IMPT for lung cancer: Physics Consideration

Xiaodong Zhang

Department of Radiation Physics, UT MD Anderson Cancer Center

THE UNIVERSITY OF TEXAS
MD Anderson
~~Cancer~~ Center

Outline

- The dose distribution and clinical outcome data
  - It is important for IMPT plan to be better in paper
- IMPT clinical implementation of thoracic cancer
  - Treatment planning
  - Motion management
  - Patient specific quality assurance/Dose verification
  - Adaptive planning

Prostate Dosimetric Data: IMRT v.s. PSPT

- MDACC: proton is worse for bladder and rectum for dose >= 40 Gy (RBE). (two lateral opposed beams, 5-8 mm margins). [Zhang et. al., IJROBP, 67, 2007, p620-629]
- MGH: proton is worse for bladder when dose > 50 Gy, for rectum when dose > 60 Gy for rectum. (10 mm margins, two lateral opposed beams) [Trofimov et. al., IJROBP, 69, 2007, p444-453]
- Florida: Proton is better for rectum at all dose levels. (allowing oblique angles toward rectum) [Vargas et. al., IJROBP, 70, 2008, p744-751]

Proton is worse for rectum at high dose using two lateral opposed beams (adopted for majority proton treatment for prostate cancer)

GI toxicity correlates with rectum V70

Int. J. Radiation Oncology Biol. Phys., Vol. 48, No. 3, pp. 635–642, 2000

0360-3016/00/$–see front matter

ELSEVIER

PII S0360-3016(00)00700-8

CLINICAL INVESTIGATION **Prostate**

COMPLICATIONS FROM RADIOTHERAPY DOSE ESCALATION IN PROSTATE CANCER: PRELIMINARY RESULTS OF A RANDOMIZED TRIAL

- **Significant increase in late rectal complications when more than 25% of rectum received 70 Gy above.**

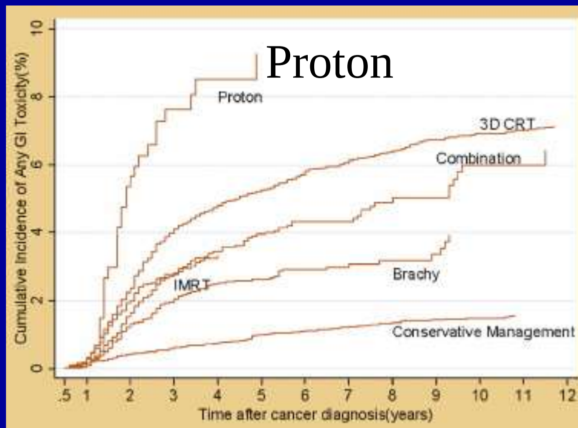
toxicity were 20% and 9% for 70-Gy and 78-Gy groups, respectively (log rank, $p = 0.8$). The 5-year risks of Grade 2 or higher late rectal toxicity were 14% and 21% for 70 Gy and 78 Gy, respectively ($p = 0.4$). Dose–volume histogram analysis of the 78-Gy patients showed a significant correlation between the percentage of rectum irradiated to 70 Gy or greater and the likelihood of developing late rectal complications. Patients with more than 25% of the rectum receiving 70 Gy or greater had a 5-year risk of Grade 2 or higher complications of 37% compared to 13% for patients with 25% or less ($p = 0.05$). All three Grade 3 complications occurred when greater than 30% of the rectum received 70 Gy or more.

Conclusion: The overall rate of complications was similar in both treatment arms. However, there is evidence for a significant increase in late rectal complications when more than 25% of the rectum received 70 Gy or greater. This parameter may serve as a benchmark for the design of future three-dimensional conformal trials. © 2000 Elsevier Science Inc.

Dose escalation, Prostate cancer, Radiotherapy, Rectal complications.

Experience and learning curve matters

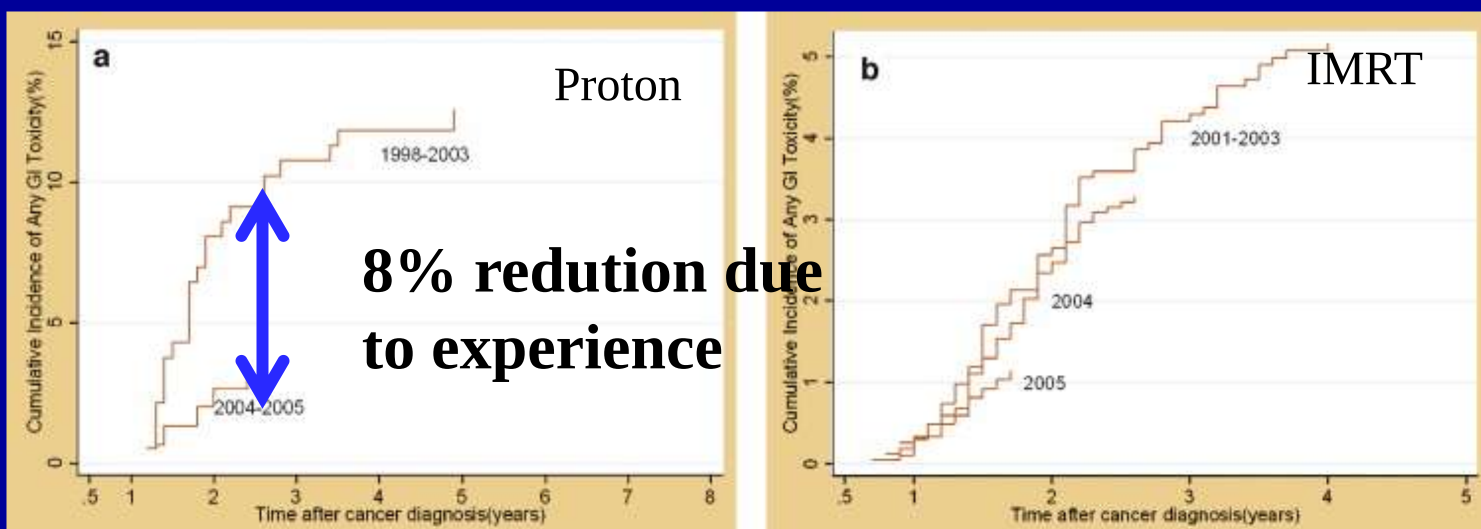
GI Toxicity



Late Gastrointestinal Toxicities Following Radiation Therapy for Prostate Cancer

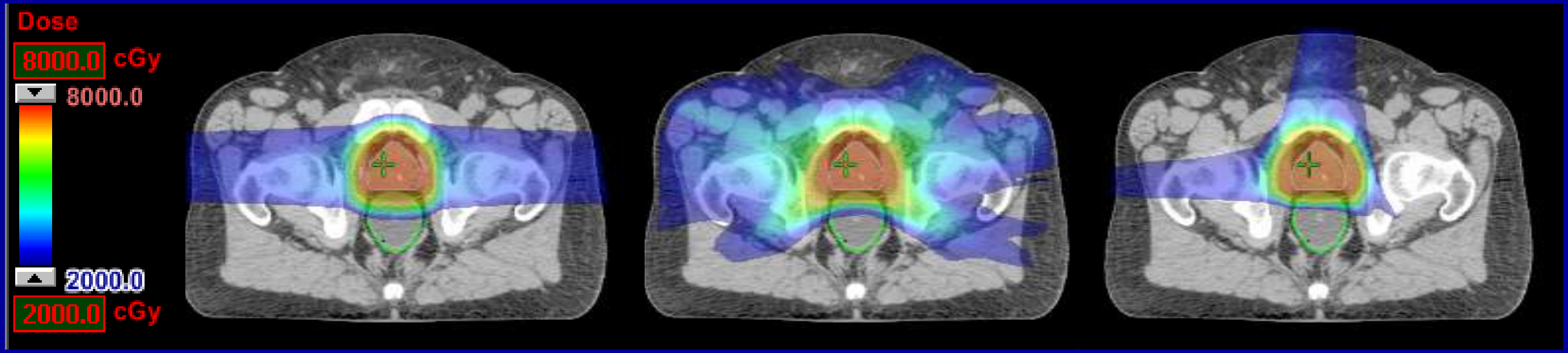
Sung Kim, Shunhua Shen, Dirk F. Moore, Weichung Shih, Yong Lin, Hui Li, Matthew Dolan, Yu-Hsuan Shao, Grace L. Lu-Yao

European Urology
Volume 60, Issue 5, November 2011, Pages 908–916

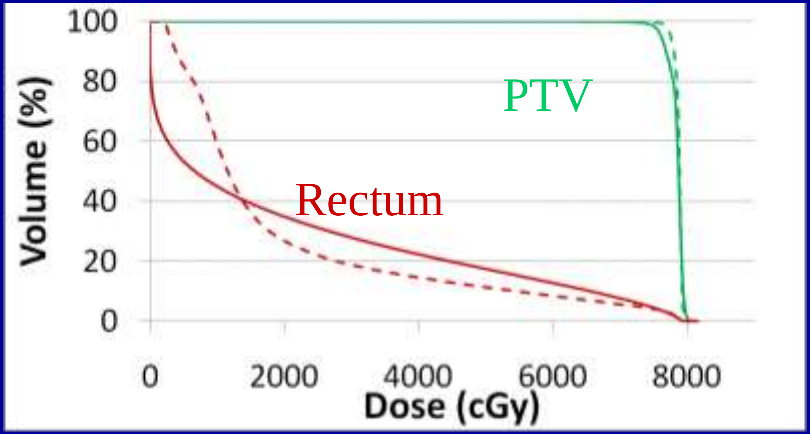


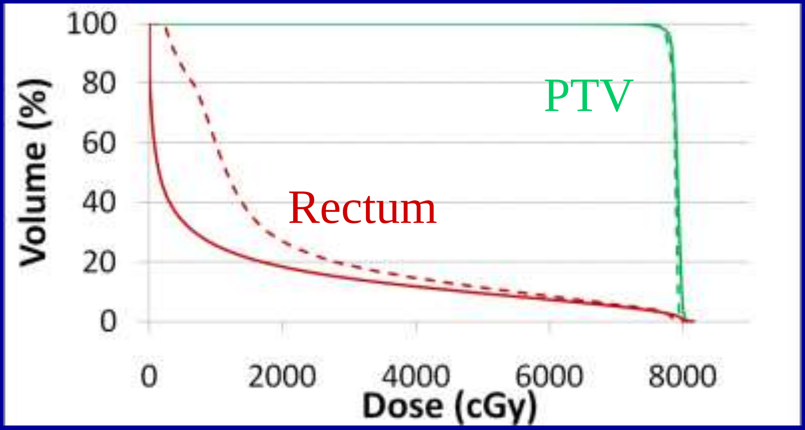
Cumulative incidence estimates of any gastrointestinal (GI) toxicity by radiation modality. Competing risk was computed by using cumulative incidence adjusting for death from any cause prior to any GI toxicity.3D CRT = three-dimensional conformal radiotherapy; Brachy = brachytherapy; IMRT = intensity-modulated radiotherapy; Proton = proton beam therapy. (41737 patients)

Better rectum sparing by IMPT and better beam direction



PSPT **VMAT/RapidArc** **IMPT-BAO**





Soild: PSPT, dashed IMRT

Soild: IMPT, dashed IMRT

- If we have the confidence to use the oblique beam (towards rectum) and we believe that what we see in the TPS is what we get, proton plan should be preferred for prostate patients.

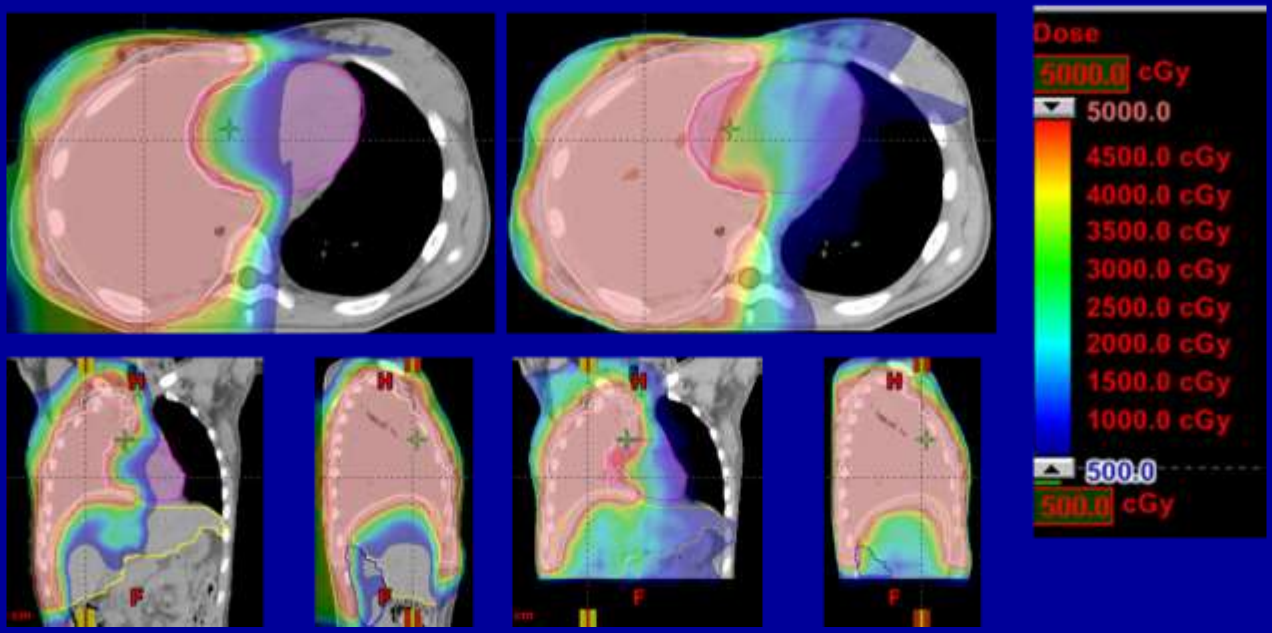
IMPT technique for lung cancer/Consideration

- IMPT plans should be significantly better than IMRT plans in terms of DVH data
  - **Treatment planning**
- IMPT plan should be robust against setup, range, motion uncertainties and anatomical change
  - **Motion management, adaptive planning, robust evaluation**
- **The dose distribution should be accurate**
  - **QA/dose verification**
- In the long run, the implementation should be cost effective
  - **Improvement**

Treatment planning

- Quality Assurance/Quality Control
  - IMPT v.s. IMRT v.s. PSPT
- Robust optimization
  - "worst-case" optimization
    - did not consider anatomical change during the treatment

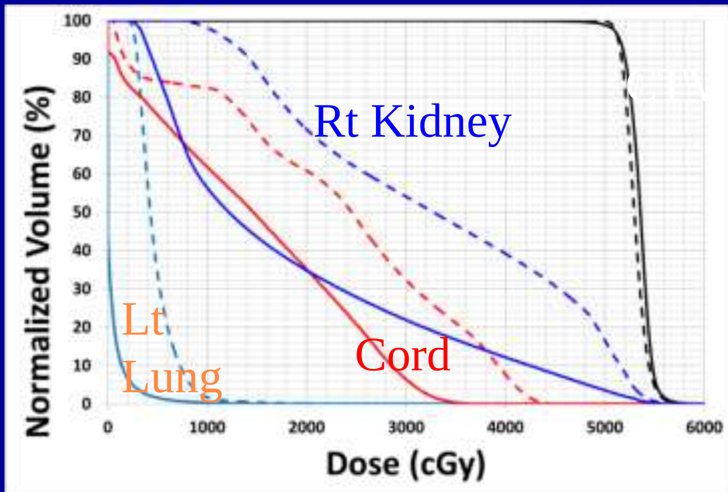
First thoracic patients treated using IMPT/MFO

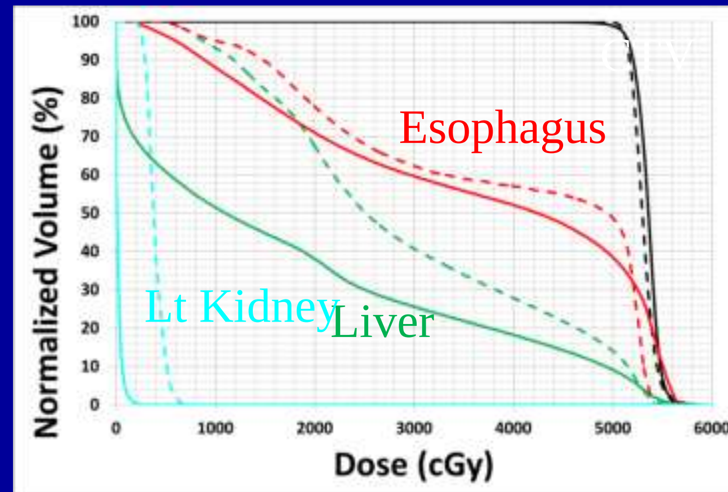


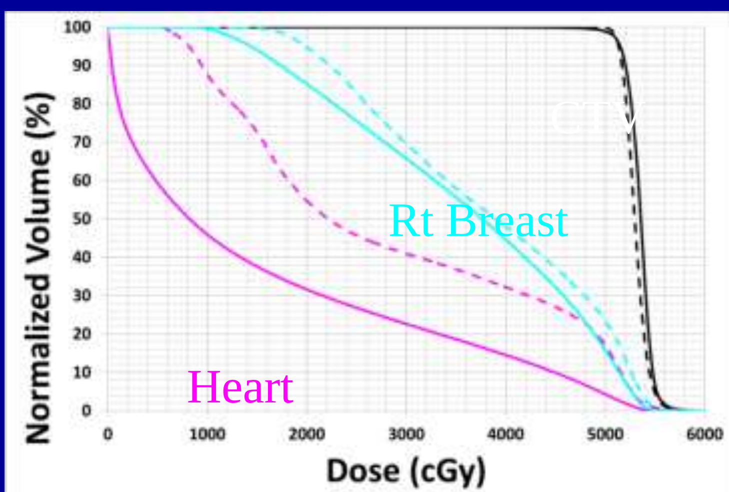
IMPT IMRT

- 17 yr old female
- Stage IV metastatic adenocarcinoma with extensive involvement of the nodular right pleural
- Treated with multiple cycles of chemotherapy
- Eventually underwent extrapleural pneumonectomy
- Large and complex CTV = 2215 cc
- Even with a H&N patient with CTV = 547 cc and various normal structures – Eclipse 8.9 could run out of memory
- In-house system running on the super-computers at TACC was used to design this plan.
- Patient started treatment using robust MFO IMPT plan on 07/30/12 and finished treatment on 08/31/12

Challenge case example: DVHs

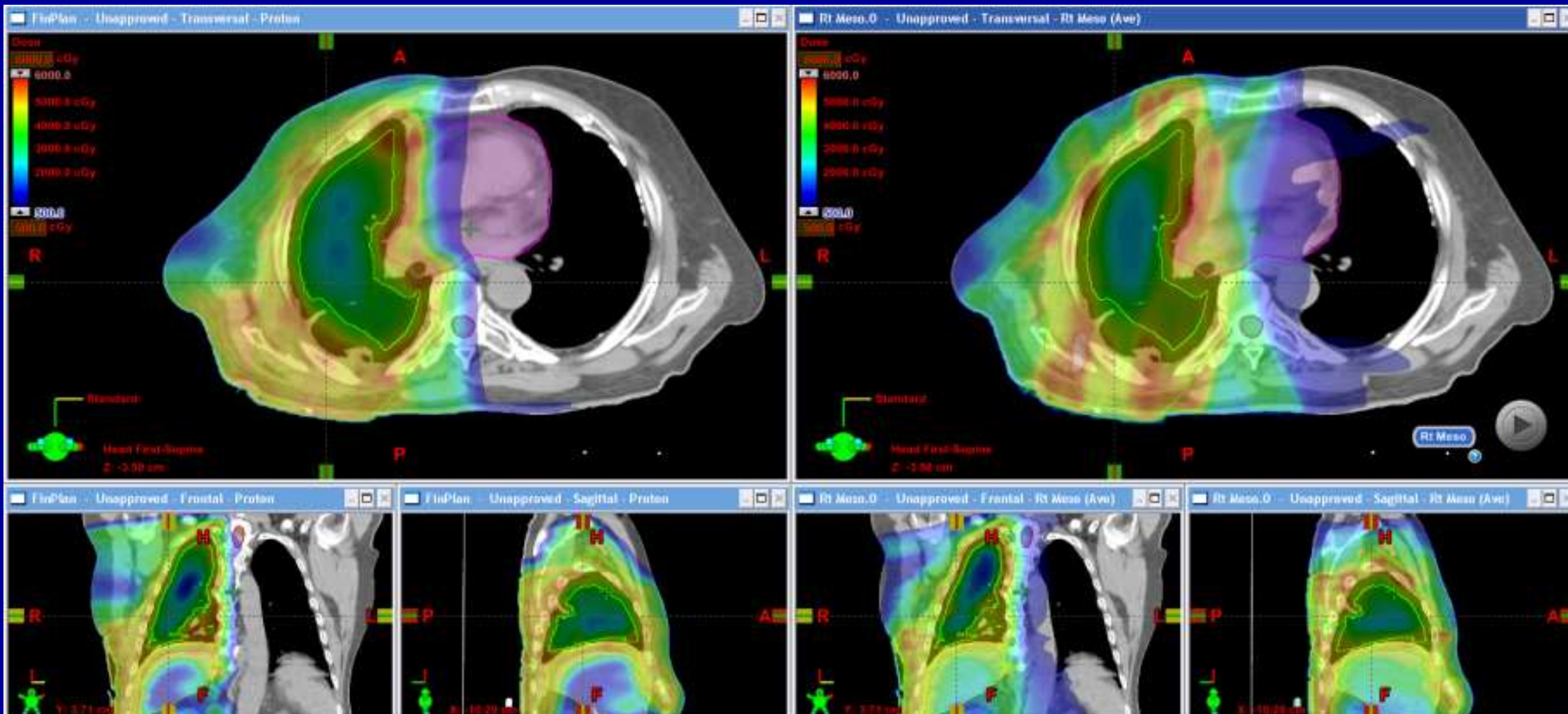


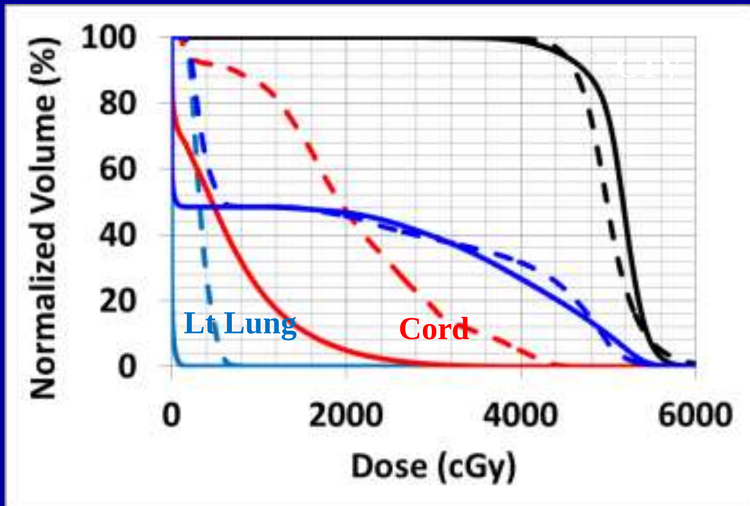


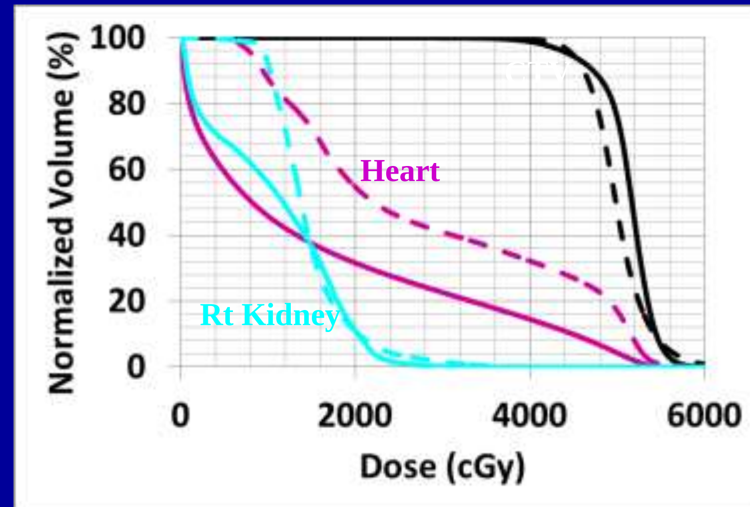


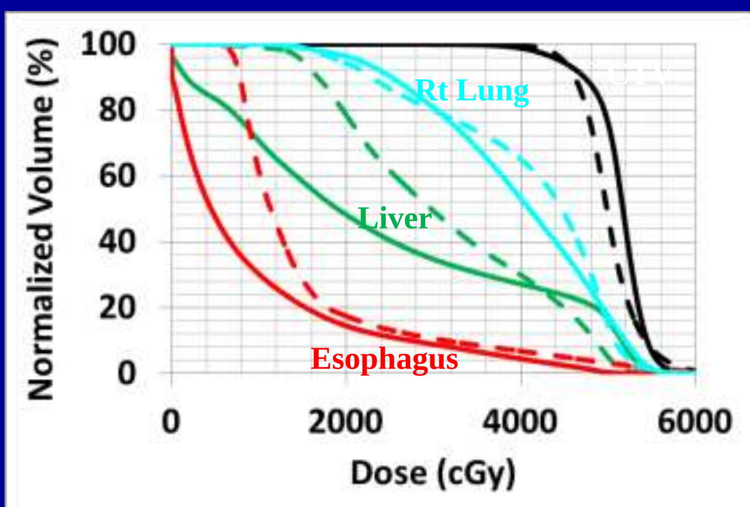
- DVH data indicated the very significant advantage of IMPT on large size tumors.

Solid: IMPT and dashed: IMRT


FinPlan - Unapproved - Transversal - Proton
Rt Meso.0 - Unapproved - Transversal - Rt Meso (Ave)
6000.0
500.0
A
R
L
P
Rt Meso
FinPlan - Unapproved - Frontal - Proton
FinPlan - Unapproved - Sagittal - Proton
Rt Meso.0 - Unapproved - Frontal - Rt Meso (Ave)
Rt Meso.0 - Unapproved - Sagittal - Rt Meso (Ave)
H
F


Normalized Volume (%)
100
80
60
40
20
0
0
2000
4000
6000
Dose (cGy)
Lt Lung
Cord


Normalized Volume (%)
100
80
60
40
20
0
0
2000
4000
6000
Dose (cGy)
Heart
Rt Kidney


Normalized Volume (%)
100
80
60
40
20
0
0
2000
4000
6000
Dose (cGy)
Rt Lung
Liver
Esophagus

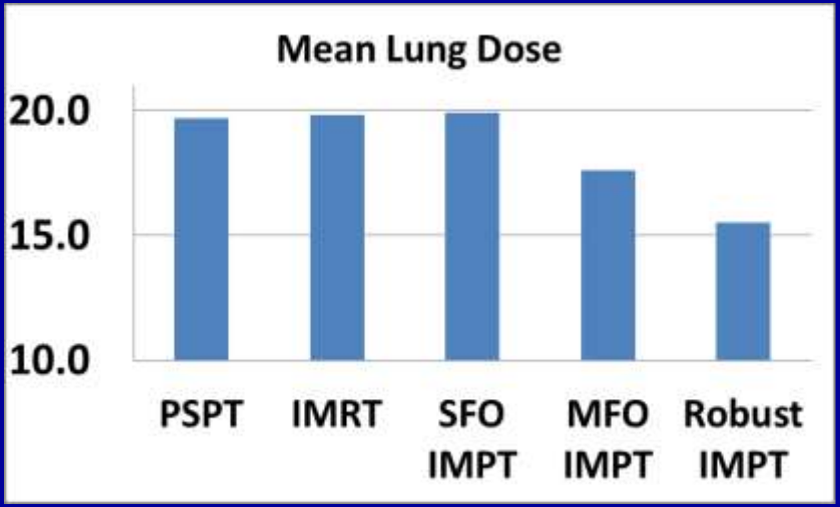
IMPT

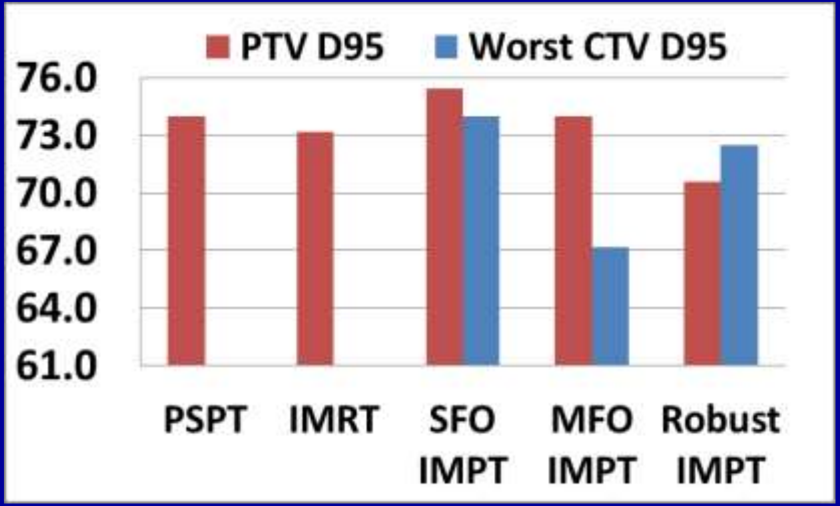
IMRT

QA/QC of Treatment Plan

- Treatment planner is still in the **learning curve** period of designing the high quality IMPT plan.
- Relatively, IMRT plan design starts to be mature and plan quality and consistency are improved significantly
  - Recent work on class solution (MDACC), database driven QC tool (JHU, Duke), automatic planning (MDACC, JHU, Duke) greatly improves the quality of IMRT plan.
  - In MDACC, proton dosimetrists are facing peer photon dosimetrist’s competition: proton/IMPT plan will not always win.

Treatment Plan QA/QC





- 5 plans were evaluated in proton planning clinic. The robust MFO IMPT was selected for patient treatment.
- 4.4 Gy reduction of mean lung dose was considered to be very clinically significant.
- Plan quality of initial SFO IMPT plan is comparable to PSPT and IMPT plan: we are still in the learning curve period of IMPT planning process

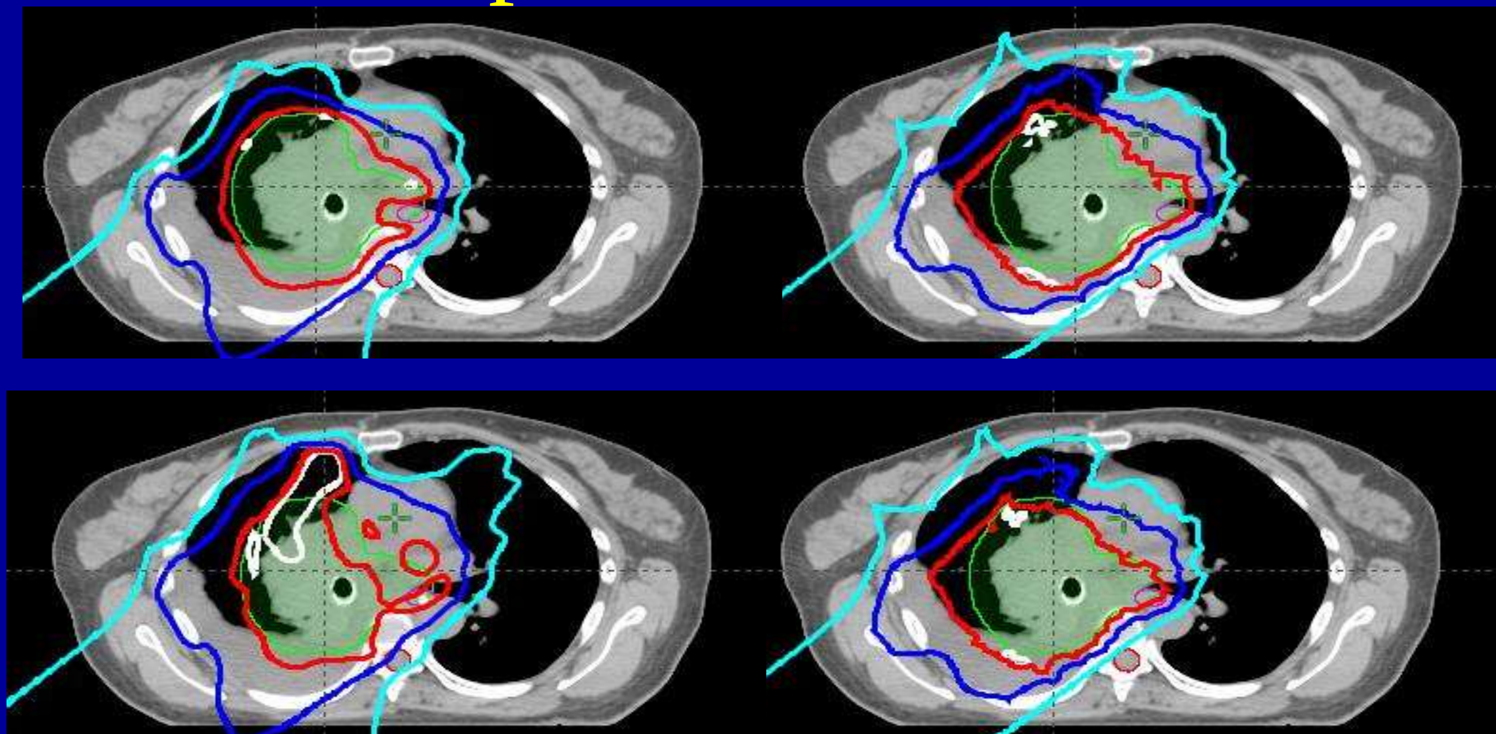
Treatment planning: robust optimization

- Plan is robust against setup and range uncertainties
- Do not use “PTV” but optimize “worst case” CTV
  - Added benefit: smaller dynamic margin leading to better normal tissue sparing

Optimization model: robust optimization

Nominal position

3.5% range overshoot



Nominal

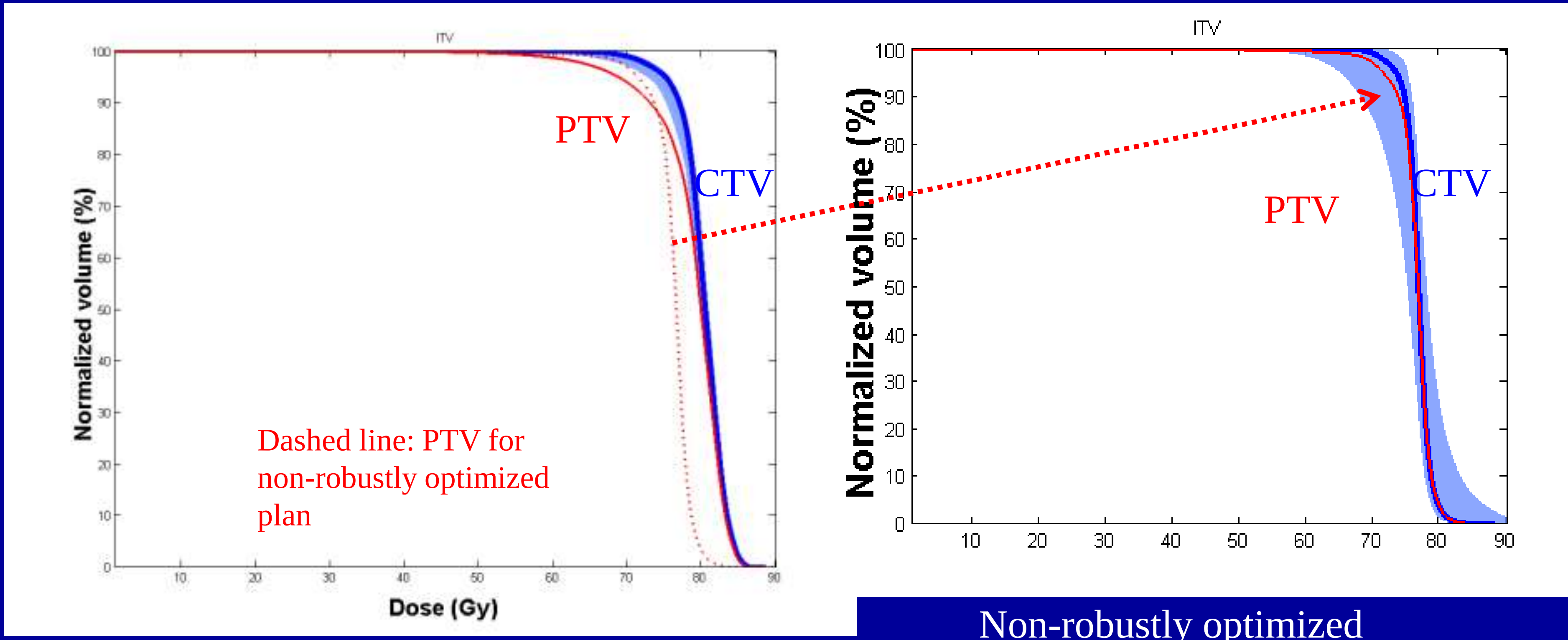
Green color wash: ITV

Robustly optimized plan

Liu W, Zhang X, Li Y, Mohan R. Robust Optimization of Intensity Modulated Proton Therapy. Medical Physics 39:1079, 2/2012.

Liu W, Li Y, Cao W, Li X, Zhang X. Influence of robust optimization in intensity-modulated proton therapy with different dose delivery techniques. Medical Physics. 39: 3089, 2012

“PTV” is not a good concept for IMPT



Robustly optimized plan

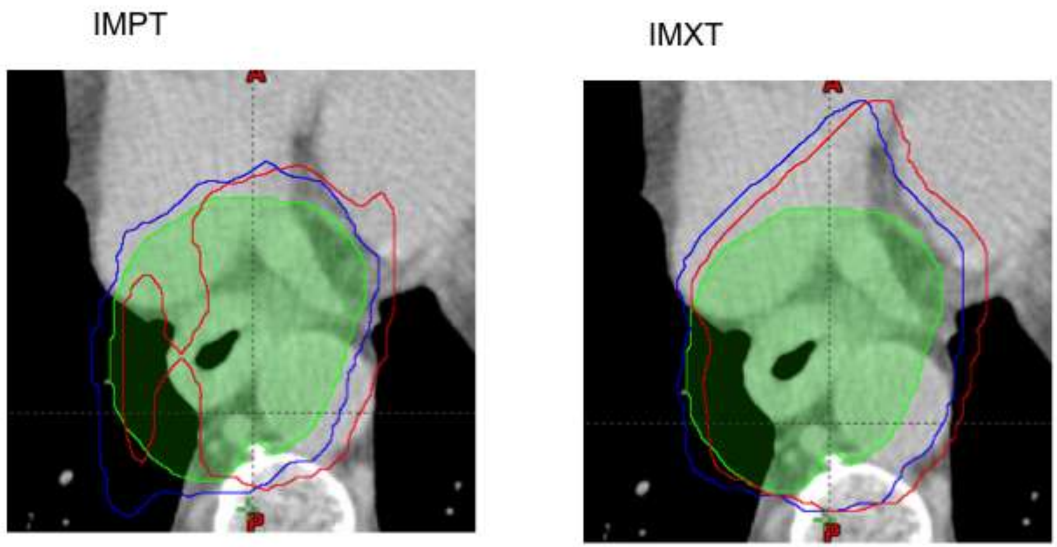
Non-robustly optimized plan

- **Better PTV coverage (dashed line) does not necessary mean better robustness of CTV coverage.**
- **worse PTV coverage but better robustness of CTV coverage leads to the better normal tissue sparing**

Robust evaluation method (principle)

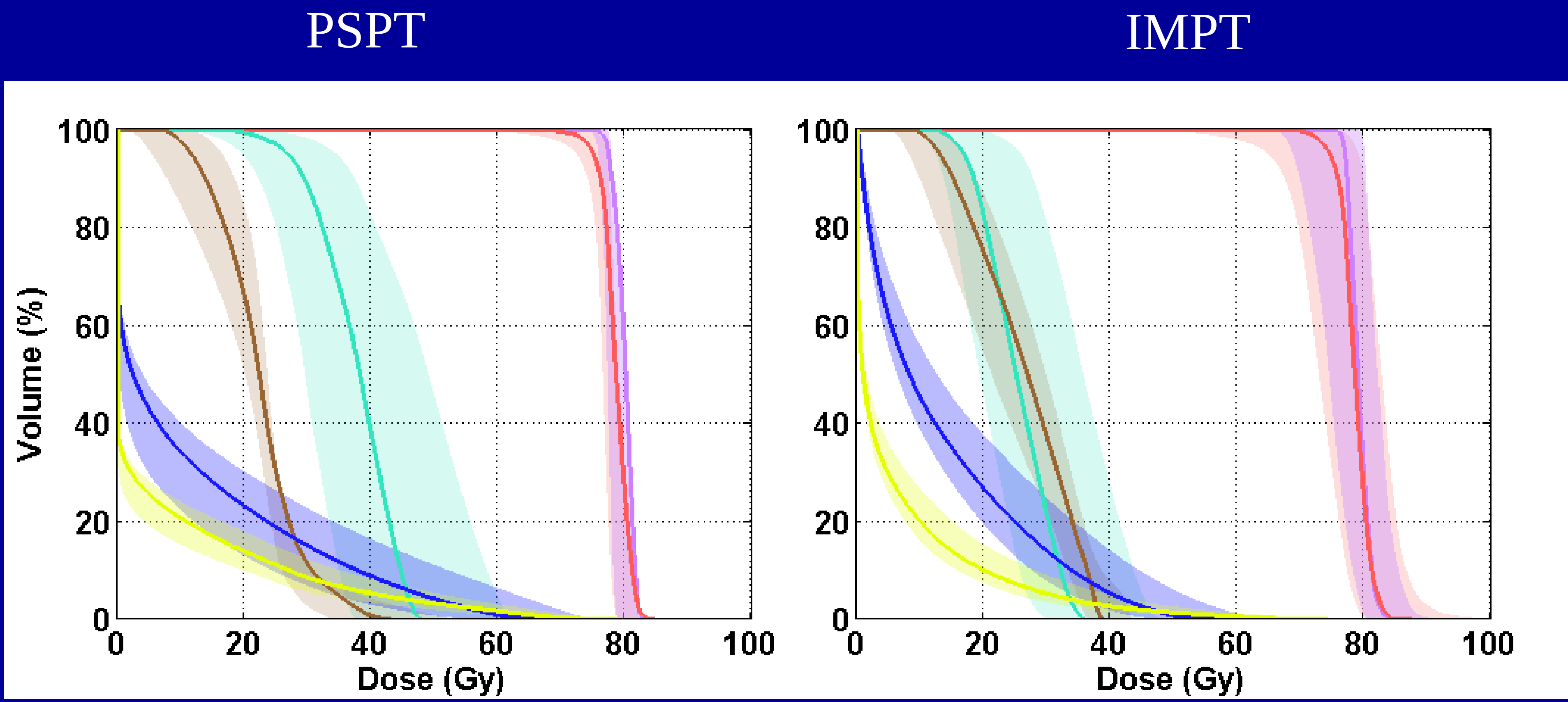
- For every scenario of perturbation/uncertainty, the dose needs to be recalculated
- Range uncertainty needs to be evaluated

Dose distribution symmetry broken under perturbation: patient example



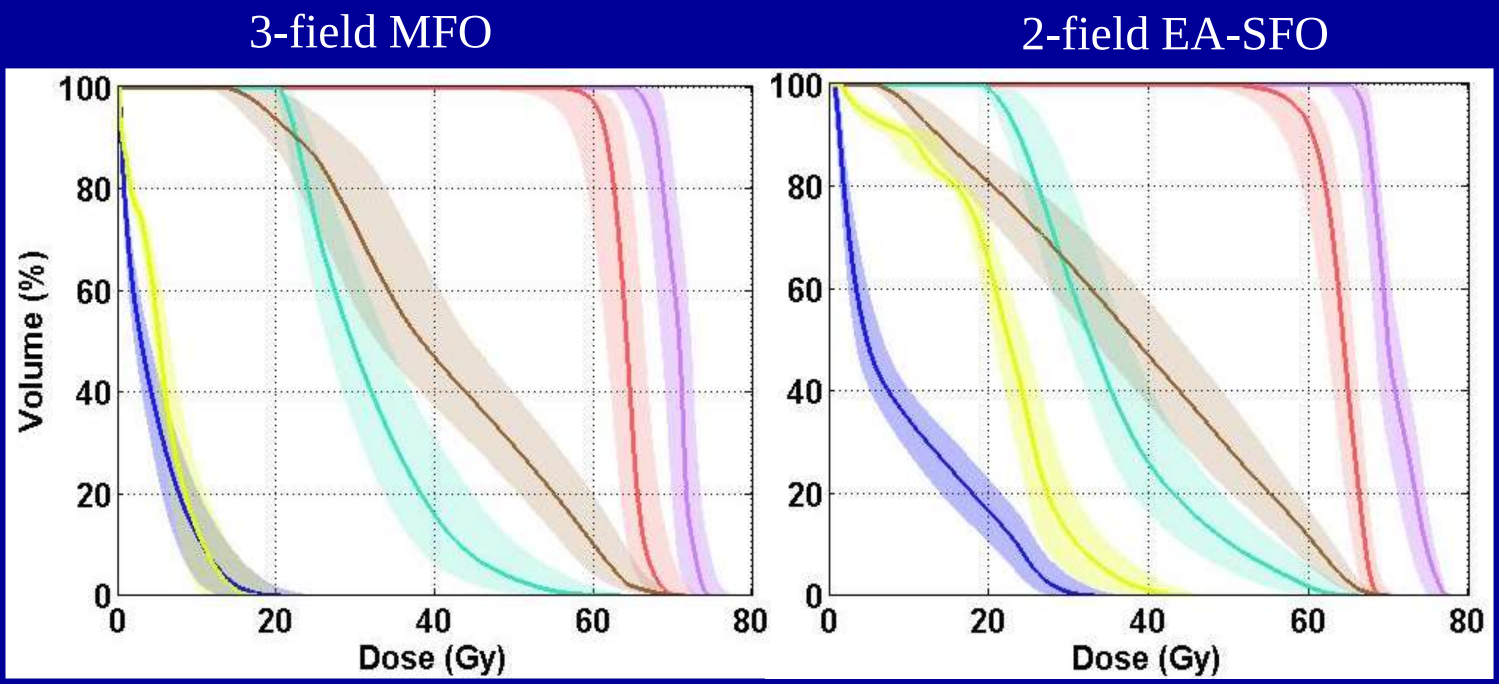
Blue: planed prescription iso-dose line; red: prescription iso-dose line if patient moves left 5mm.

Banded DVHs



GTV CTV Brainstem Left temporal lobe Optic chiasm Right optic nerve

Banded DVHs



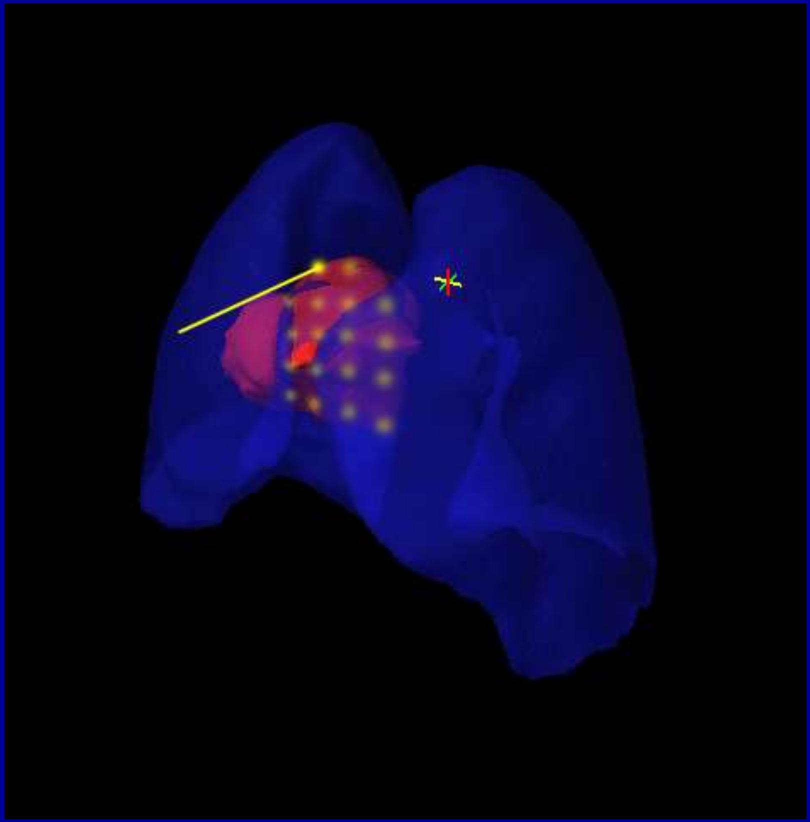
- The nominal plan of 2-field EA-SFO achieved target coverage that is close to 3-field MFO
- The 2-field EA-SFO plans yielded average band width reduction of 38.5% in the targets, indicating improved plan robustness

Experiences on robust evaluation

- SFO/PSPT plan are robust, we normally do not perform robust evaluation for SFO/PSPT patients
- We performed robust evaluation for all MFO IMPT plans

Motion management: Interplay Effects:

- Two dynamic motions interplay:
  - Dynamic scanning spot delivery
  - breathing motion



Motion analysis

- Due to interplay effects for scanning beam, IMPT plans are more sensitive to tumor motion than PSPT plans. Treating patient with large motion is not ready using scanning beam at this time.
  - **Motion less than 5mm is considered acceptable**
- A patient specific 4D water equivalent thickness (WET) motion analysis software developed by Peter Park is also used for motion analysis.
  - **It is also acceptable if more than 80% of range uncertainties caused by motion can be accommodated by 5mm margin**

Only treat the patient with motion less than 5mm

We really want to treat more patients using IMPT techniques

Liao,Zhongxing
ent: Mon 10/29/2012 4:30 PM
o: Zhang,Xiaodong; Yang,Claire Chunyi; Ukegbu,Lerma T
c: Korulla,Aleyamma; Koshy,Suja M; Zhu,Xiaorong Ronald; Lin,Steven Hsesheng

We will treat this patient with pspt to 66 Gy as jacques has planned. She will remain on 2008-0133 group 3.
Thank you all.

From: Zhang,Xiaodong
Sent: Monday, October 29, 2012 04:03 PM
To: Liao,Zhongxing; Yang,Claire Chunyi; Ukegbu,Lerma T
Cc: Korulla,Aleyamma; Koshy,Suja M; Zhu,Xiaorong Ronald
Subject: RE: Hahn 756876 final decision 2011-1058

I attach you the motion analysis report for this patient. Significant motions are detected for this patient. From our physics point of view, it is not ready for us to recommend to treat this patient using MFO IMPT.
I guess it is your discretion to make the final decision on the treatment of this patient.

Xiaodong

It is not recommended based on motion analyss

From: Liao,Zhongxing
Sent: Monday, October 29, 2012 2:12 PM
To: Zhang,Xiaodong; Yang,Claire Chunyi; Ukegbu,Lerma T
Cc: Korulla,Aleyamma; Koshy,Suja M
Subject: Re: Hahn 756876 final decision 2011-1058

Hope we can pit her on trial. Thanks

Hope we can put her on trial

From: Zhang,Xiaodong
Sent: Monday, October 29, 2012 02:06 PM
To: Liao,Zhongxing; Yang,Claire Chunyi; Ukegbu,Lerma T
Cc: Korulla,Aleyamma; Koshy,Suja M
Subject: RE: Hahn 756876 final decision 2011-1058

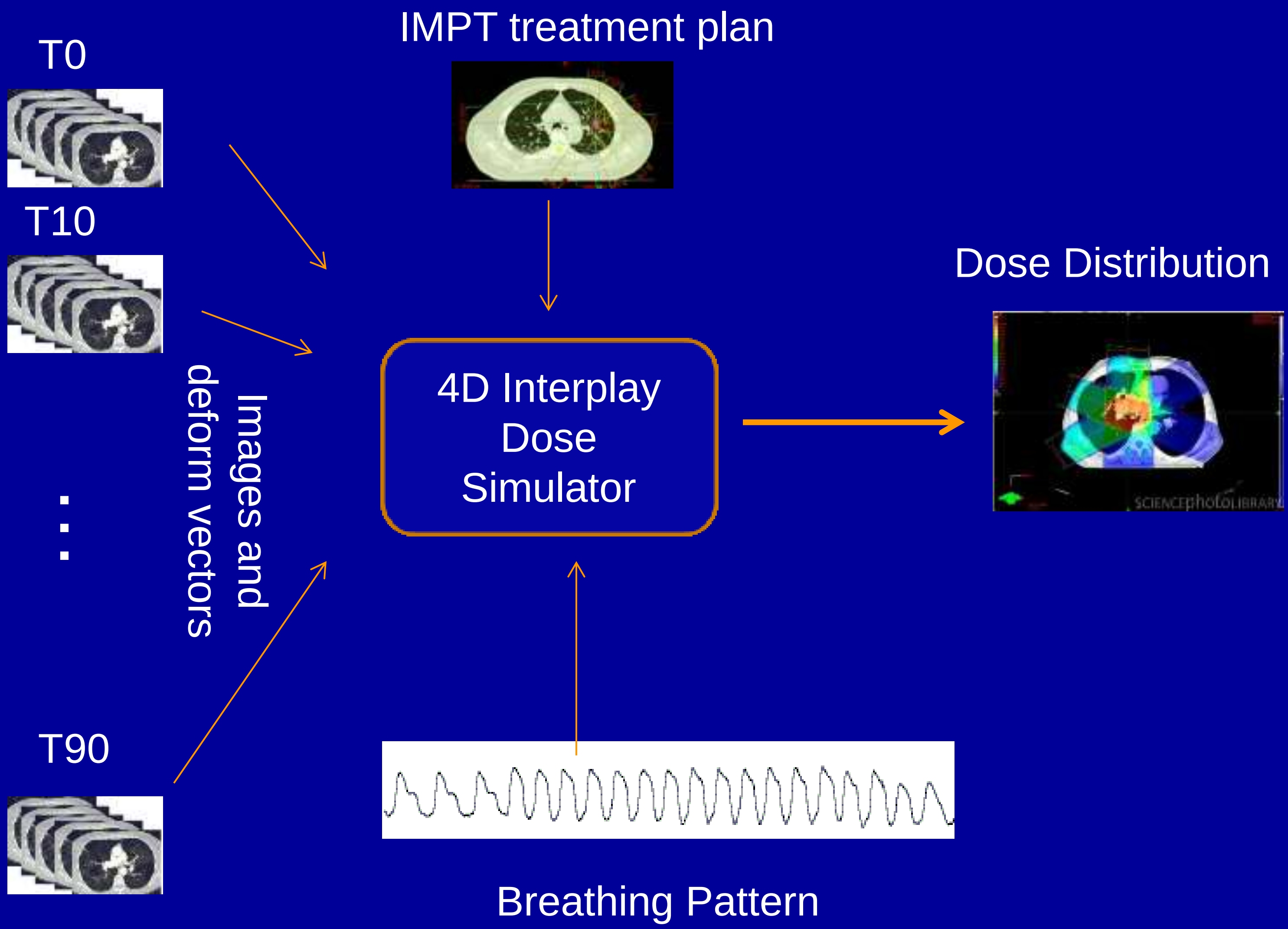
We are waiting for the WET analysis report. We physics team now makes our recommendation partly based on that report. I will inform you as soon as possible.

Xiaodong

From: Liao,Zhongxing
Sent: Monday, October 29, 2012 2:04 PM
To: Zhang,Xiaodong; Yang,Claire Chunyi; Ukegbu,Lerma T
Cc: Korulla,Aleyamma; Koshy,Suja M
Subject: Re: Hahn 756876 final decision 2011-1058

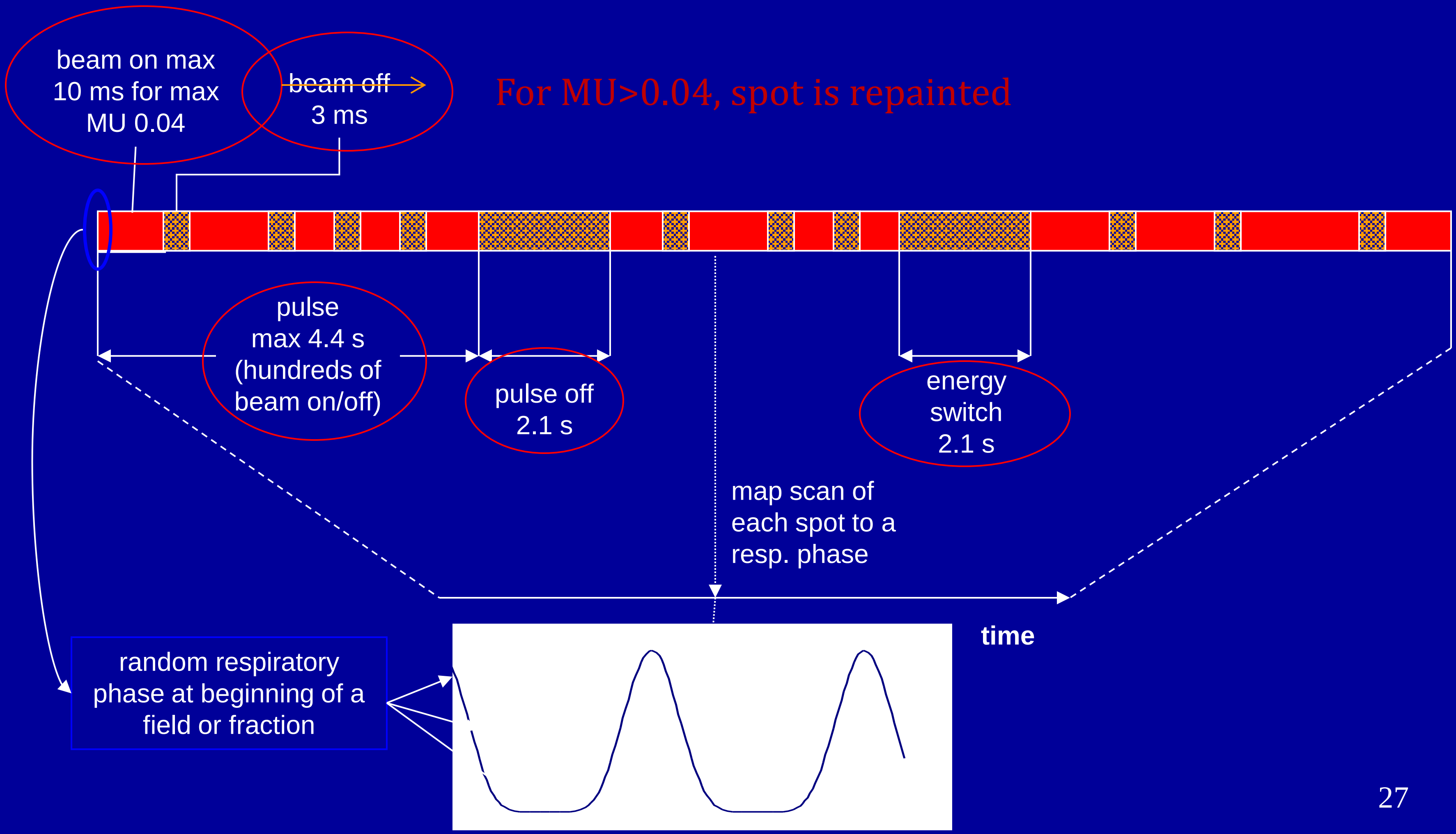
That is too bad. Can she still be treated with impt sib off protocol?

4D Interplay/dynamic Dose



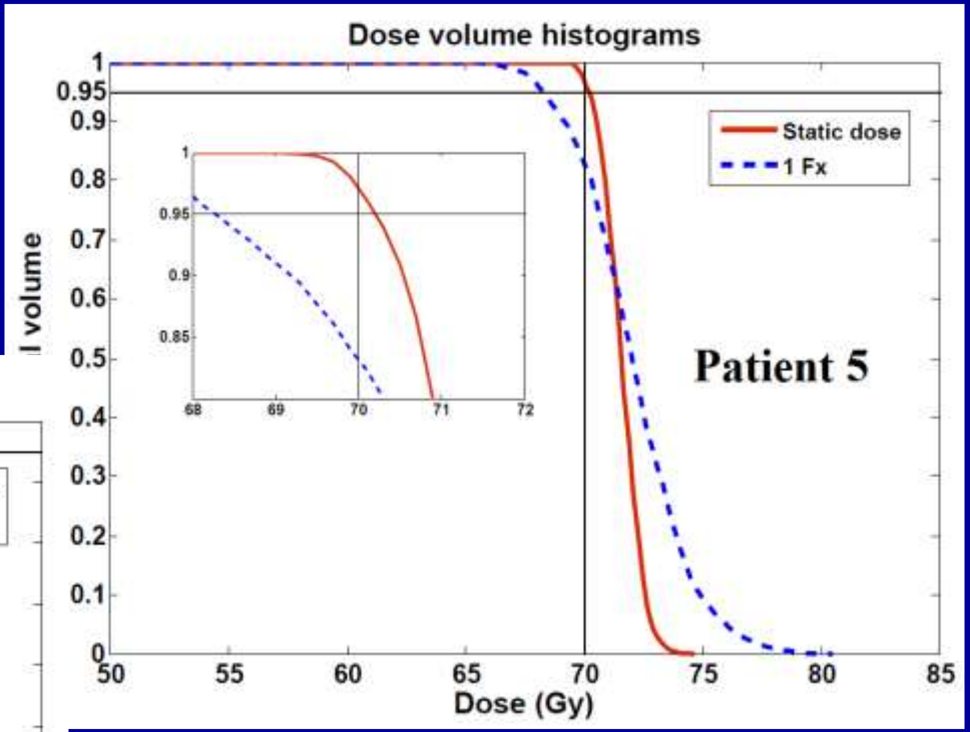
Time Stamps in the Spot Scanning

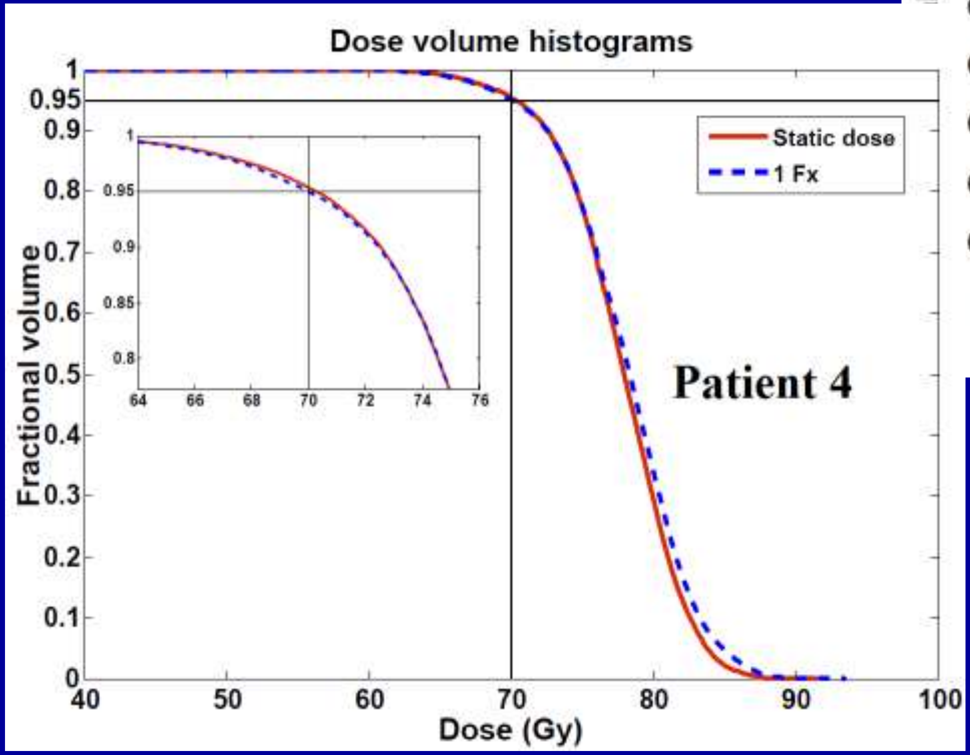
For MU>0.04, spot is repainted



"1FX dynamic dose" as a surrogate to evaluate the robustness the plan against interplay effects

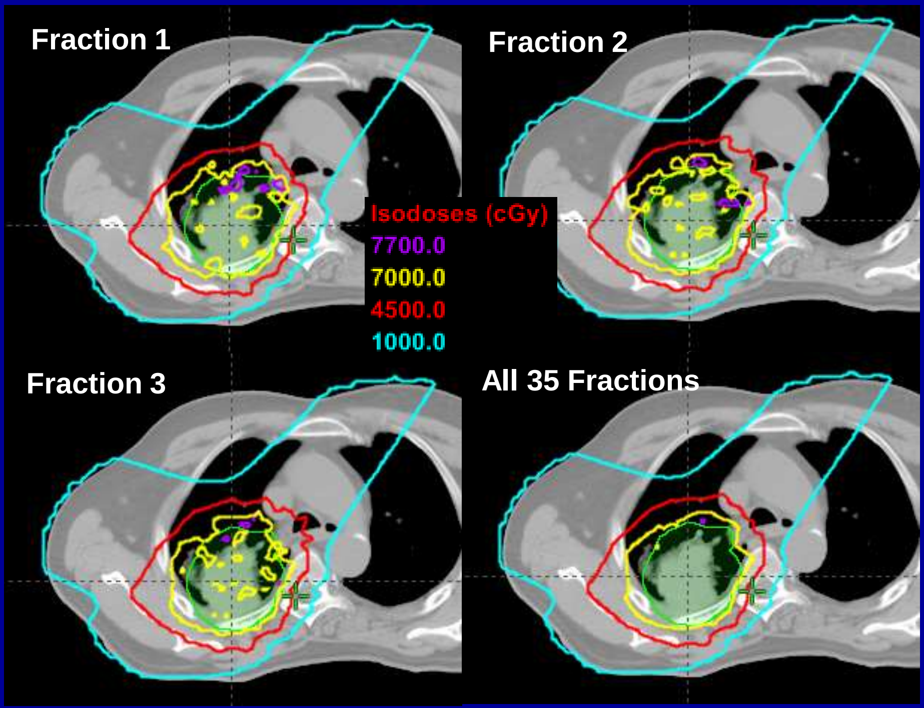
volume = 358.24 cc
motion = 0.46 cm

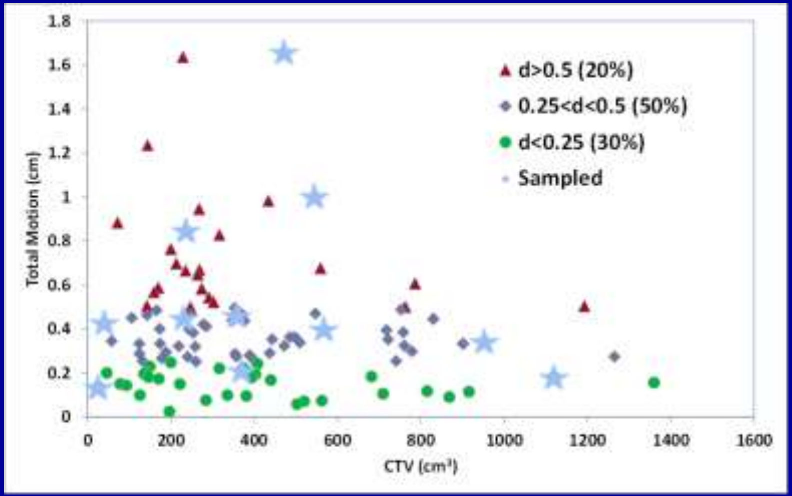




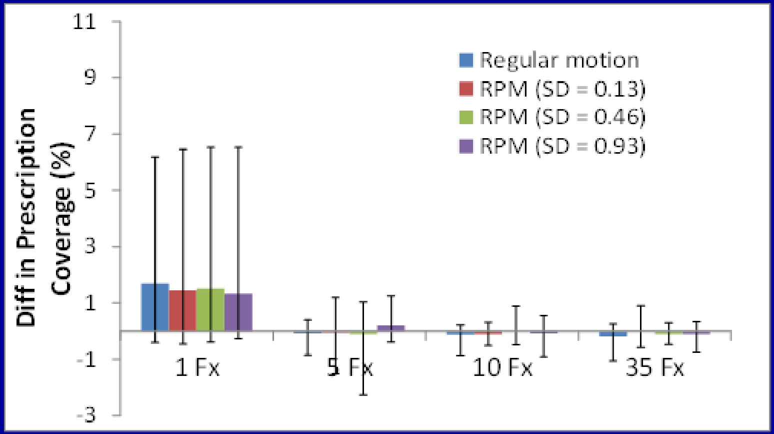
volume = 40.38 cc
motion = 0.43 cm

“washed out” effects with multiple fractional delivery

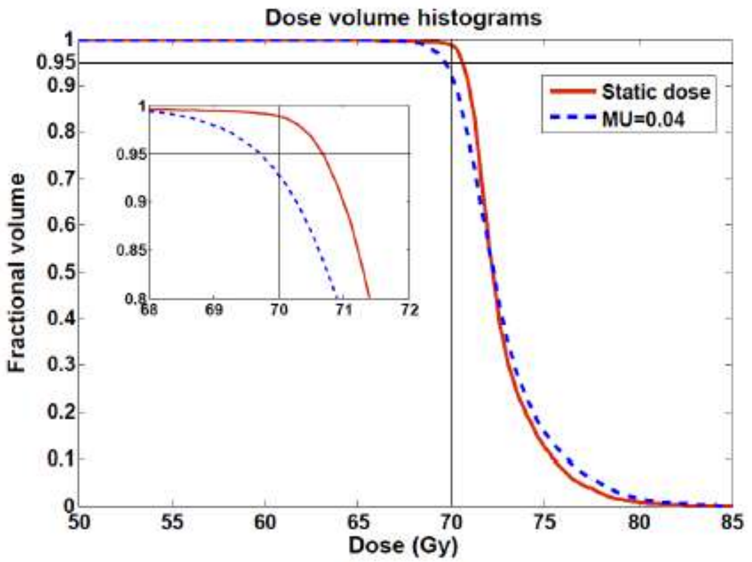




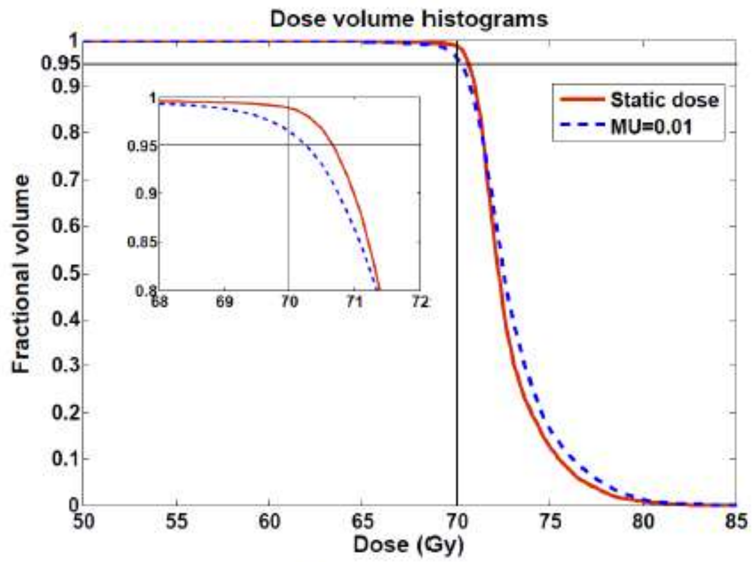
11 patients sampled from 110 patients



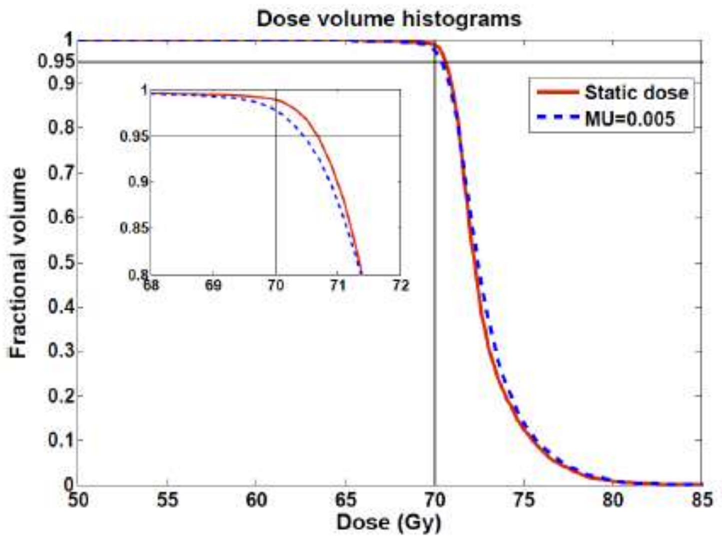
Intra-fractional iso-layer repainting



(a) MU=0.04



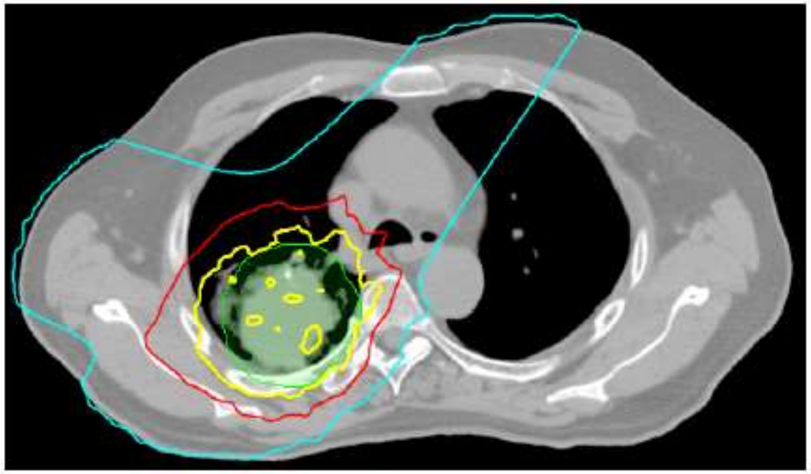
(b) MU=0.01



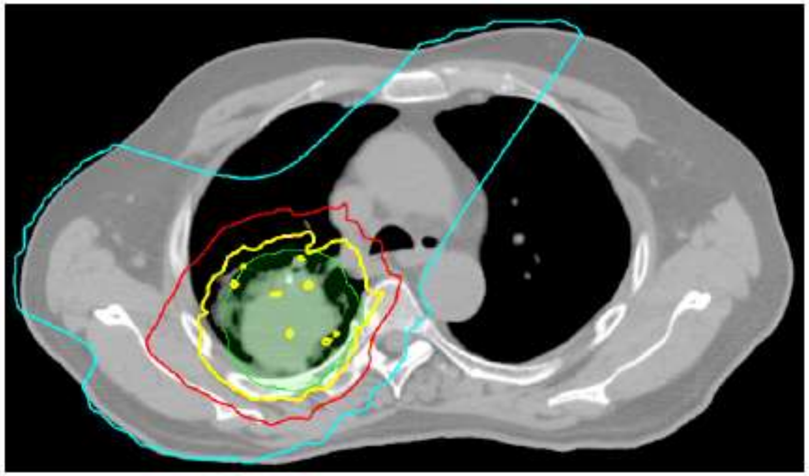
(c) MU=0.005

- Reduce the max MU for each spot $\rightarrow$ Effectively increase number of isolayer repainting and treatment delivery time

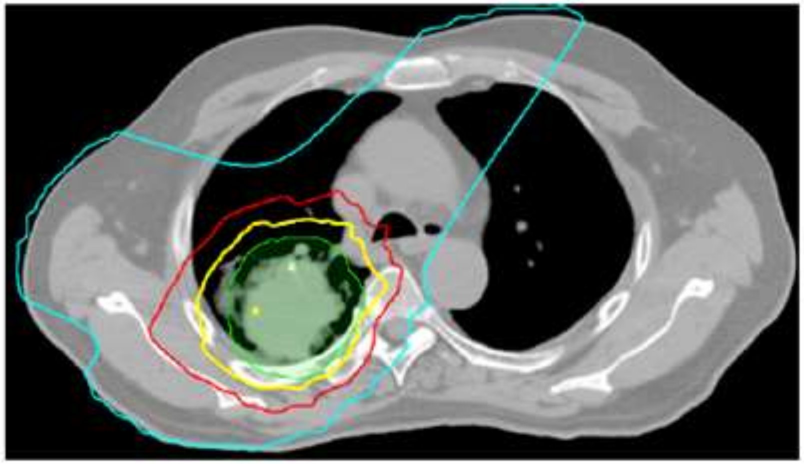
Reduce the max MU for each spot: iso-layer repainting



(a) MU=0.04



(b) MU=0.01

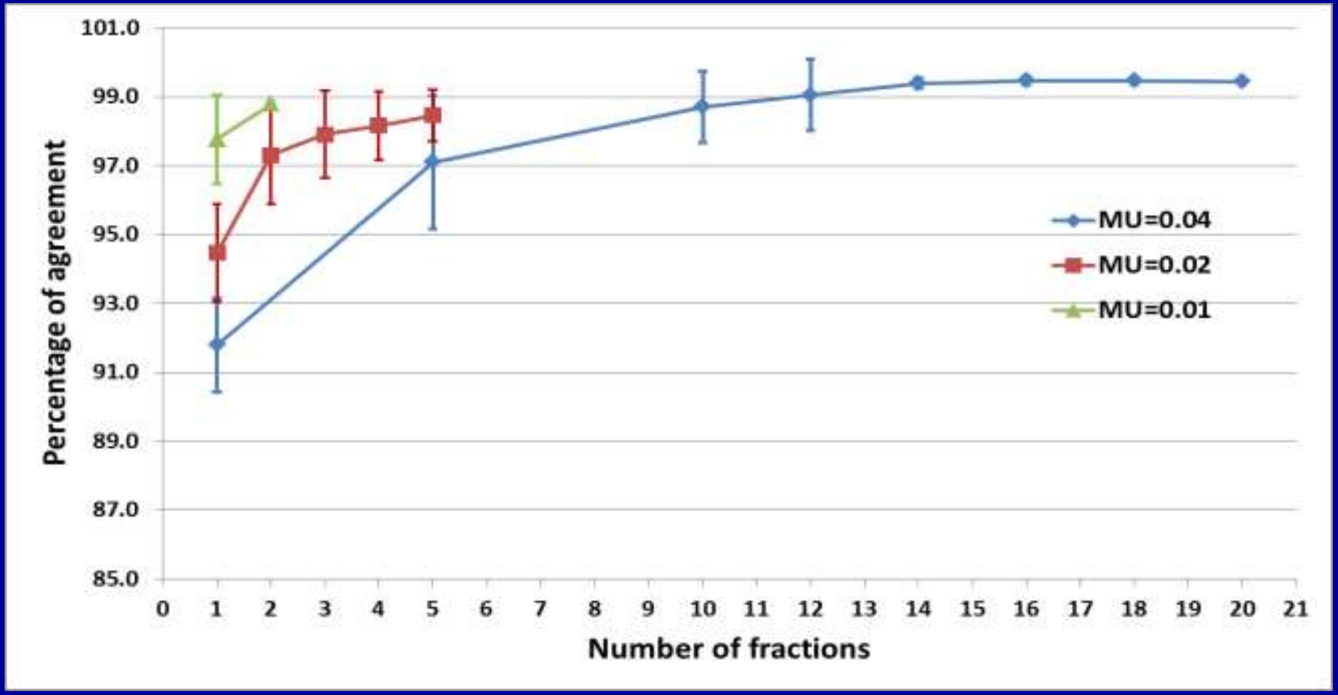


(c) MU=0.005

- These results are consistent with a recent general study – Increase treatment time will help!

Experimental Validation

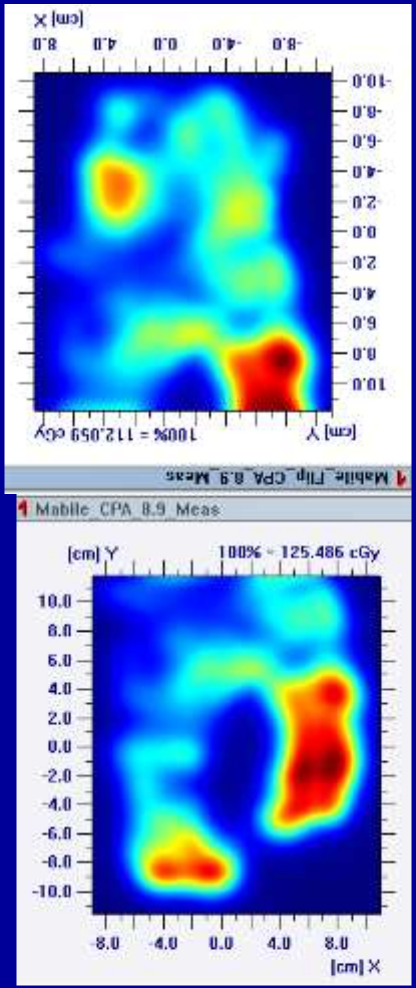
- Wash-out effects of Multiple fractions
- Intra-fractional iso-layer repainting

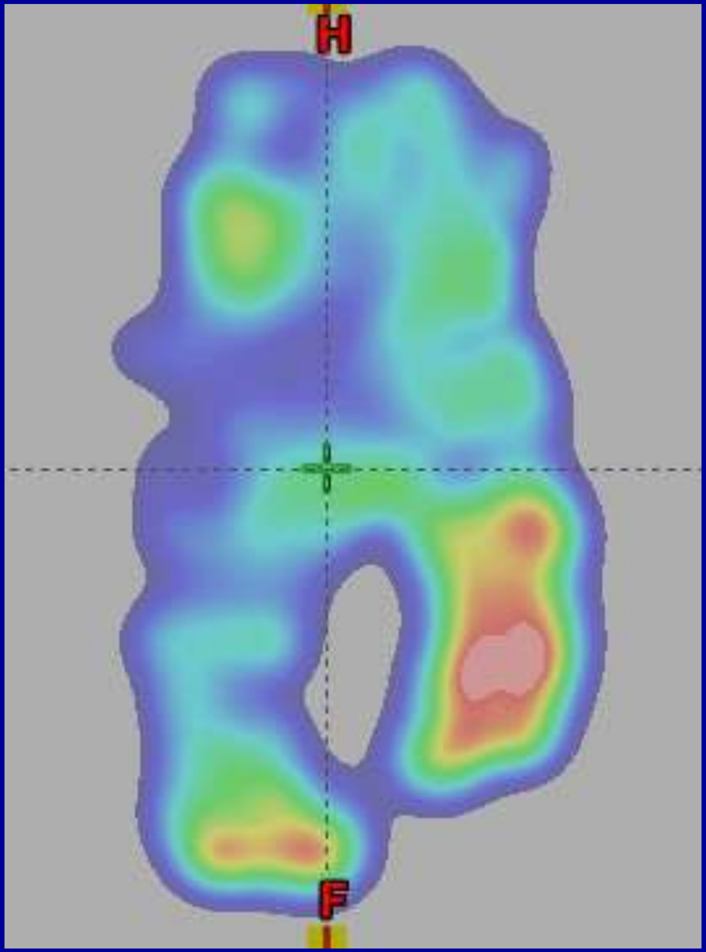


Patient Specific QA

- Mosaiq measurement
  - End-to-end data transfer
  - Verifying beam steering
  - Uploading the required bending magnet fields
  - Verifying dose to the center of the target
- Depth measurement
  - Several 2-D dose verification at 2 to 5 different depths for each field to verify the 3D dose distribution.
- Total time per patient: 8 hours for MFO IMPT

For very large field, two measurements were done to obtain the dose distribution of the full plane

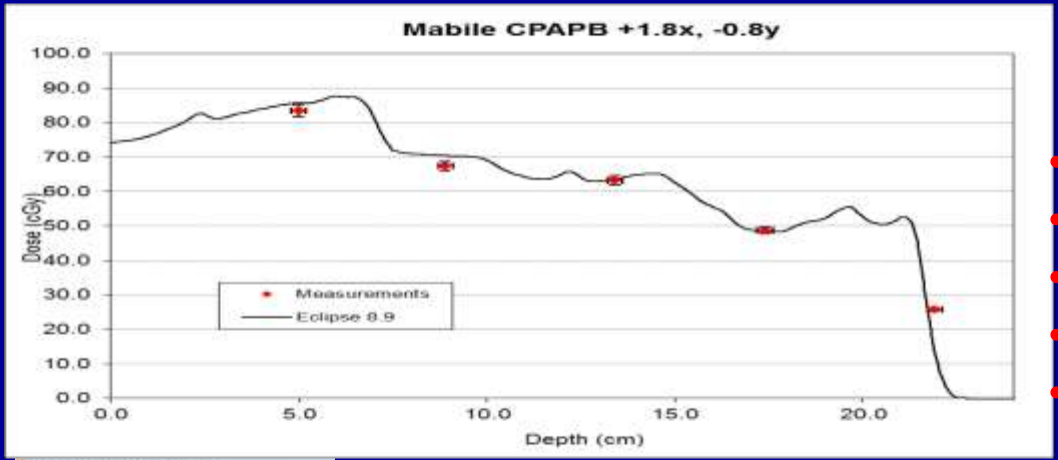




Two measurements using Matrix for this plane

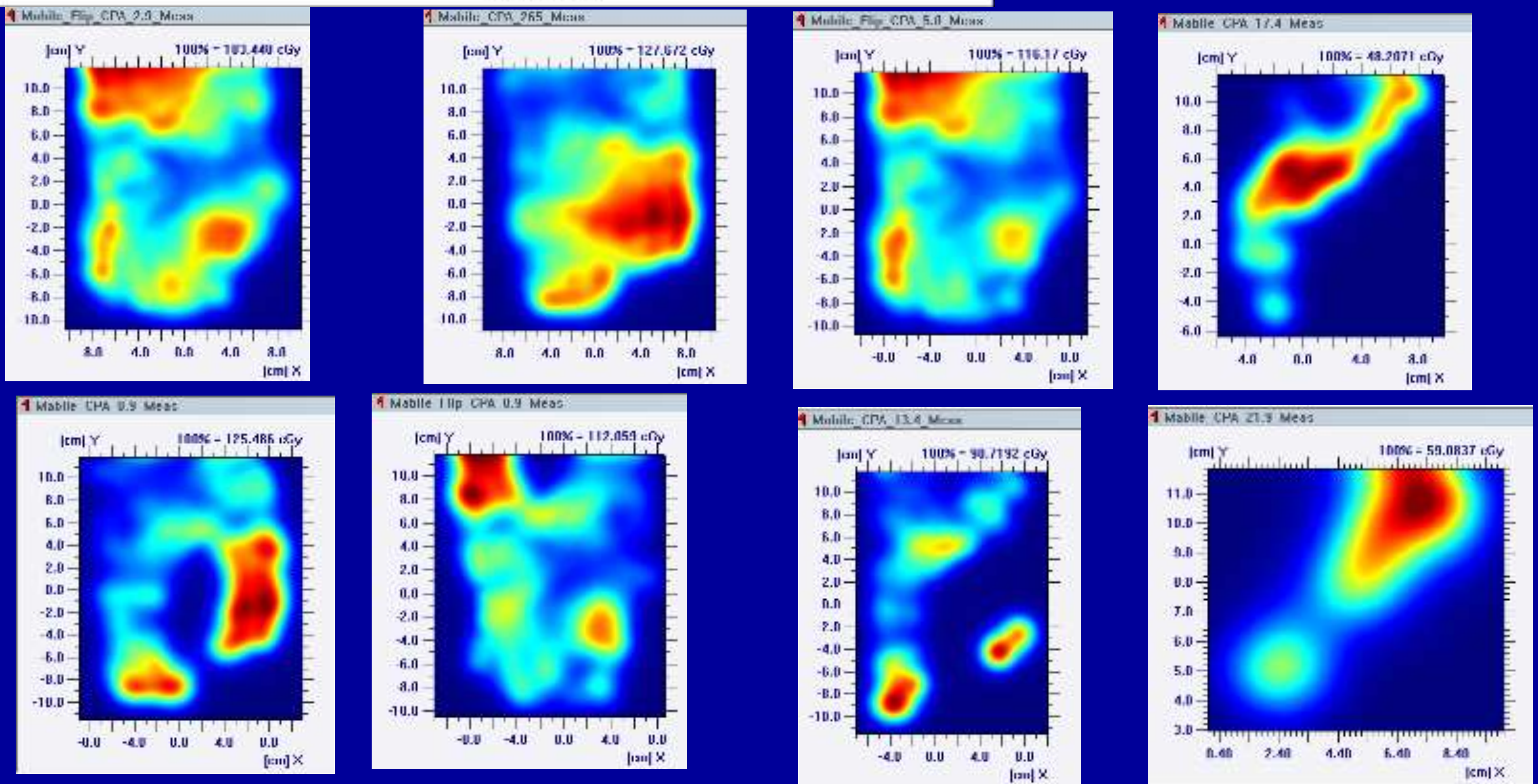
Dose plane in TPS

QA challenge

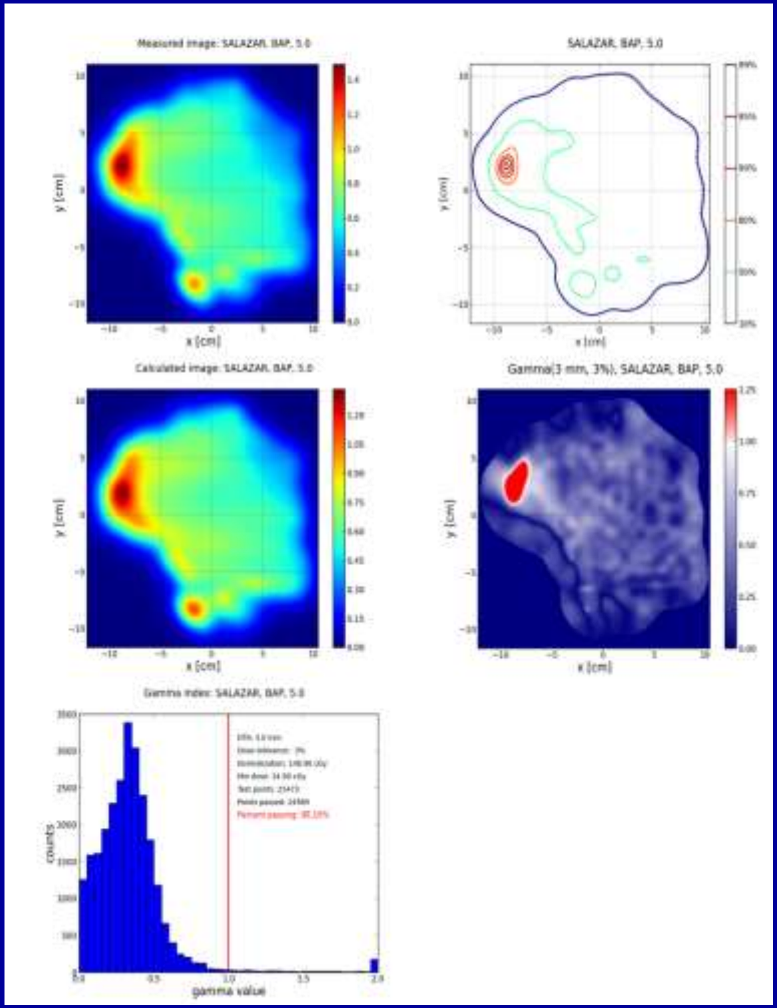


QA	6/25/2013	23:43	1Fld		
		23:43	AAPPE	QA	299.2 MU
QA	6/26/2013	0:12	3Flds		
		0:12	BLPPE	QA	233.9 MU
		0:18	CPAPE	QA	401.9 MU
		0:40	DLAPE	QA	406.2 MU

- 10 minutes for one measurement
- 8 measurement for one beam
- 4 beam total
- 320 minutes measurement time
- 2 night QA time which used Machine



QA result for one beam



- 98% percent of region passed 3mm/3% criteria
- Small region (2%), 9% difference between calculation and measurement

Physics QA

Salazar Mosaiq Measurement Analysis

Kerr,Matthew D

Sent: Tue 4/9/2013 6:26 AM

To: Zhang,Xiaodong; Poenisch,Falk; Zhu,Xiaorong Ronald

Cc: Mackin,Dennis Stephen; Taylor,Michael B

Show stopper

There are a few problems with the Mosaiq measurements for Salazar, who is scheduled to start tonight at 8:30PM in G3. The first issue, which Falk might consider to be a "show stopper" at first glance, is that the dose difference at Dmax for the BAPPB field is 9.2%. The second issue is that the gammas at 2%/2mm for fields ALPPB and CLAPB are somewhat low at 82.01% and 77.04%, respectively. The third issue is that the point-dose measurements extracted from the Mosaiq measurement planes are all about 4 percent higher than the depth dose-curves.

It's not all bad though. The gammas at 3%/3mm for all three fields are in the high 90 percentiles. Also, it appears the only place field BAPPB doesn't agree well is in close proximity to Dmax. In fact, BAPPB has the highest 2%/2mm gamma of the three fields at 95.89%. The dose difference at the central axis is 3.4%

	ALPPB	BAPPB	CLAPB
Diff (%)	1.0%	9.2%	0.5%
Histogram Pass Percent (3%/3mm)	99.34%	98.67%	97.97%
Histogram Pass Percent (2%/2mm)	82.01%	95.89%	77.04%

Since this is the last patient scheduled to be treated today for all of PTC, I could do the depth measurements for field BAPPB and analyze them before the patient gets treated. It would take about an hour and a half, and the treatment would need to be pushed back to 10pm. Otherwise, the depth measurements for this patient will be done tonight after treatment.

I exported the ASCII files and put them in the patient folder. I also sent the verification plan to HPlusQA. If Dennis has time today, he can see how the HPlusQA Mosaiq measurement planes compare.

- The physics QA measurement was performed during midnight by our physicist colleagues and the Mosaiq measurement results were sent to physicists at early morning (6:26 AM).
- There is "large" discrepancy between TPS calculation and measurement

QA measurements done Monday/Tuesday
Midnight and results was sent to us 6:26 AM
Tuesday morning, 04/09/13

Physicist’s recommendation and physician's response

RE: Salazar Mosaiq Measurement Analysis

Poenisch,Falk

Sent: Tue 4/9/2013 11:50 AM
To: Zhu,Xiaorong Ronald
Cc: Zhang,Xiaodong; Kerr,Matthew D; Mackin,Dennis Stephen; Taylor,Michael B

Ron,
We have further analyzed the Mosaiq measurements.
The problem arises that dmax for field B is around a depth of 5 cm.
The maximum dose in that depth is 148 cGy(RBE), whereas the measured data is 148 cGy,
i.e. there is a difference of 9% in that location.
In other areas, e.g. normalized to CAX, we have about 3% agreement (meas higher).
In my opinion the QA failed.
We have 2 options:
a) start pt’s Tx and work on new plan
b) postpone pt and work on new plan
In the meanwhile we can do the HP+ run.
I need to send Dr Nguyen feedback.

Thank

- Start pt’s TX and work on new plan
- Postpone pt and work on the new plan

Physicist’s recommendation and physician’s decision on 04/09/13

Sent: Tue 4/9/2013 2:05 PM
To: Poenisch,Falk
Cc: Zhu,Xiaorong Ronald; Zhang,Xiaodong; Kerr,Matthew D; Georges,Rola H

Please start pt tonight and work on another plan.

Xiadong, can you please let me know when you have a plan? The MFOorp plan was good but the dose to the stomach too high. Can you use that plan and reduce the dose to stomach to 50-54 Gy max?

Thanks
QN

New plan and new QA

Kerr,Matthew D

Sent: Wed 4/10/2013 11:20 AM

To: Zhang,Xiaodong; Poenisch,Falk; Zhu,Xiaorong Ronald

Cc: Taylor,Michael B; Holmes Jr,Charles E; Mackin,Dennis Stephen

The analysis of the Mosaiq-like measurements for the MFORBnew plan (the robust plan, but with a higher stomach dose) looks good. The only blemish is the 4.1% dose difference at Dmax for Field 1. The dose differences for the other two fields are low and the gammas are all great.

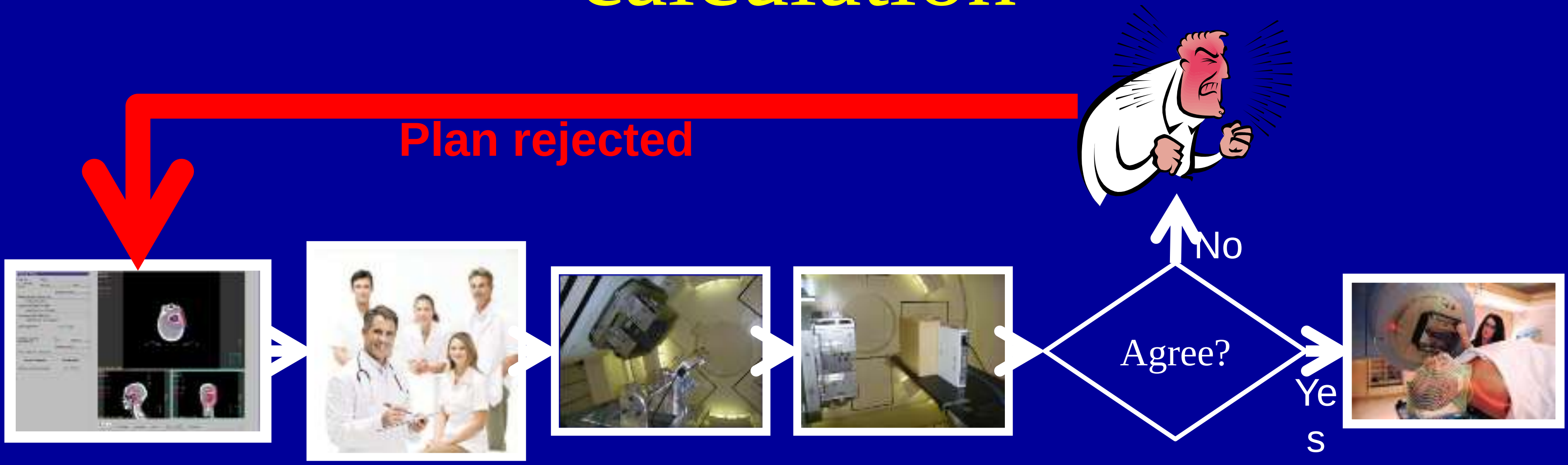
	Field 1	Field 2	Field 3
Diff (%)	4.1%	0.8%	1.1%
Histogram Pass Percent (3%/3mm)	99.59%	100.00%	100.00%
Histogram Pass Percent (2%/2mm)	94.02%	99.98%	98.66%

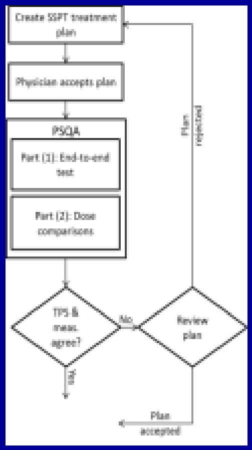
-Matt

- For the new plan, it is not perfect but it will pass our QA

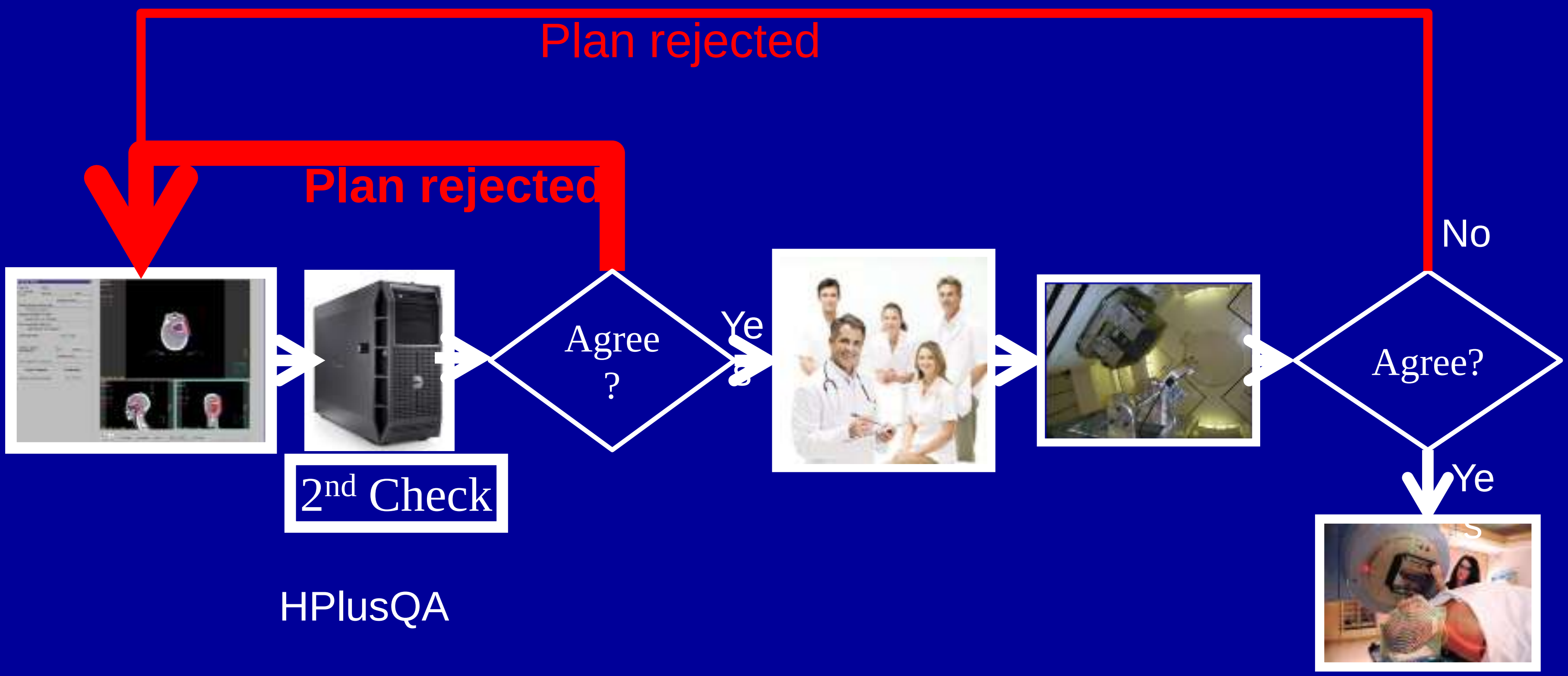
New possible plan and QA for not approved new possible plan on 04/09/2013

Current "QA" workflow to check the accuracy of the dose calculation

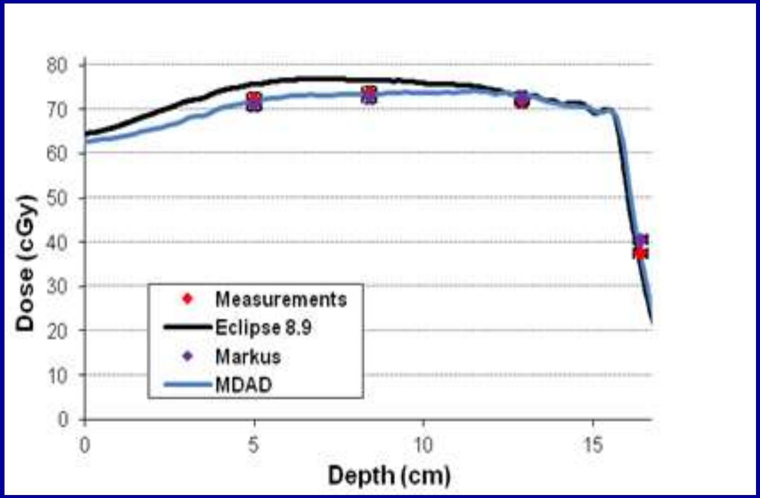


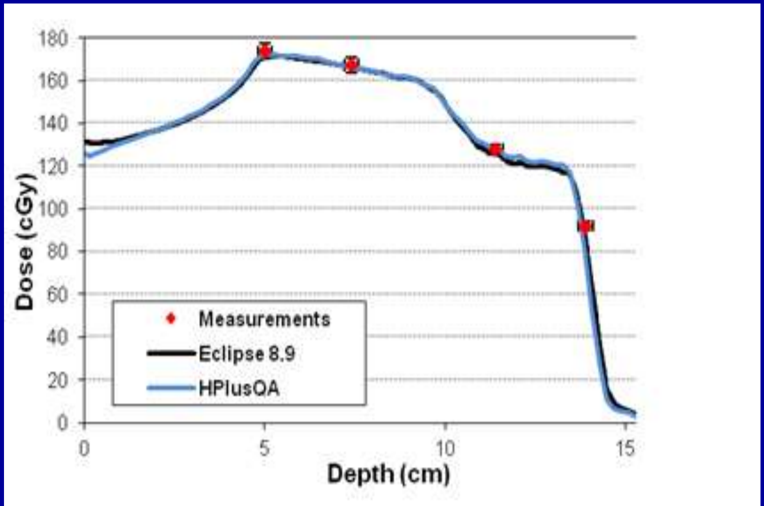


Propose workflow to address some “accuracy” issue



How HPlusQA is helping this process?

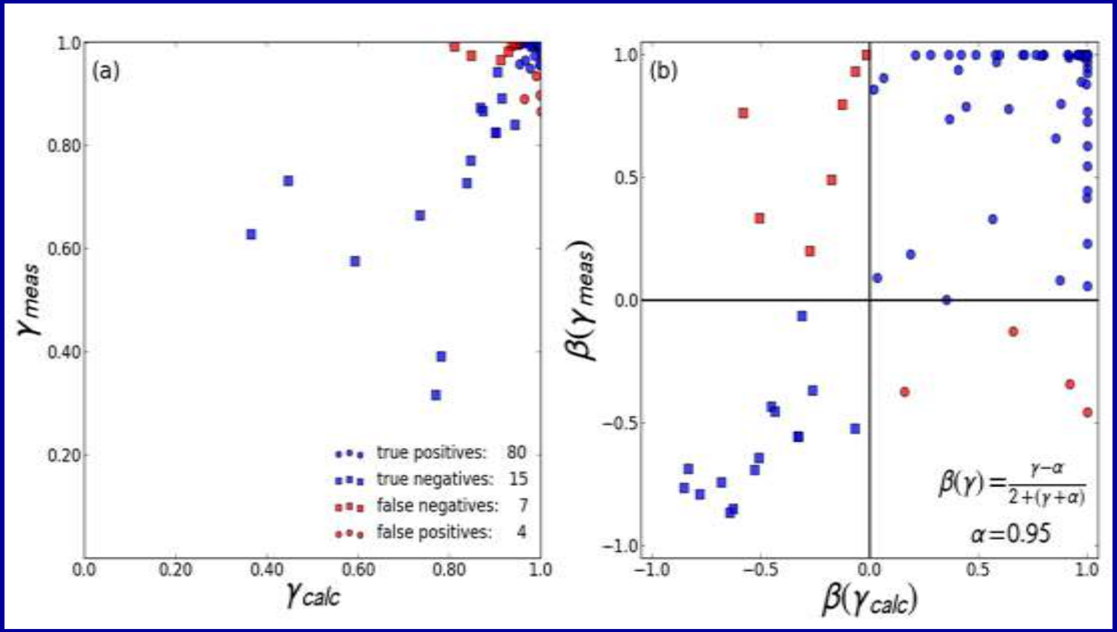




Disagreement with measurement was detected early for a patient: plan was rejected by HPlusQA before the measurement

Plan accepted by HPlusQA was also accepted by final physics QA measurement

HPlusQA

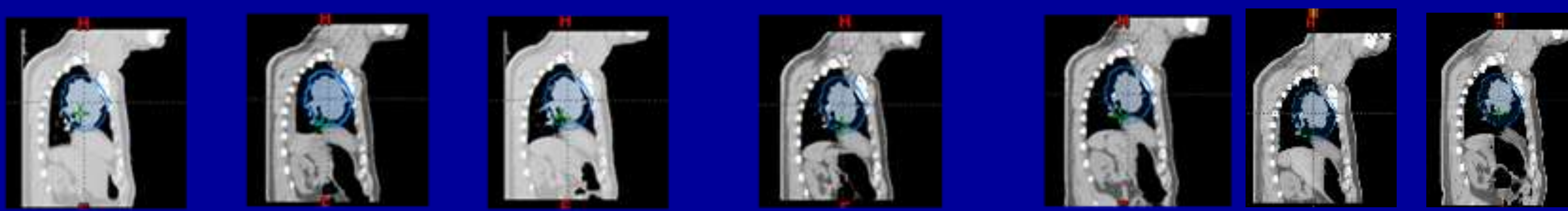


- 95 out of 106 success rate for HPlusQA

Adaptive planning/Verification

- Robust optimization did not consider anatomical change
- Weekly 4D CT to monitor change and redesign plan to adapt change
- It is very “Expensive” to do an adaptive plan now
  - New patient (new contours, new plan, new QA, new chart check …)
  - Proton has more trouble
    - We really see changes (from Dr. Chang)

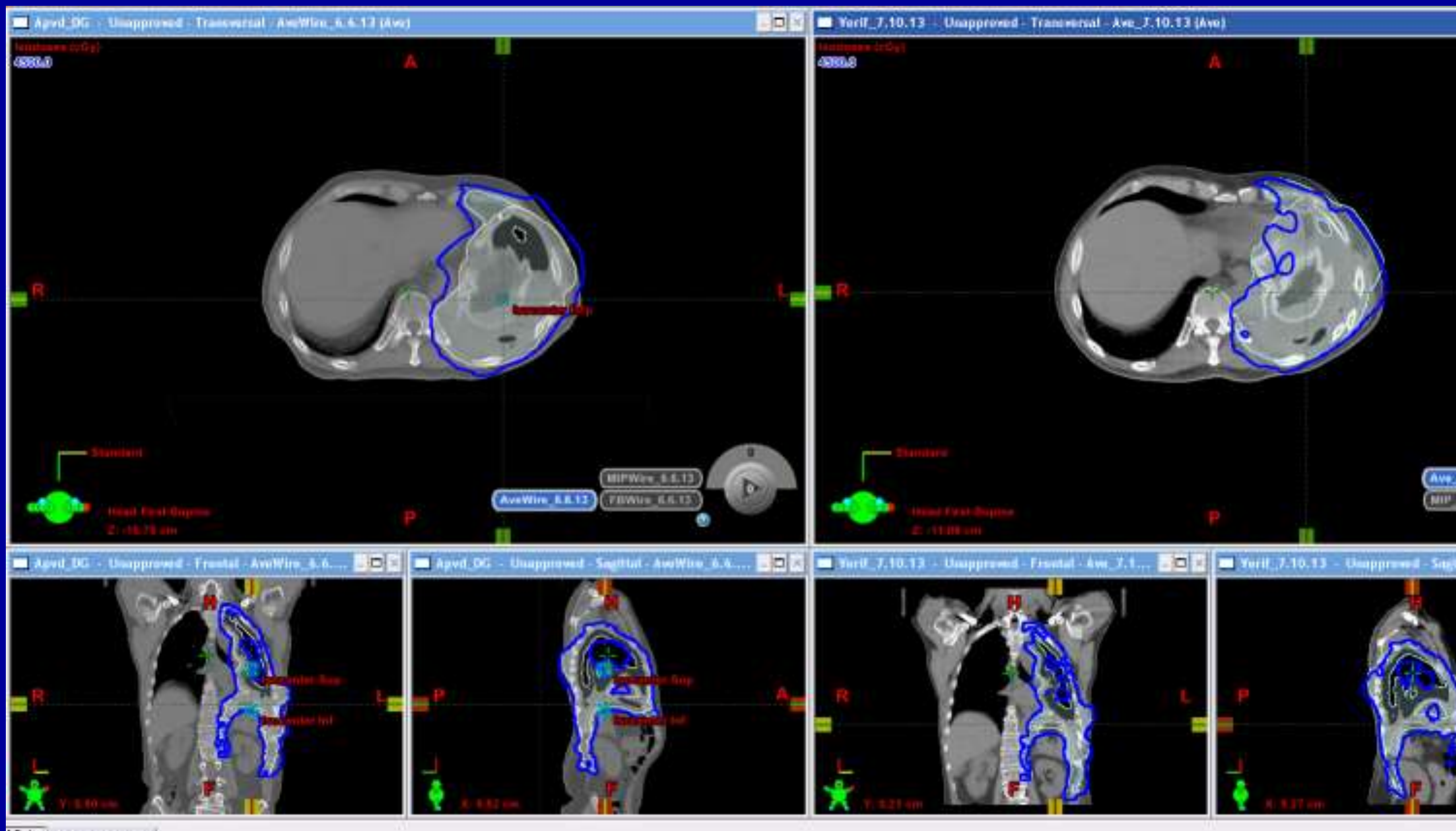
Monitor tumor change using 4D weekly CT



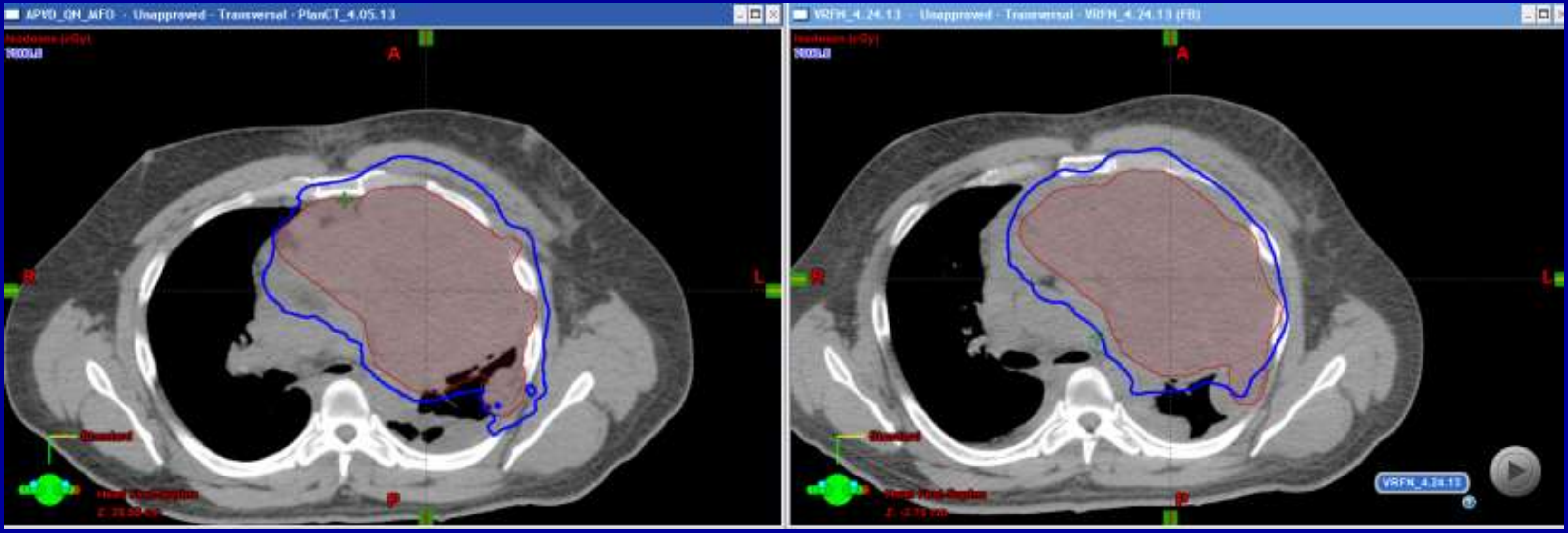
4D CT Date	08/22/12	09/20/12	09/26/12	10/3/12	10/10/12	10/17/12	10/24/12
Conra. Lat. Lung (Gy)	0.84	0.88	1.10	1.27	1.62	0.86	1.21
Cord Dmax (Gy)	9.2	15.6	15.7	22.8	20.8	14.8	19.9

- No adaptive re-plan for this patient during the course of the treatment

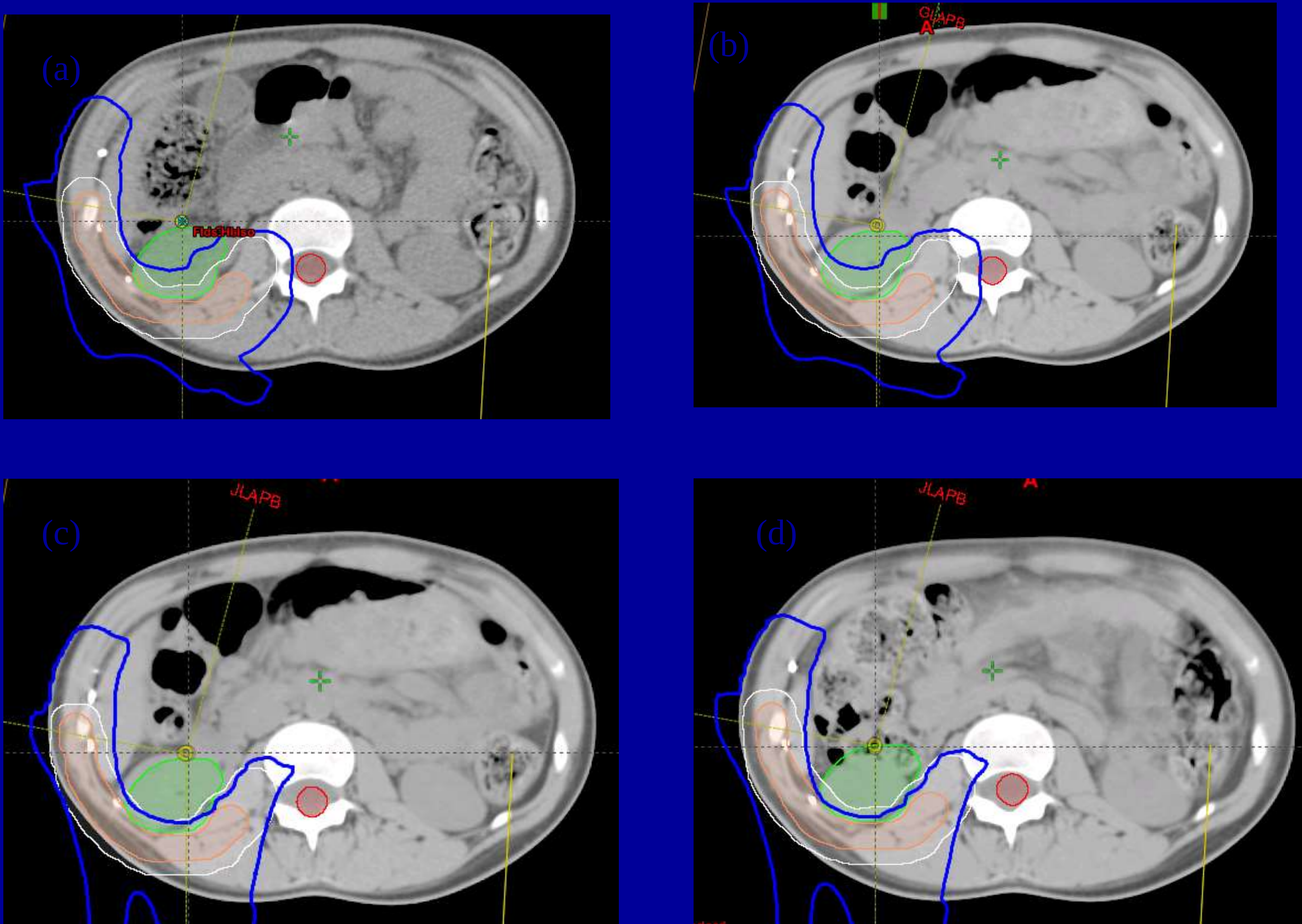
Lung Collapse



Lung Collapse



Tumor response



Stomach gas

Summary

- IMPT is great and we can treat most challenged and extremely hard cases
- IMPT is more trouble
  - TPS is not ready …
  - Plan is more vulnerable for change ..
  - Machine delivery are more trouble some … (too much overriding…)
  - QA is more time consuming …
  - IMRT challenge …
  - Pressure from Public …
  - Pressure to treat more patients …
- However: It is rewarding to be a proton physicist to push the limit …

Acknowledgements

All the physicists from our department who have contributed to our proton therapy efforts

Radiation Oncologists for their support

Dosimetrists for creating great plans

Hitachi engineers for their support

Proton Physics Fellows: past and present

Physics Assistants
Mengping Zhu
Craig Martin
Michael B.Taylor
Jon P. Oliver
Charles Holmes
Mathew Kerr
John Zullo (2006-2008)

All Physics Residents: past and present

Postdoctoral Fellows who were / are involved in proton therapy related projects

UTGSBS Medical Physics Graduate students who were / are involved in proton therapy related projects,

Clinical outcome and dosimetric data

Among the cases examined in this study, Patient 5, who received 70 CGE to 26.5%, and 75 CGE to 21.3% of the whole rectal volume, according to the clinical 3D-CPT plan,

mon treatment option.

The uncertainty in the particle penetration depth is the main factor that limits sparing of healthy tissue with proton

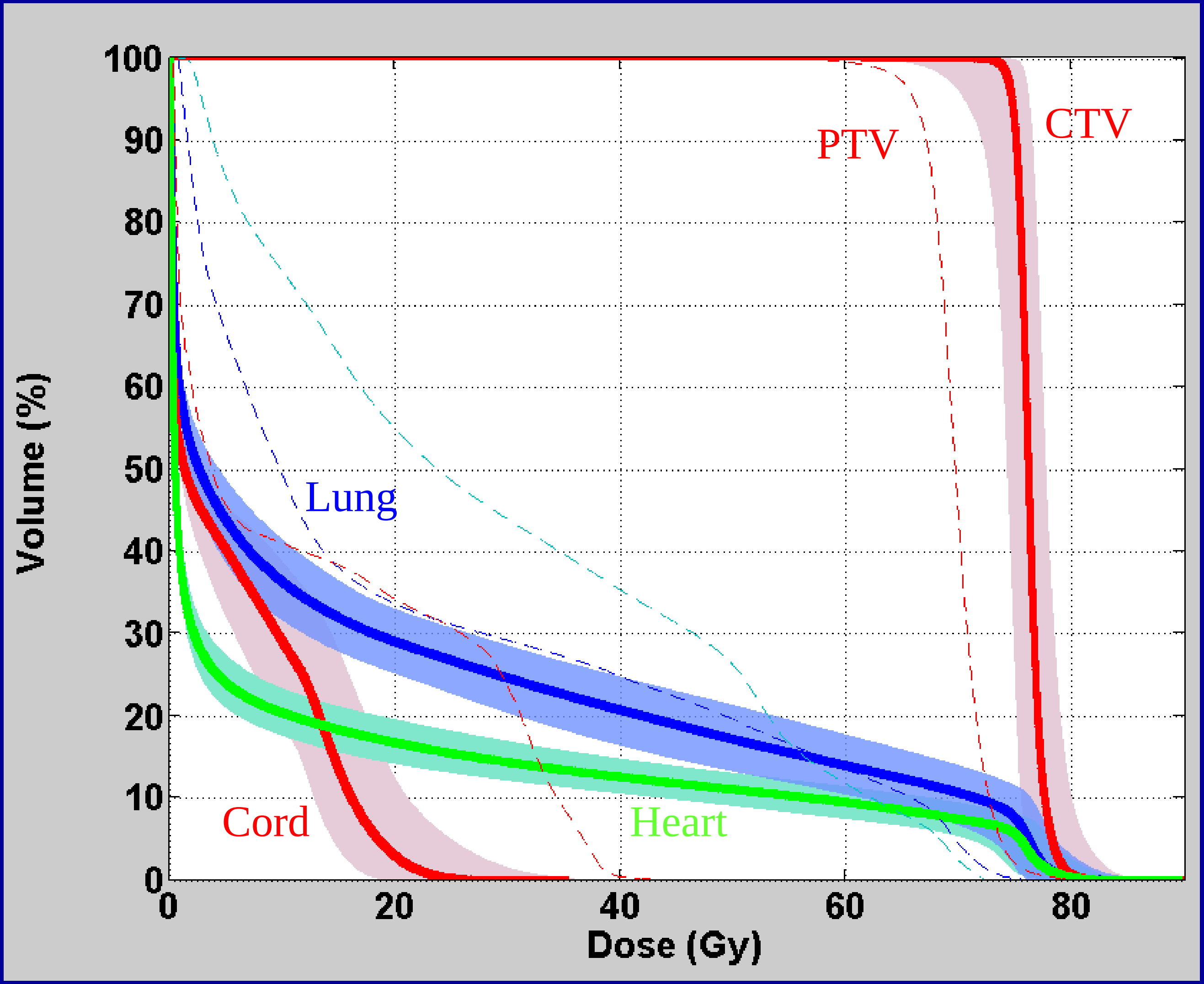
- **Patient 5, who received 70 CGE to 26.5 % of whole rectal volume according to the clinical 3D CPT plan, indeed suffered form acute rectal toxicity. In the respective IMRT plan, only 16.6% of the rectal volume received 70 Gy more.**

RADIOTHERAPY TREATMENT OF EARLY-STAGE PROSTATE CANCER WITH IMRT AND PROTONS: A TREATMENT PLANNING COMPARISON

Alexei Trofimov, Ph.D., Paul L. Nguyen, M.D., John J. Coen, M.D., Karen P. Doppke, M.S., Robert J. Schneider, C.M.D., Judith A. Adams, C.M.D., Thomas R. Bortfeld, Ph.D., Anthony L. Zietman, M.D., Thomas F. DeLaney, M.D., and William U. Shipley, M.D.

Department of Radiation Oncology, Massachusetts General Hospital and Harvard Medical School, Boston, MA

IMPT robust plan for lung



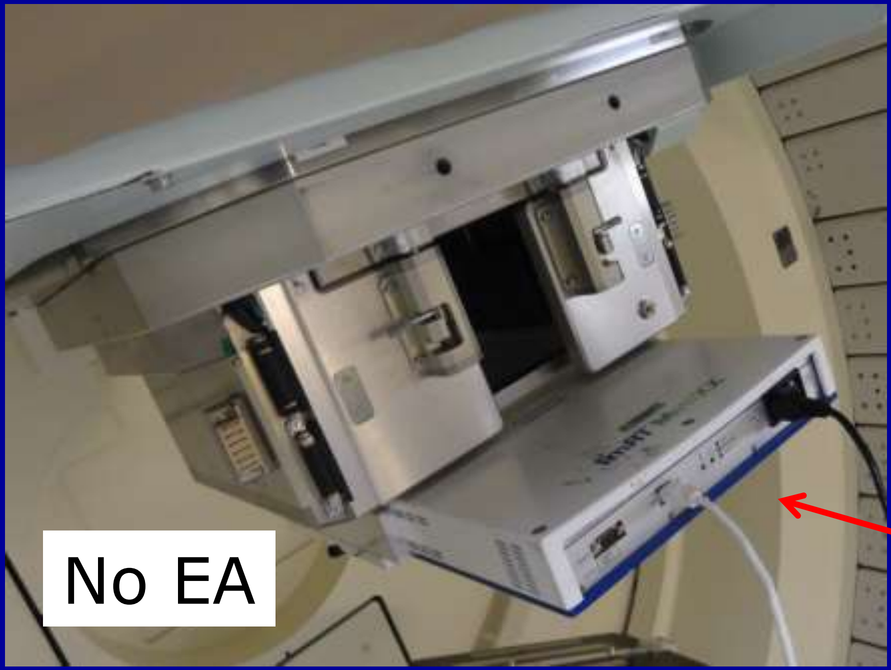
Dashed line: IMRT plan.

In-house method used for robust evaluation: Cold and Hot plan

- Nominal/clinical plan using margins adopted in Clinic.
- 6 plans by changing the position of the isocenter by +/- positioning uncertainty margin [3 or 5 mm, CTV to PTV margin]
- 2 plans by varying the CT numbers/stopping powers by + / - range uncertainty [3.5%]
- Computing the "hot" and "cold" dose distribution obtained by
  - Cold plan: assigning to each voxel of calculated volume the minimum dose to that voxel on any of the 9 plans.
  - Hot plan: assigning to each voxel of calculated volume the maximum dose on any of the 9 plans
- The resulting "cold" and "hot" plans were imported to TPS for Physicians and Physicists' evaluation
- The dose-volume histograms with band were plotted and sent to Physicians and Physicists via email in PPT format

Patient QA Measurements

- ACS: Tx & EMR: QA
- ACS: Phys & EMR: N/A



ACS: Tx mode