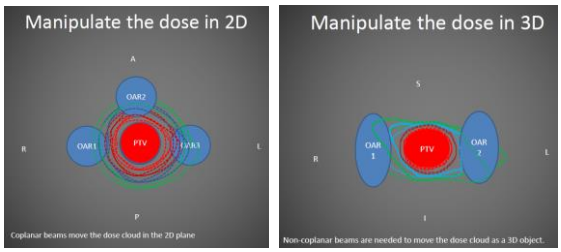


FIG. 2. Modulation index (solid) as a function of gantry angle for the HN case 1, after an initial VMAT treatment plan is optimized with uniformly distributed control points. Three arcs (shown in shaded areas) are added to the initial one-arc VMAT plan. The dashed line indicates the modulation index for the updated one-arc VMAT plan after the combined system is optimized. The modulation index significantly decreases at those gantry angles with boosted segments.

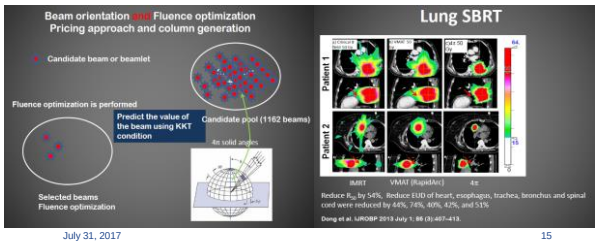
JOHNS HOPKINS MEDICINE

4 π (K. Sheng, D. Low et. al.) UCLA



JOHNS HOPKINS MEDICINE

4 π (K. Sheng, D. Low et. al.) UCLA



Positional uncertainty

JOHNS HOPKINS MEDICINE

- Adaptive
- Robust

INSTITUTE OF PHYSICS PUBLISHING PHYSICS IN MEDICINE AND BIOLOGY
Phys. Med. Biol. **50** (2005) 5463–5477 doi:10.1088/0031-9155/50/23/003

Robust optimization for intensity modulated radiation therapy treatment planning under uncertainty

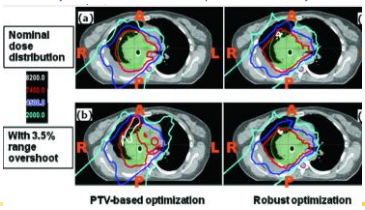
Millie Chu[1], Yuriy Zinchenko[1], Shane G Henderson[1] and Michael B Sharpe[2]

[1] School of Operations Research & Industrial Engineering, Cornell University, Ithaca, NY 14853, USA
[2] Princess Margaret Hospital, Toronto, ON M5G 2M9, Canada

Robust optimization

JOHNS HOPKINS MEDICINE

- Not all IMRT plans are equal with patient motion
- Goal is to create an IMRT plan that degrades less with setup and motion uncertainty from the patient
- Solution is to include the motion uncertainty in the calculation of the objective functions to drive the optimization to delivery solutions that are



W. Liu et al Med Phys 39(2) IMPT Plan

Automation

JOHNS HOPKINS MEDICINE

POINT/COUNTERPOINT

Suggestions for topics suitable for these Point/Counterpoint debates should be addressed to Colin G. Orton, Professor Emeritus, Wayne State University, Detroit: ortonc@comcast.net. Persons participating in Point/Counterpoint discussions are selected for their knowledge and communicative skill. Their positions for or against a proposition may or may not reflect their personal opinions or the positions of their employers.

Within the next ten years treatment planning will become fully automated without the need for human intervention

Michael B. Sharpe, Ph.D.
Radiation Medicine Program, UHN Princess Margaret Cancer Centre and Department of Radiation Oncology, University of Toronto, Toronto, Ontario M5G 2M9, Canada
(Tel: 416-946-4501 ext. 5025; E-mail: Michael.Sharpe@rmp.uhn.on.ca)

Kevin L. Moore, Ph.D.
Department of Radiation Medicine and Applied Sciences, University of California, La Jolla, San Diego, California 92093-0865
(Tel: 858-822-6056; E-mail: kevinmoore@ucsd.edu)

Colin G. Orton, Ph.D., Moderator

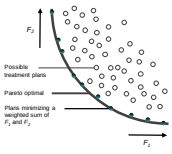
(Received 11 August 2014; accepted for publication 13 August 2014; published 10 November 2014)

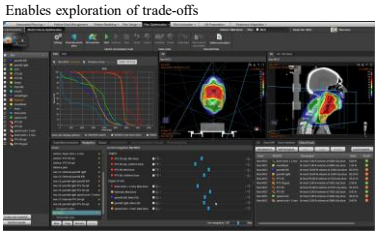
[http://dx.doi.org/10.1118/1.4894496]

Multi-criteria Optimization

JOHNS HOPKINS MEDICINE

Enables exploration of trade-offs





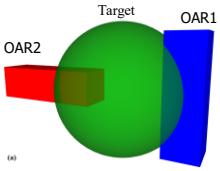
What makes a high quality plan?

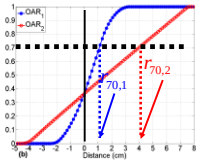
JOHNS HOPKINS MEDICINE

- Are all dose protocol guidelines met?
- Is the conformity and uniformity of dose in the targets appropriate?
- Are the contours correct?
- Is the sparing of organs at risk at the limit of the delivery capabilities?
- Is there a proper balance of dosimetric trade-offs between organs at risk?

OVH: serial vs parallel

JOHNS HOPKINS MEDICINE

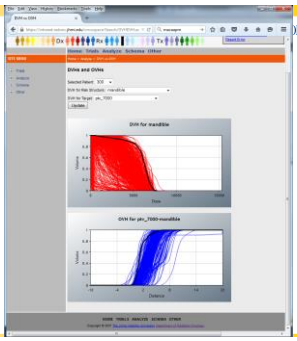




For parallel organs, **OAR2** is more easily spared.
For serial organs, **OAR1** is more easily spared.

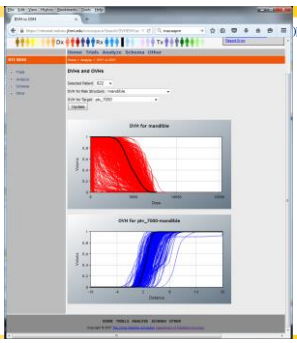
Mandible vs PTV_7000

pt: 300



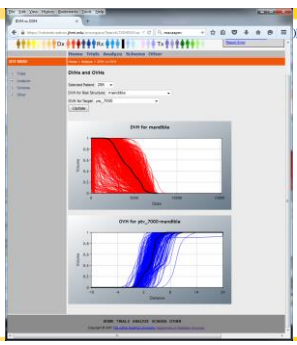
Mandible vs PTV_7000

pt: 822



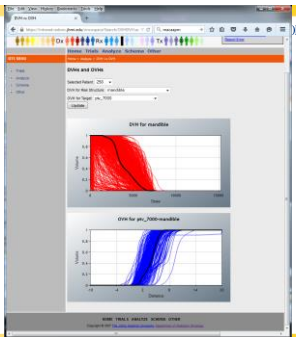
Mandible vs PTV_7000

pt: 295



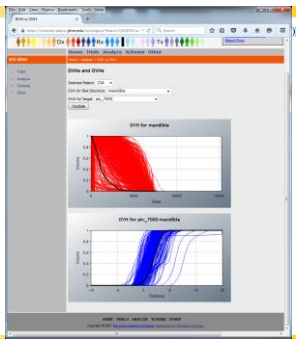
Mandible vs PTV_7000

pt: 258



Mandible vs PTV_7000

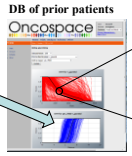
pt: 234



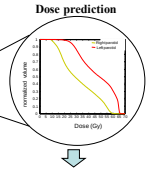
Shape-dose relationship for radiation plan quality

Shape relationship

DB of prior patients



Dose prediction

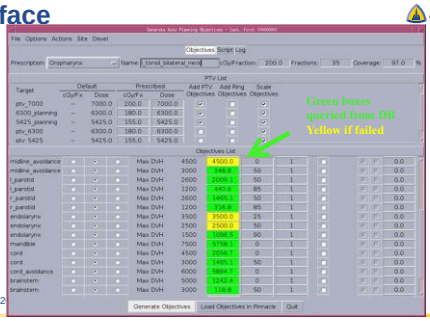


For a selected Organ at Risk and %V, find the lowest dose achieved from all patients whose %V is closer to the selected target volume?

Decisions:

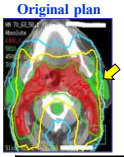
- Plan quality assessment
- Automated planning
  - IMRT objective selection
- Dosimetric trade-offs

Interface

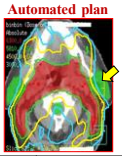


Sample automated radiation planning result (B. Wu et al)

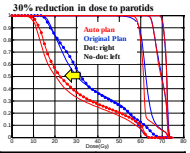
Original plan



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

Clinical implementation of dose-volume histogram predictions for organs-at-risk in IMRT planning

K L Moore[1,2], L M Appenzoller[1], J Tan[1], J M Michalski[1], W L Thorstad[2] and S Mutic[1]

[1] Department of Radiation Medicine and Applied Sciences, University of California, San Diego, La Jolla, CA 92093, USA
[2] Department of Radiation Oncology, Washington University in St. Louis, St. Louis, MO 63110, USA

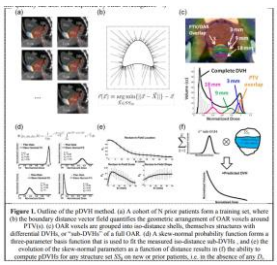


Figure 1. Outline of the pDVH method. (a) A cohort of N prior patients form a training set, where (b) the boundary distance vector field quantifies the geometric arrangement of OAR voxels around PTV(s). (c) OAR voxels are grouped into iso-distance shells, themselves structures with differential DVHs, or "sub-DVHs" of a full OAR. (d) A skew-normal probability function forms a three-parameter basis function that is used to fit the measured iso-distance sub-DVHs , and (e) the evolution of the skew-normal parameters as a function of distance results in (f) the ability to compute pDVHs for any structure set S_N on new or prior patients, i.e. in the absence of any $f(\cdot)$.

Pinnacle IMRT Alpha Demo

JOHNS HOPKINS MEDICINE

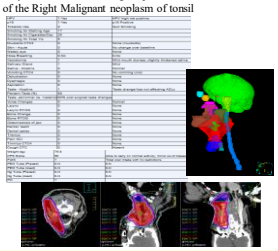
"What I really want to do is have the patient fill out a questionnaire telling me what is most important to them and have the computer design the best plan for that patient?"

unidentified senior
radiation oncologist
(circa ASTRO 2001)

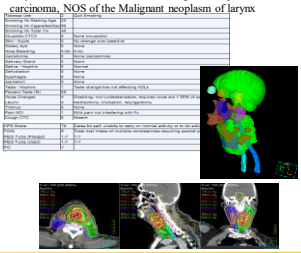
Which patient will do better?

JOHNS HOPKINS MEDICINE

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

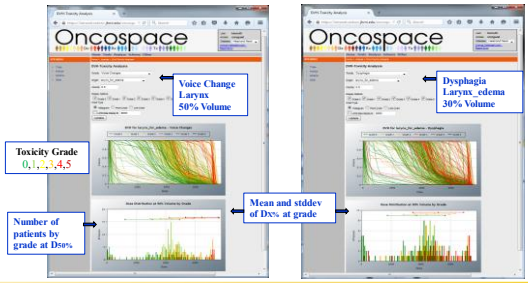


63-year-old man with T3 N2b M0 Stage IVA Squamous cell carcinoma, NOS of the Malignant neoplasm of larynx

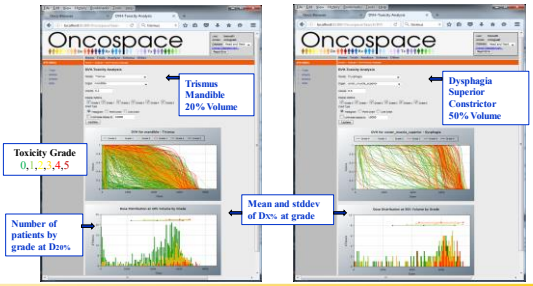


DVH, Toxicities and Grade distributions

JOHNS HOPKINS MEDICINE

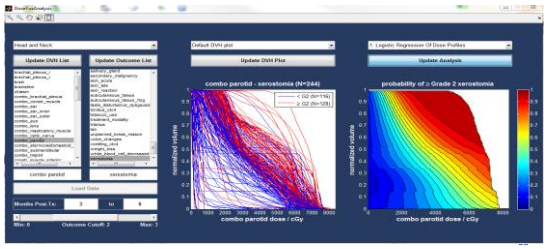


DVH, Toxicities and Grade distributions

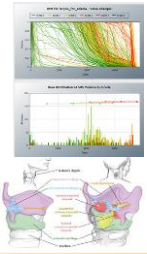


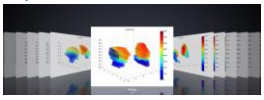
Toxicity and Dose Volume Histogram

(Scott Robertson et al…)



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





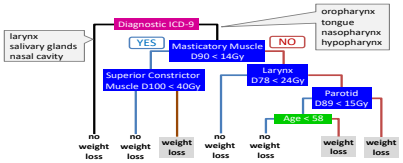
Method	Voice dysfunction n=99, n_+=8, n_-=91	Xerostomia n=364, n_+=275, n_-=89
Bagged Naive Bayes (1000 iterations)	0.915	0.743
Bagged Linear Regression (1000 iterations)	0.905	0.737
Naïve Bayes	0.900	0.734
Linear Regression	0.896	0.731
Random Forest (1000 trees)	0.724	0.683
$NTCP_{LKB}$	0.596	0.700

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

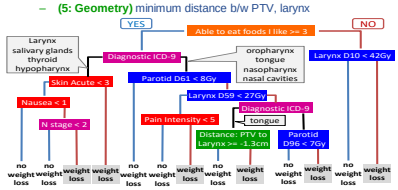
AUC	0.773
Sensitivity	0.766
PPV	0.426
NPV	0.901

Results: Weight loss prediction during RT

Endpoint: > 5kg loss at 3 months post RT

Sierra Zhi Cheng MD MS
Minoru Nakatsagawa PhD

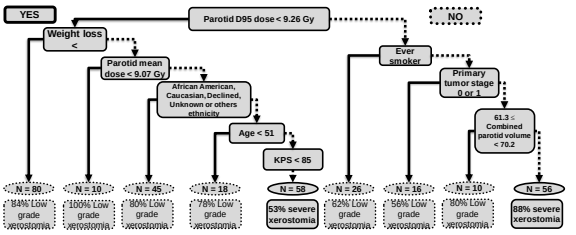
- Predictors:
  - **(1: QOL)** patient reported oral intake
  - **(2: Diagnosis and staging)** ICD-9, N stage
  - **(3: Dosimetry)** dose to larynx, parotid
  - **(4: Toxicity)** skin toxicity, nausea, pain
  - **(5: Geometry)** minimum distance b/w PTV, larynx



Prediction result

AUC	0.821
Sensitivity	0.977
PPV	0.462
NPV	0.986

Xerostomia Prediction (3-6 m post RT)



AUC	Accuracy	Sensitivity	Specificity
0.627	0.687	0.536	0.784

Xuan Hui MD MS

In the future…

Automated real-time biologically data-driven robust adaptive planning capabilities that provide easy trade-off evaluation and progressively lowers dose outside of the targets where possible.

Which is something I may have said at my last Mike talk…

…a true friend and confidant

Miss you buddy!

What's Next in IMRT

- Delivery Advancements
- True automation
- Data-driven "biological" models
- Real-time planning and adaptation
  - with MR Linac

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

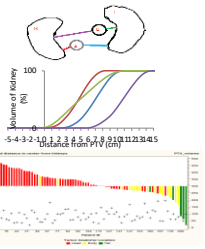
- Delivery methods
  - Tomo
  - Fixed beam
  - VMAT
  - Proton
- Optimization
  - Stochastic vs Gradient
  - Biological
  - Global Minimum – What Objective
  - Multi-criteria
  - Drive down dose
  - Data driven
  - Robust

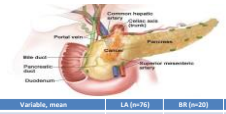
- How do we know we found the global minimum... turns out we don't even know the right objective.

- Did biological work?
- Well, let's try Pareto multi-criteria
- Continuous driving down of dose
- Then data driven...

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*

46

Professional Guidance

Medical Physics Volume 30, Issue 8, 1 August 2003, Pages 2089-2115

Guidance document on delivery, treatment planning, and clinical implementation of IMRT: Report of the IMRT subcommittee of the AAPM radiation therapy committee(Article)

Ezzell, G.A, Galvin, J.M.b, Low, D.c, Palta, J.R., Rosen, I., Sharpe, M.B., Xia, P., Xiao, Y., Xing, L., Yu, C.X.

International Journal of Radiation Oncology Biology Physics Volume 58, Issue 5, 1 April 2004, Pages 1616-1634

Implementing IMRT in clinical practice: A joint document of the American Society for Therapeutic Radiology and Oncology and the American Association of Physicists in Medicine(Article)

Galvin, J.M. Ezzell, G., Eisbrauch, A., Yu, C., Butler, B., Xiao, Y., Rosen, I., Rosenman, J., Sharpe, M., Xing, L.b, Xia, P.b, Lomax, T.b, Low, D.A.b, Palta, J.

7/31/2017 47