CONNECTING LIFE AND SCIENCE

# Practical Workflow and the Cost of Adaptive Therapy

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NCCN National Comprehensive Cancer Network®

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# Disclosures

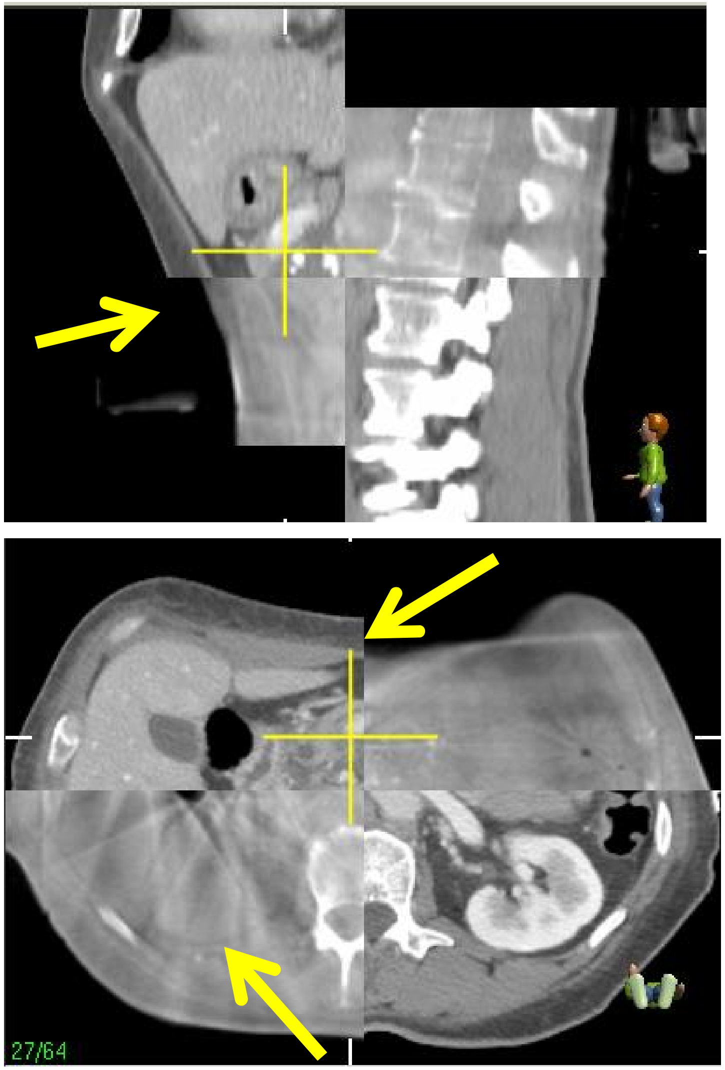
- Travel expenses paid by ViewRay Inc. for on-site software testing

# Learning Objectives

- Describe the overall process for online adaptive therapy
- Describe the tools required for online quality assurance
- Discuss the uncertainties associated with the various steps in the process
- Discuss the roles and responsibilities of team members
- Understand the resources and cost of online adaptive therapy

# Introduction

- Adaptive therapy is not a new concept
- Hundreds of publications in the past two decades
- Most importantly, we do this in the clinic every day:
  - Patients lose weight
  - Anatomical changes - tumor shrinkage and growth, change in organs at risk
  - CBCT or other volumetric imaging allows us to see changes in the patient's external surface but little information on the actual changes in the internal anatomy



# Current Adaptive Workflow (Offline)

| Patient Simulation | Image Registration | Contouring | Planning and Evaluation | Patient QA Physics checks |
|---|---|---|---|---|
| 1 – 2 hours | 1 hour | 3 – 4 hours | 1/2 day to several days | 3 – 6 hours |

- The current process is slow
- There is wait time in between each step which can vary depending on the availability of clinical resources
- The overall process takes a minimum of 1.5 to 2 days resulting in delay in patient treatment

# Online Adaptive Workflow

| Setup Image | Image Registration | Contouring | Planning and Evaluation | Patient QA Physics checks |
|---|---|---|---|---|
| 2 – 5 minutes | 2 minutes | 10 – 15 minutes | 3 – 5 minutes | 4 – 5 minutes |

- To take this process online, with the patient on the table, we need to go from hours to minutes

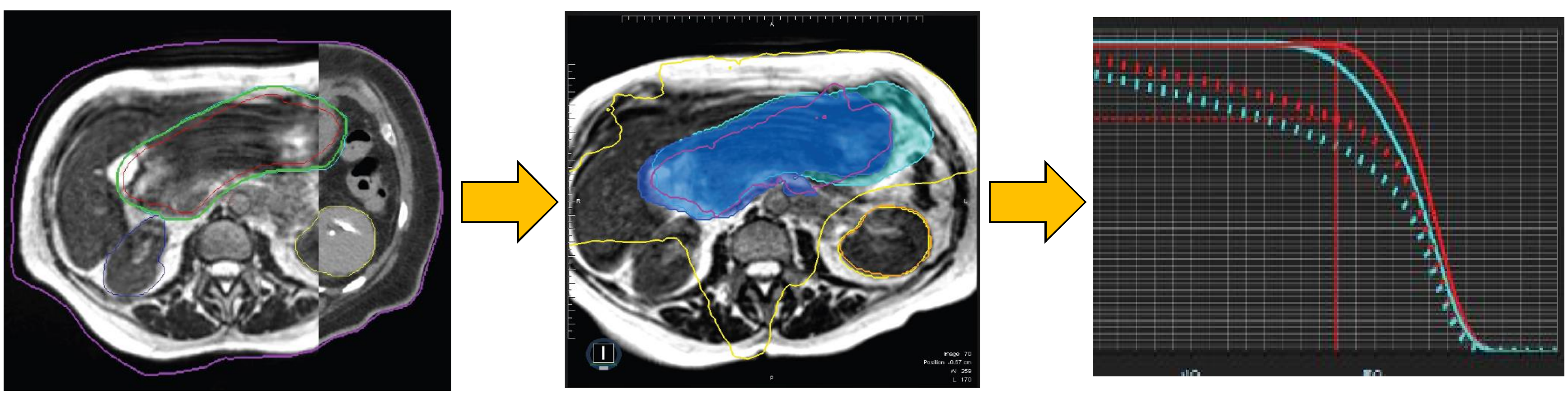
# Online treatment adaptation

What would be required in order to do this while the patient is on the table?

1. Volumetric images to determine changes in the internal and external anatomy
2. Electron density
3. Fast and automated contouring tools with tools for manual corrections
4. Fast dose calculation and re-optimization
5. Independent plan and dose verification tools in place of patient specific measurements

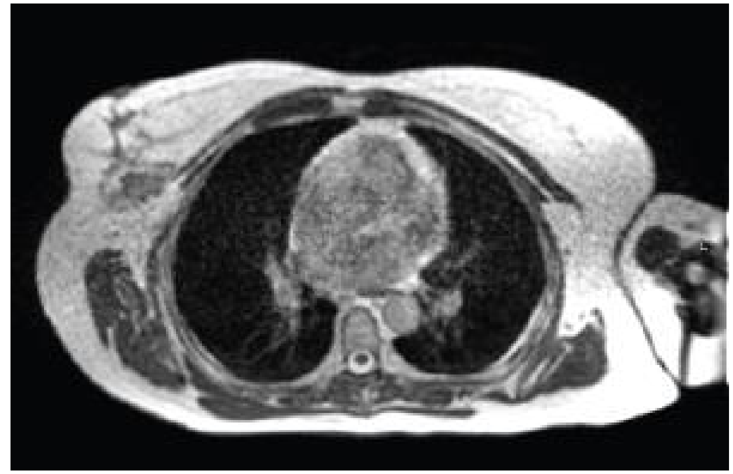
# Online adaptive planning workflow

- Volumetric imaging
- Image registration
  - Rigid or deformable
- Contour and electron density mapping
- Dose prediction
- Plan re-optimization
- Independent plan evaluation prior to delivery

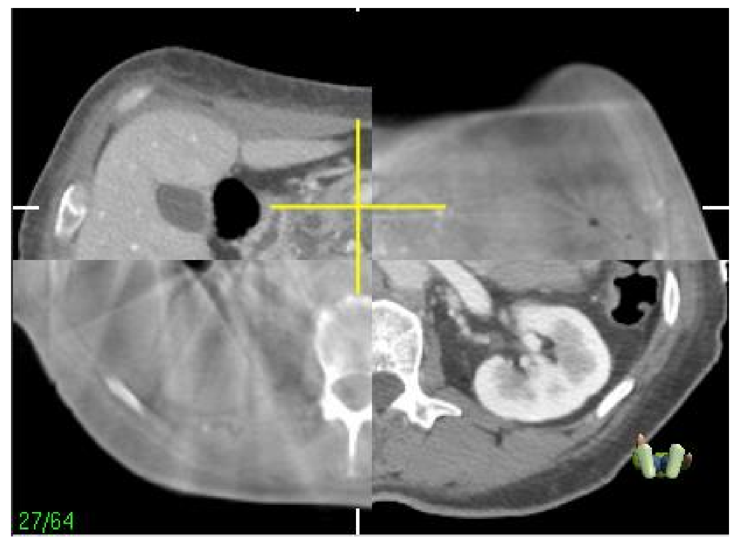


# Volumetric image characteristics

- Volumetric MR image
  - In-room MR
  - 0.35 T MR, produces high quality images while reducing dosimetric effect of MR field

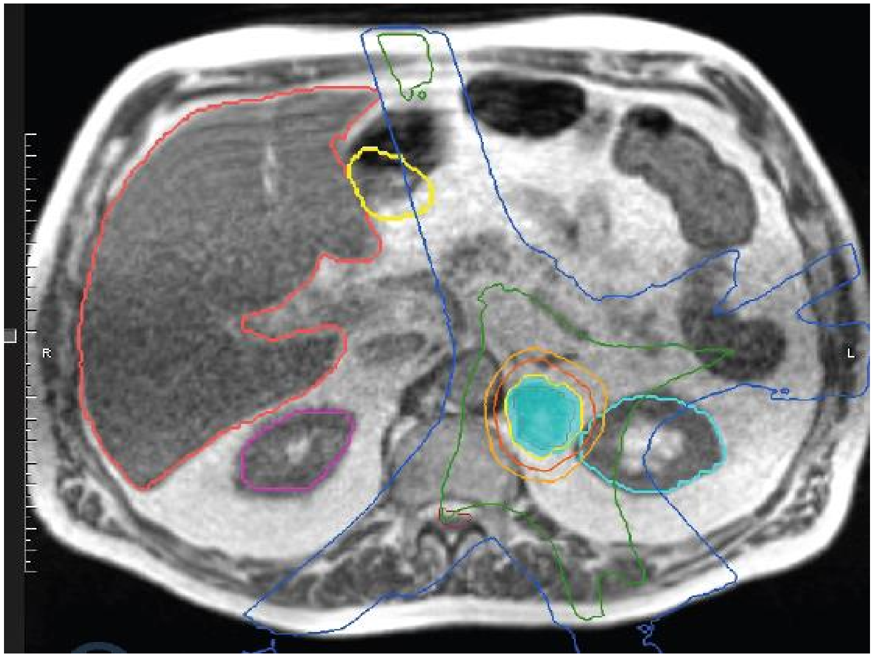


- In-room CT or ConeBeam CT
  - CBCT is not sufficient on it's own, but may be useable in combination with other information and tools



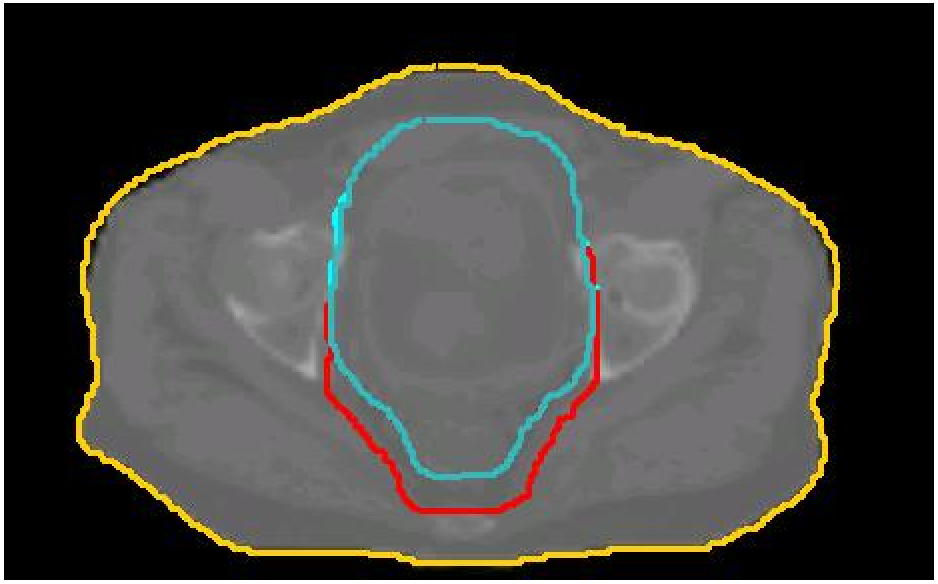
# Contour and electron density mapping

- Primary reference image can be registered to the volumetric image of the day:
  - Rigid or deformable
  - Same registration is applied to both contours and electron density
  - System allows manual edits to the contours and electron density map to correct for errors in deformable registration



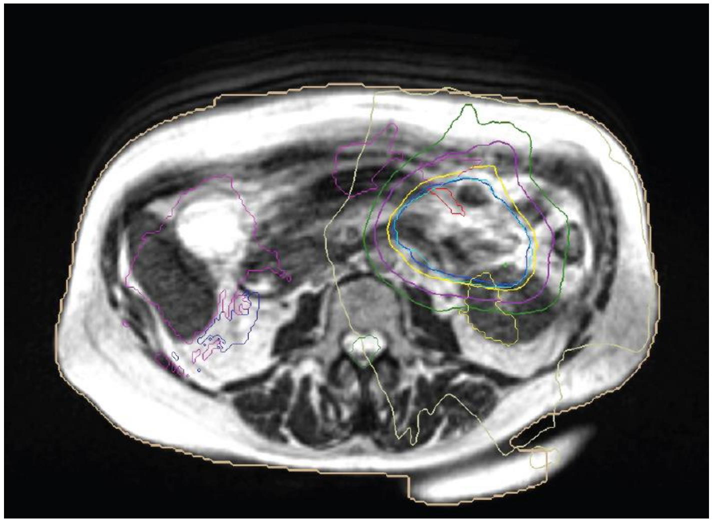
# Contour and electron density mapping

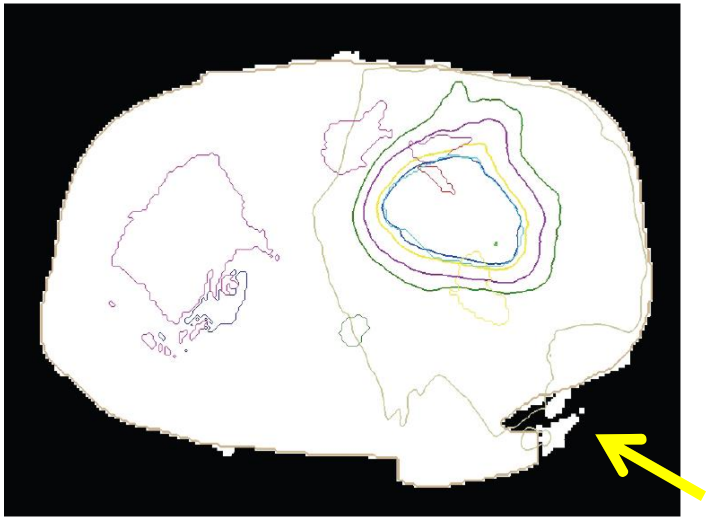
- Electron density is transferred from primary density map to image of the day
  - Based on the deformation map if CT is used
  - Along with the transferred contours if bulk density overrides are used



# Contour and electron density mapping

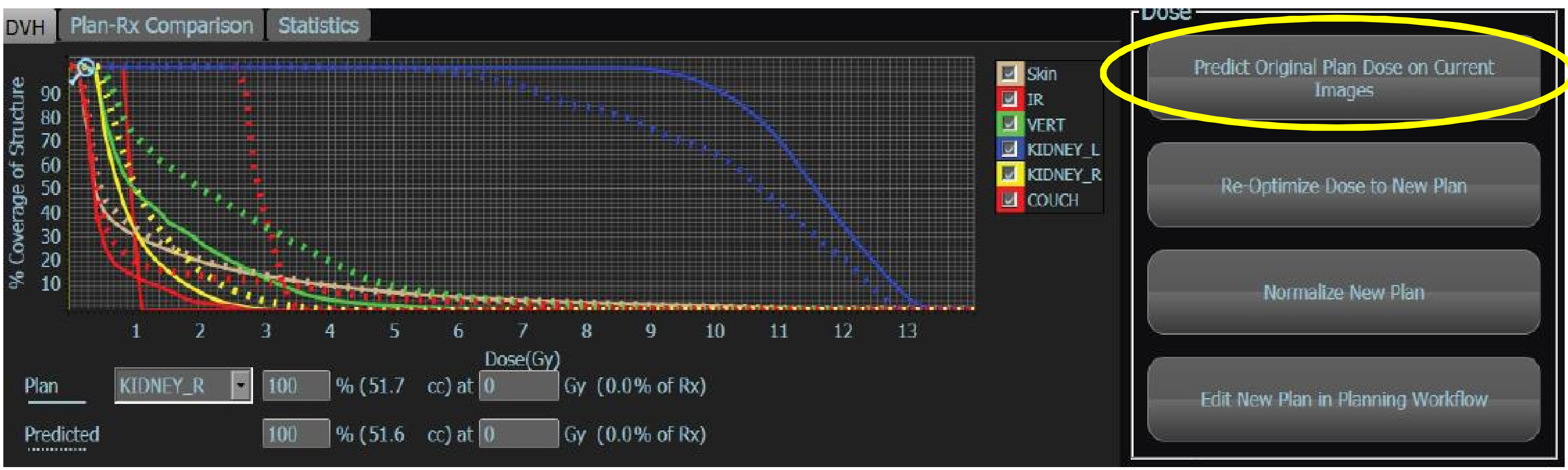
- Errors in electron density map
  - Unlike contours that can be edited manually, the errors in deformation will propagate to the electron density map
  - Any significant deviations observed, can be resolved with manually overriding the density to air, or water





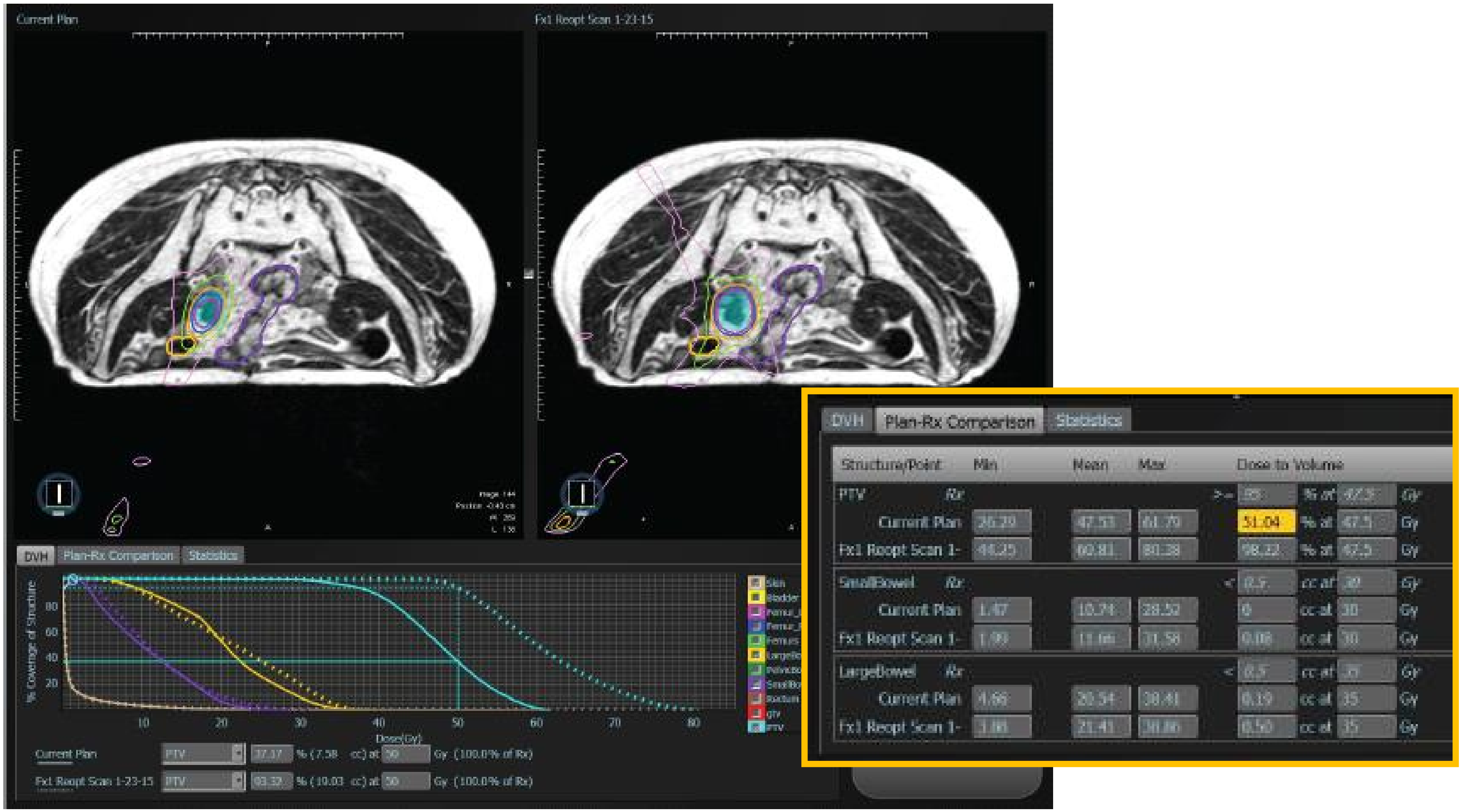
# Dose prediction

- Original plan needs to be calculated on the current electron density map
  - Why not deform the dose along with the contours ?



# Dose prediction

- DVHs can be evaluated for the new contours



# The accuracy of mapping and accumulating the dose for adaptive therapy is limited by:

20% 1. Errors in electron density map

20% 2. Relative location of the errors in deformable registration and the dose gradient

20% 3. Errors in deformable registration alone

20% 4. Difference between original and new image resolution

20% 5. There are no concerns regarding dose accumulation if the registration is verified.

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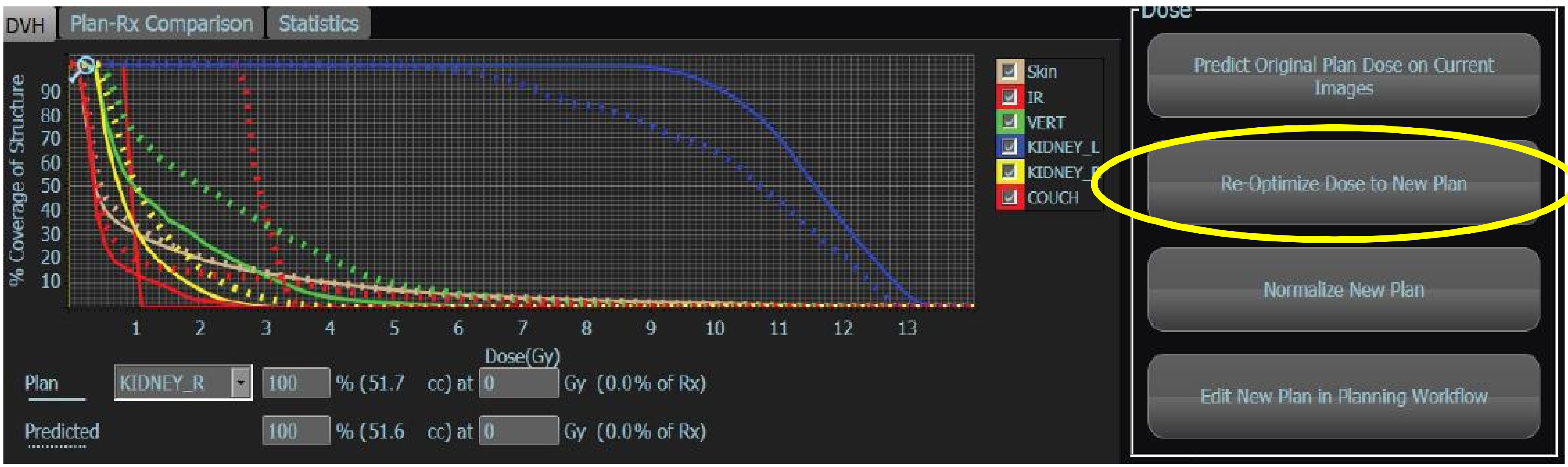
1. Errors in electron density map
2. Relative location of the errors in deformable registration and the dose gradient
3. Errors in deformable registration alone
4. Difference between original and new image resolution
5. There are no concerns regarding dose accumulation if the registration is verified.

Murphy MJ, et al. ñA method to estimate the effect of deformable image registration uncertainties on daily dose mapping.òMed Phys. 2012; 39: 573-580.

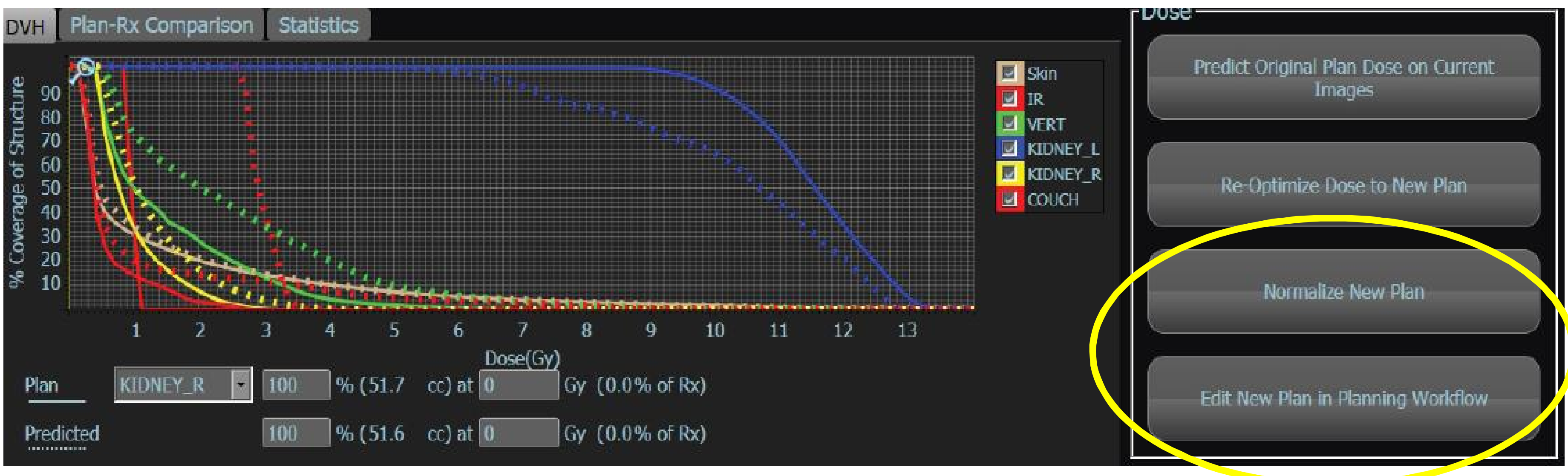
# Plan Re-optimization

- Selection of beam angles is dependent on the delivery method and the delivery system
  - Preserving the beam angles of the original plan may be beneficial in simplifying the QA
  - Original beams may not be optimal for the new geometry
    - Within our system, beams may be turned off during optimization



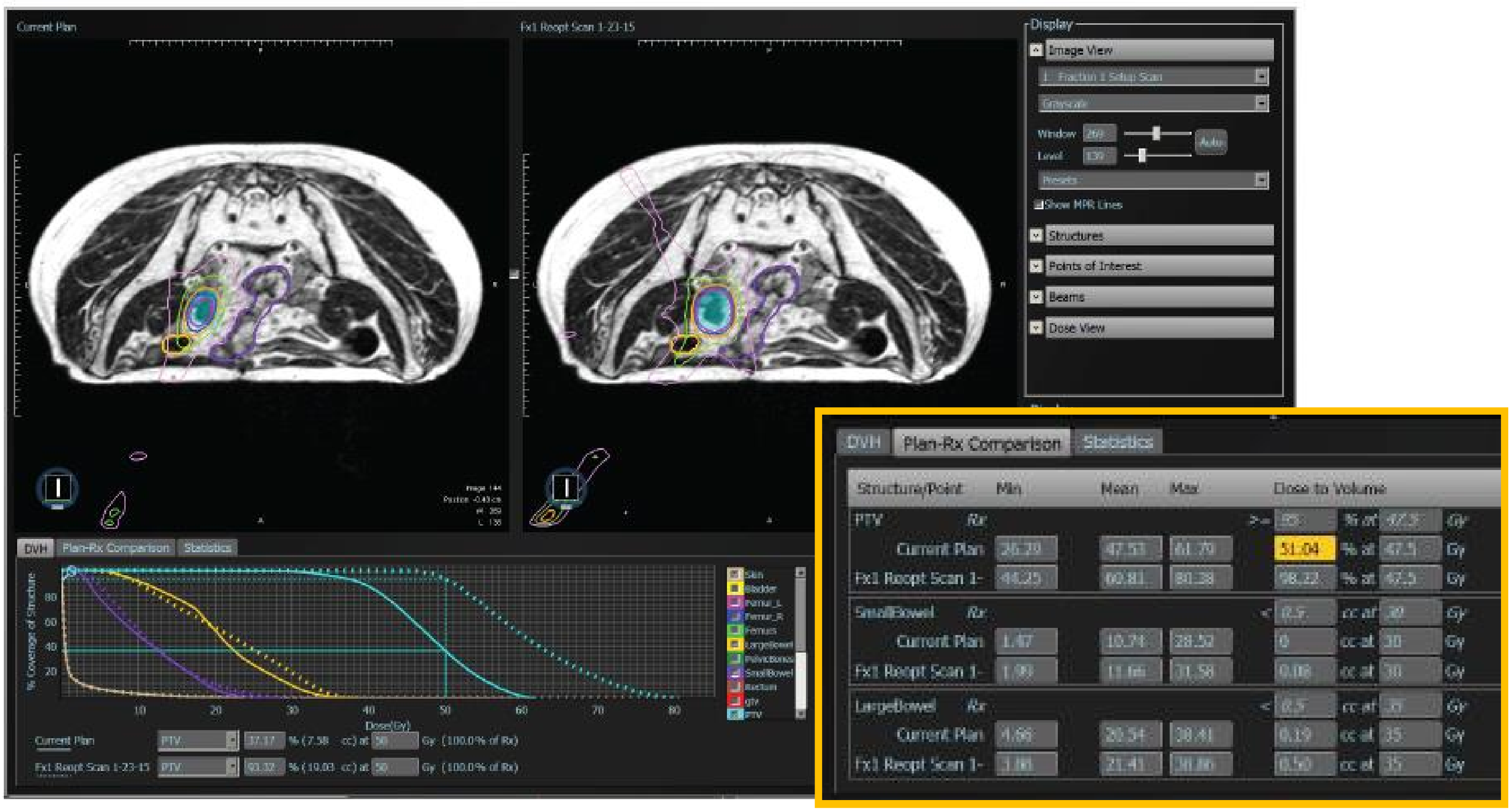
# Plan Re-optimization

- Original plan's optimization parameters can be used as a starting point
  - May not be optimal considering the new patient geometry
  - Availability of tools to adjust the parameters is useful but requires good understanding of the the optimizer



# Plan Evaluation

- Plan quality can be evaluated manually
  - DVHs points
  - Isodoses



# Now that we have a new plan, what's next?

- Primary limitation in proceeding to treatment is QA
  - We cannot take the patient off the table to do phantom measurements. But is it necessary ?

**Patient-specific QA for IMRT should be performed using software rather than hardware methods**

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Colin G. Orton, Ph.D., Moderator

(Received 23 February 2013; accepted for publication 25 February 2013; published 31 May 2013)

# Is patient specific phantom measurement necessary?

**Argument against measurement**

- Measurement inaccuracies
- Insensitivity of the QA devices
- Measurements cannot separate the source of the error

**Argument for measuremt**

- Measurement is the only way to test deliverability of the plan
- Measurement can save us from catastrophic errors

**Patient-specific QA for IMRT should be performed using software rather than hardware methods**

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# A passing patient specific IMRT QA measurement indicates :

| | | |
|---|---|---|
| 20% | 1. | That the patient will be treated correctly |
| 20% | 2. | That the plan is deliverable and is not exceeding any machine limits |
| 20% | 3. | That the tissue heterogeneities are accounted for in the planning system. |
| 20% | 4. | That the plan transfer to the delivery system is correct at every fraction |
| 20% | 5. | That the plan quality is optimal |

10

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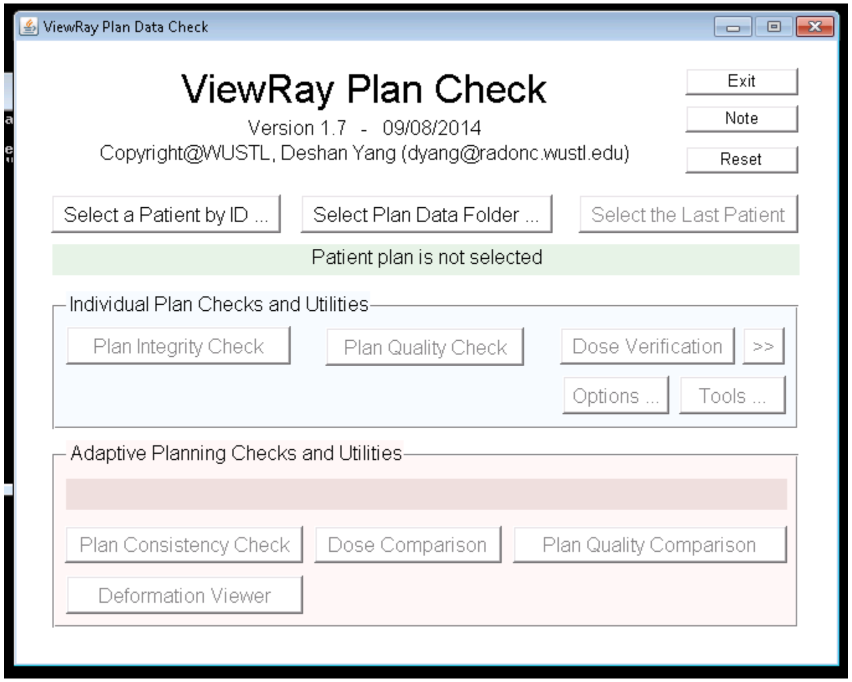
5. That the plan quality is optimal

Siochi, A, Molineu A, Patient-specific QA for IMRT should be performed using software rather than harder methord. MedPhys 2013, point counter point.

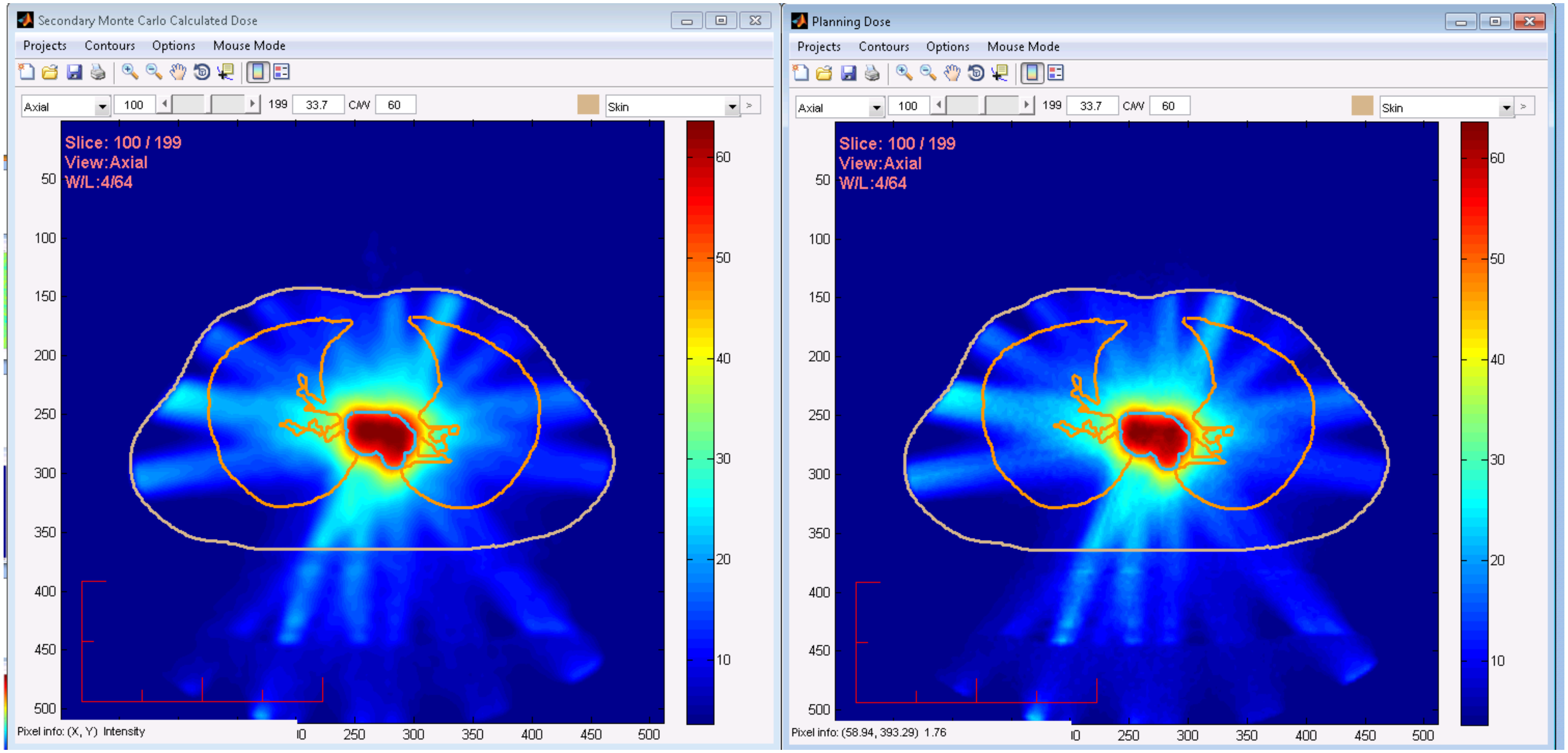
# Independent plan evaluation prior to delivery

- Beam parameters, electron density map, structures, and dose distribution are exported for the new plan
- In-house tool developed Deshan Yang and Tianyu Zhao
  - Independent Monte Carlo dose calculation within 2 mintes
  - Plan consistency checks can be performed:
    - Gantry angles
    - Number of segments
    - Beam on times
    - Fluence calculation and PTV overlay
    - Structure volumes



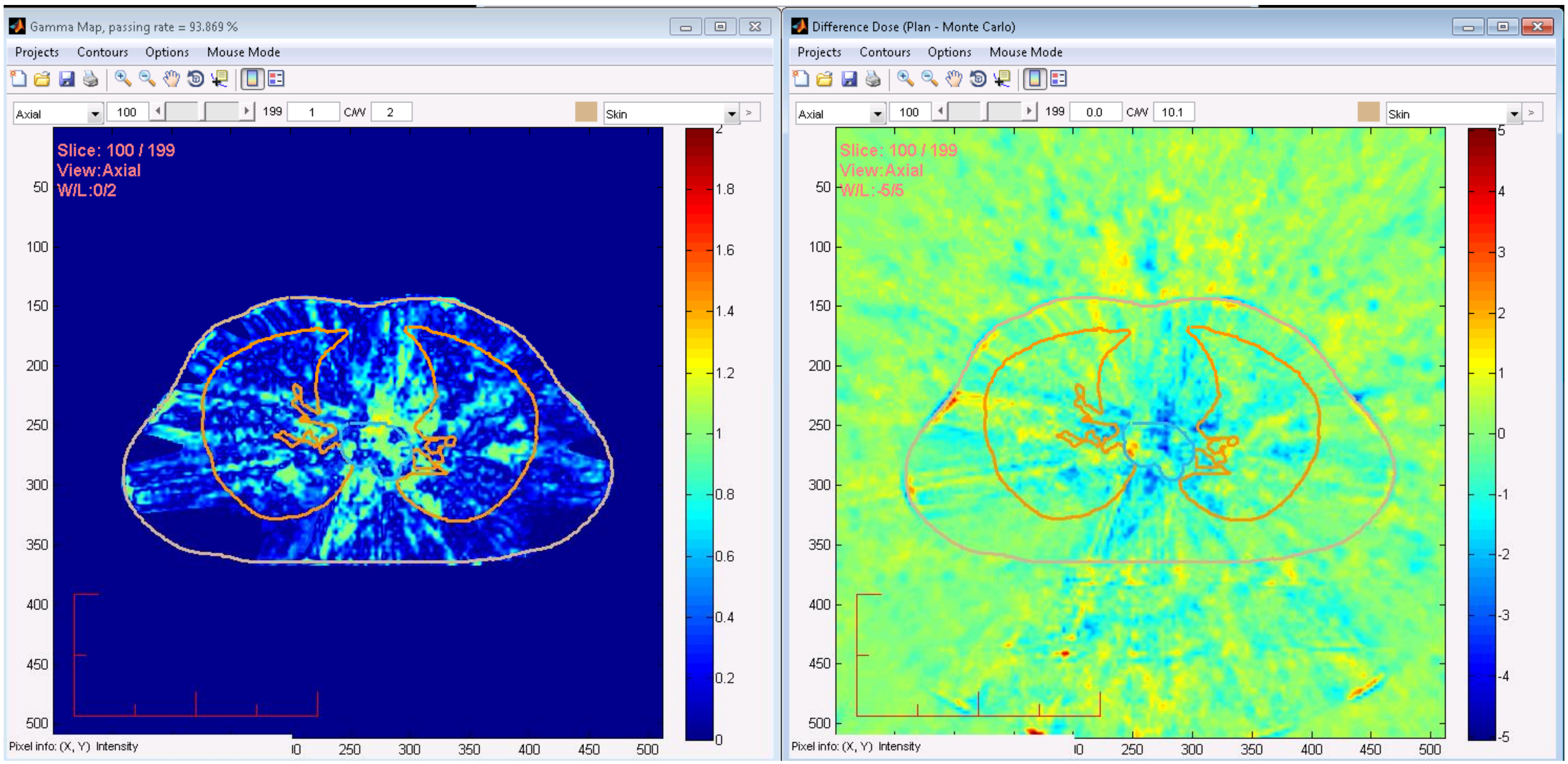
# Independent plan evaluation prior to delivery

– Monte Carlo dose calculation on the electron density map in 2 min (100K)
– Accuracy is less at interfaces, in air, and inside the treatment couch



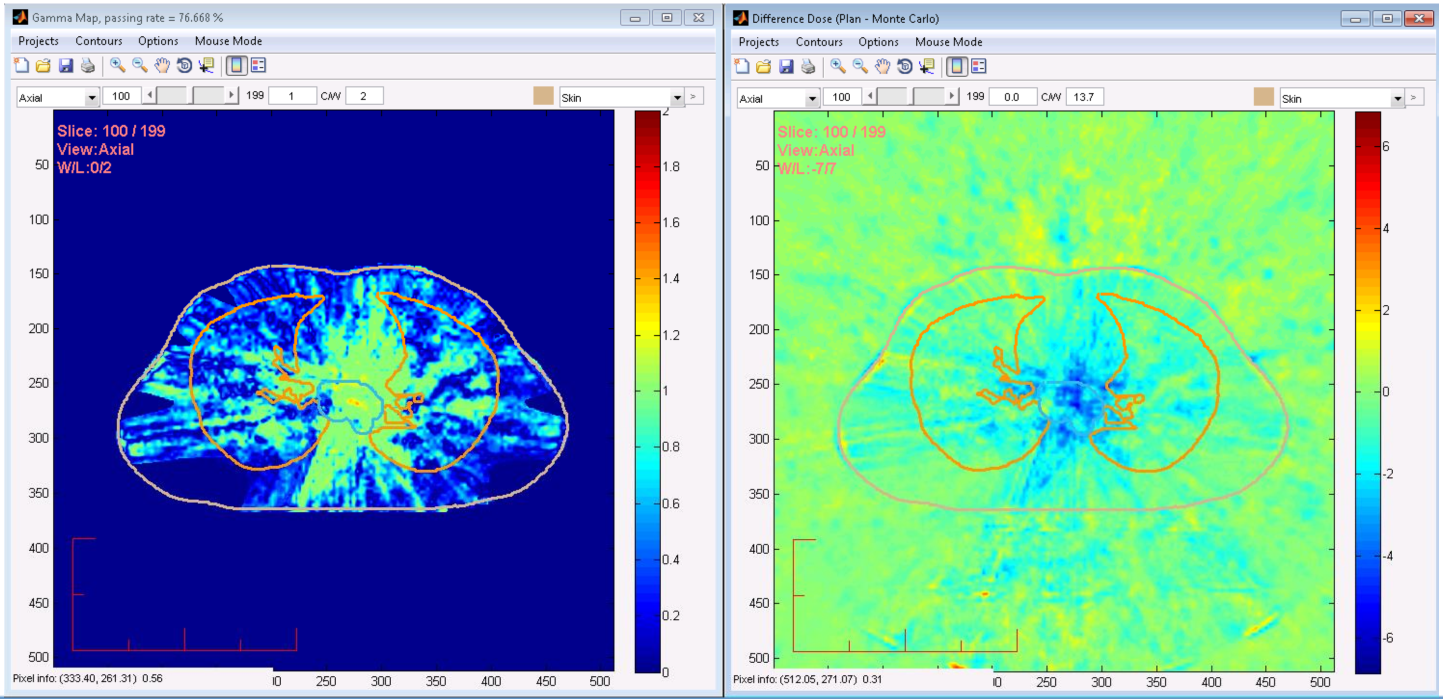
# Independent plan evaluation prior to delivery

- 3D gamma calculation over the full volume with 3%, 3 mm criteria
- Everything outside the skin is ignored



# Independent plan evaluation prior to delivery

- How do we trust this over actual measurements?
  - Dose calculated by this tool was compared to actual patient specific measurements – ArcCheck, ion chamber
  - Sensitivity of the analysis to errors in dose was verified by introducing known errors
    - Introducing a 3% error in dose results in gamma pass rate dropping to 76% from 93%



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ViewRay Plan Consistency ...

| | | | |
|---|---|---|---|
| Number of Contours | 31 | 31 | Pass |

## Density Overrides (Reference Plan / Plan)

| # | ROI Name | Density | Priority |
|---|---|---|---|
| 1 | BOWEL CONTRAST / BOWEL CONTRAST | 1 / 1 | 25 / 25 |
| 2 | IV CONTRAST / IV CONTRAST | 1 / 1 | 24 / 24 |

## RealTarget Settings (Reference Plan / Plan)

| # | POI Name | Coordinate | Tracking Enabled |
|---|---|---|---|
| 1 | Isocenter / Isocenter | -0.1, 25.4, -9 / 0, 0, 0 | No / No |

## Optimization Constraints (Reference Plan / Plan)

| # | ROI Name | Type | Upper Importance | Upper Power | Threshold | Rx | Lower Importance | Lower Power | Offset |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Skin / Skin | Critical Structure / Critical Structure | 2 / 2 | 2 / 2 | 18.5 / 18.5 | - | - | - | - |
| 2 | LargeBowel / LargeBowel | Critical Structure / Critical Structure | 2 / 2 | 2 / 2 | 51 / 51 | - | - | - | - |
| 3 | SmallBowel / SmallBowel | Critical Structure / Critical Structure | 20 / 20 | 20 / 20 | 46.5 / 46.5 | - | - | - | - |
| 4 | Ostomy / Ostomy | Critical Structure / Critical Structure | 2 / 2 | 2 / 2 | 51 / 51 | - | - | - | - |
| 5 | PTV_5750 / PTV_5750 | Target / Target | 2 / 2 | 2 / 2 | - | 57.5 / 57.5 | 2.5 / 2.5 | 2 / 2 | 1.5 / 1.5 |
| 6 | PTV 50-(SB+4MM) / PTV 50-(SB+4MM) | Target / Target | 1 / 1 | 2 / 2 | - | 50 / 50 | 3 / 3 | 2.5 / 2.5 | 1.5 / 1.5 |
| 7 | PTV50-PTV57.5 / PTV50-PTV57.5 | Target / Target | 1 / 1 | 1 / 1 | - | 46.5 / 46.5 | 2 / 2 | 2 / 2 | 1.5 / 1.5 |
| 8 | PTV45-(PTVs) / PTV45-(PTVs) | Target / Target | 1 / 1 | 2 / 2 | - | 45 / 45 | 3 / 3 | 2 / 2 | 1 / 1 |
| 9 | OSTOMY OPTI / OSTOMY OPTI | Critical Structure / Critical Structure | 1 / 1 | 1 / 1 | 26 / 26 | - | - | - | - |
| 10 | PTV50-(PTV57.5+5MM) / PTV50-(PTV57.5+5MM) | Critical Structure / Critical Structure | 3.5 / 3.5 | 3 / 3 | 53.5 / 53.5 | - | - | - | - |
| 11 | SB+4MM / SB+4MM | Critical Structure / Critical Structure | 3 / 3 | 3 / 3 | 50.5 / 50.5 | - | - | - | - |
| 12 | POST AVOID / POST AVOID | Critical Structure / Critical Structure | 1 / 1 | 1 / 1 | 40 / 40 | - | - | - | - |

## Contours (Reference Plan / Plan)

| # | ROI Name | Volume |
|---|---|---|
| 1 | Skin / Skin | 27066.61 / 22919.26 |
| 2 | Bladder / Bladder | 184.54 / 197.03 |
| 3 | Femur_R / Femur_R | 159.16 / 159.24 |
| 4 | Femur_L / Femur_L | 155.59 / 156.02 |
| 5 | LargeBowel / LargeBowel | 314.84 / 309.28 |
| 6 | PelvicBones / PelvicBones | 841.72 / 841.29 |
| 7 | SmallBowel / SmallBowel | 378.51 / 374.71 |
| 8 | GTV / GTV | 526.96 / 538.55 |
| 9 | CTVnodal_mcr / CTVnodal_mcr | 893.23 / 893.56 |
| 10 | CTV_4500 / CTV_4500 | 1421.14 / 1492.77 |
| 11 | CTV_5000 / CTV_5000 | 1185.93 / 1230.82 |
| 12 | CTV_5750 / CTV_5750 | 3.13 / 3.35 |
| 13 | PTV_4500 / PTV_4500 | 1941.51 / 1940.24 |
| 14 | PTV_5000 / PTV_5000 | 1641.57 / 1641.21 |
| 15 | PTV_5750 / PTV_5750 | 15.81 / 15.6 |

Should be identifical

## Beams (Reference Plan / Plan)

| # | Head | Angle | Number of Segments | Total BeamOn Time |
|---|---|---|---|---|
| 1 | 1 / 1 | 32 / 32 | 8 / 4 | 5.8224 / 2.8197 |

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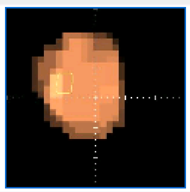
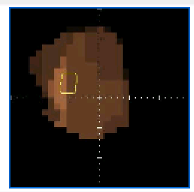
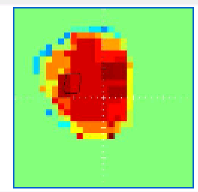
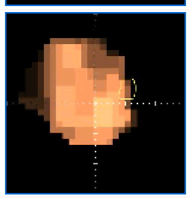
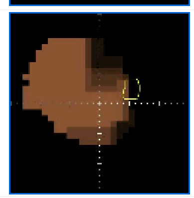
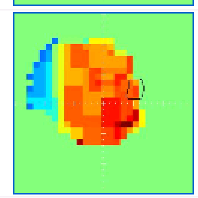
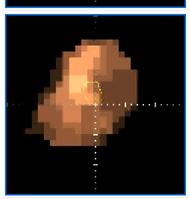
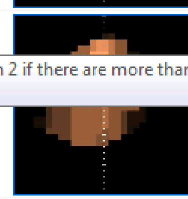
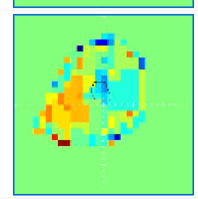
ViewRay Plan Consistency ...

## Beams (Reference Plan / Plan)

| # | Head | Angle | Number of Segments | Total BeamOn Time |
|---|---|---|---|---|
| 1 | 1 / 1 | 32 / 32 | 8 / 4 | 5.8224 / 2.8197 |
| 2 | 2 / 2 | 152 / 152 | 8 / 6 | 7.0257 / 3.45 |
| 3 | 3 / 3 | 272 / 272 | 7 / 7 | 7.2672 / 6.5936 |
| 4 | 1 / 1 | 40 / 40 | 7 / 5 | 4.9853 / 2.3364 |
| 5 | 2 / 2 | 160 / 160 | 9 / 7 | 8.4852 / 3.9147 |
| 6 | 3 / 3 | 280 / 280 | 7 / 7 | 7.166 / 7.0467 |
| 7 | 1 / 1 | 56 / 56 | 7 / 5 | 5.2627 / 3.174 |
| 8 | 2 / 2 | 176 / 176 | 10 / 5 | 10.456 / 4.9302 |
| 9 | 3 / 3 | 296 / 296 | 8 / 6 | 7.2285 / 4.693 |
| 10 | 1 / 1 | 64 / 64 | 7 / 5 | 5.486 / 2.7142 |
| 11 | 2 / 2 | 184 / 184 | 9 / 8 | 10.206 / 7.8638 |
| 12 | 3 / 3 | 304 / 304 | 8 / 6 | 7.2375 / 5.0139 |
| 13 | 1 / 1 | 80 / 80 | 7 / 7 | 5.921 / 5.7587 |
| 14 | 2 / 2 | 200 / 200 | 9 / 7 | 9.0855 / 8.53 |
| 15 | 3 / 3 | 320 / 320 | 8 / 4 | 6.4144 / 4.8173 |
| 16 | 1 / 1 | 88 / 88 | 7 / 3 | 6.7265 / 1.2877 |
| 17 | 2 / 2 | 208 / 208 | 8 / 6 | 6.9904 / 6.8761 |
| 18 | 3 / 3 | 328 / 328 | 7 / 5 | 7.2371 / 7.9063 |
| 19 | 1 / 1 | 96 / 96 | 7 / 5 | 6.0948 / 4.6858 |
| 20 | 3 / 3 | 336 / 336 | 7 / 5 | 8.1905 / 10.159 |
| 21 | 2 / 2 | 264 / 264 | 7 / 7 | 6.2588 / 8.2884 |
| 22 | 3 / 3 | 24 / 24 | 10 / 7 | 8.5702 / 7.8883 |

## Beams Fluence Maps

| # | Head # | Angle | Reference Plan | Plan | Difference |
|---|---|---|---|---|---|
| 1 | 1 | 32 |  |  |  |
| 2 | 2 | 152 |  |  |  |
| 3 | 3 | 272 |  |  |  |

Difference should be within 2 if there are more than 2 segments

# The goal of online patient specific QA for adaptive radiotherapy:

| | | |
|---|---|---|
| 20% | 1. | is to validate the accuracy of the treatment planning system's heterogeneity correction |
| 20% | 2. | is to ensure patient did not move during treatment |
| 20% | 3. | is to verify patient setup accuracy |
| 20% | 4. | is to validate the accuracy of re-optimized plan and identify any large deviations |
| 20% | 5. | online QA cannot be sufficient under any conditions and should never be used |

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# The goal of online patient specific QA for adaptive radiotherapy:

1. is to validate the accuracy of the treatment planning system's heterogeneity correction

2. is to ensure patient did not move during treatment

3. is to verify patient setup accuracy

4. **is to validate the accuracy of re-optimized plan and identify any large deviations**

5. online QA cannot be sufficient under any conditions and should never be used

Taoran Li, Quality assurance for online adapted treatment plans: Benchmarking and delivery monitoring simulation, Med. Phys. 42 (1), January 2015

# The cost and resources for online adaptive RT

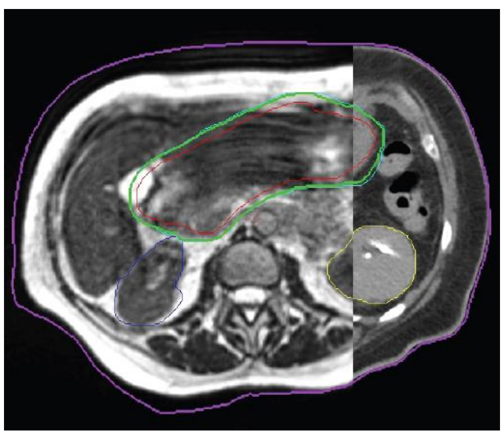
| Setup Image | Image Registratio n | Contouring | Planning and Evaluation | Patient QA Physics checks |
|---|---|---|---|---|
| 2 – 5 minutes | 2 minutes | 10 – 15 minutes | 3 – 5 minutes | 4 – 5 minutes |

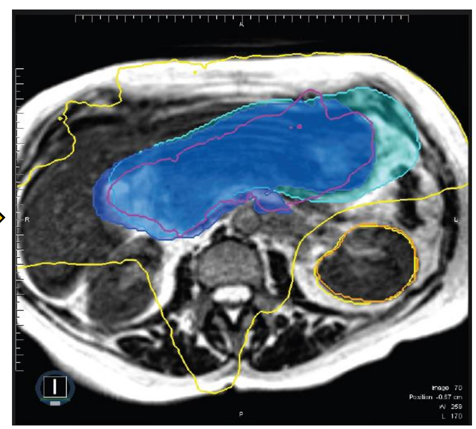
- The cost of adaptive can be discussed in terms of the required resources and time

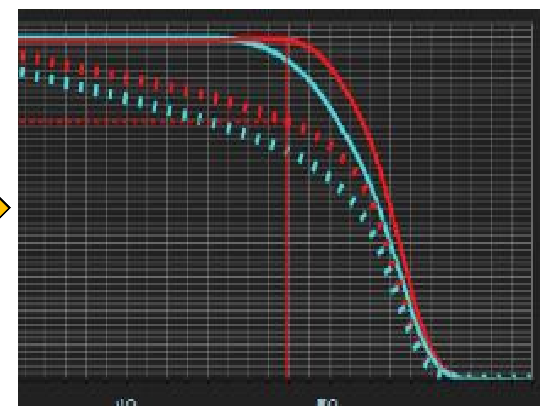
# How long does this process take ?

- Volumetric imaging and contour propagation – 2 - 4 minutes
- Dose prediction – 1.5 - 3 minutes
- Plan reoptimization – 2 - 4 minutes
- Independent dose and plan evaluation – 4 - 5 minutes

→ Total time : 10 – 15 minutes







# How long does this process take ?

- Volumetric imaging and contour propagation – 2 - 4 minutes
  - Contour evaluation and manual edits: 5 to 15 minutes (or more )
  - This is system and implementation dependent and will vary
- Dose prediction – 1.5 - 3 minutes
  - Manual edits to the electron density: 2 minutes (Not always necessary)
- Plan re-optimization – 2 - 4 minutes
  - If normalization or additional modification to the plan parameters is needed: 3 – 5 min
- Independent dose and plan evaluation – 4 - 5 minutes

→ Total time : 20 – 30 minutes

# Required Resources

- Volumetric imaging
  - Performed by therapists (same as a setup scan)
- Contour propagation and evaluation
  - Physician is required to be present for contour edits
  - Physicist is required to be present for margin expansions and Boolean operations
- Dose prediction
  - Physician and physicist
- Plan re-optimization
  - Physician and physicist
- Independent dose and plan evaluation
  - Physicist only

# Costs and Reimbursement

**Additional ART Sim, Planning Procedure**

- Simulation [Simple 77280, Complex 77290]: [$226 ($135-$355), $610 ($365-$959)]
- Planning 77295: $803 ($481-$1,263)
- Dose Calc 77300, per angle, up to 10*): $84 ($51-$133)
- MLC Check 77334: $188 ($113-$296)

**Additional one-time costs per ART patient (these charges can be difficult to get reimbursed per re-plan)**

- Special Physics Consult 77370 (1-time): $147 ($88-$231)
- Special Tx Procedure 77470 (1-time): $297 ($178-$467)

# Costs and Reimbursement

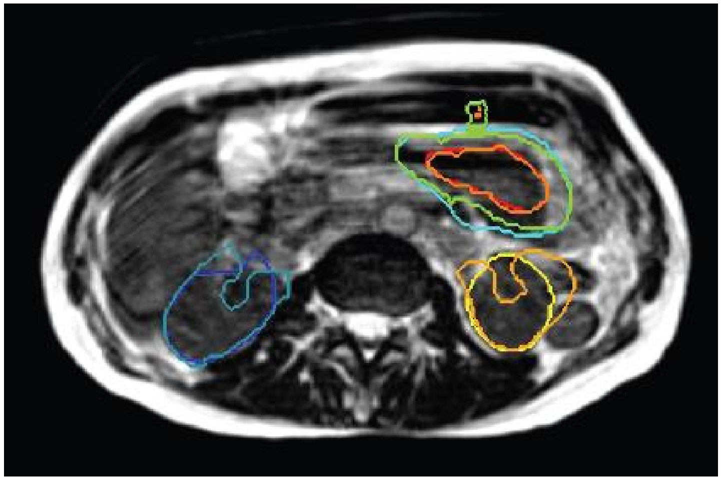
**In summary:**

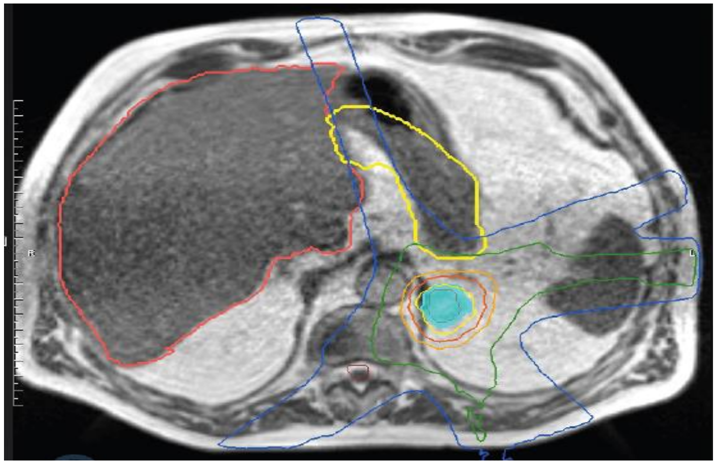
- Additional one-time charges on top of conventional IG-IMRT, excluding re-plans = $444 ($266 -$698)
- Additional charge per ART plan = $2097 ($1239 - $3848)

"Cost-Effectiveness of Modern Radiotherapy Techniques in Locally Advanced Pancreatic Cancer." James D Murphy, M.D., M.S., Daniel T Chang, M.D., Jon Abelson, M.D., Megan E Daly, M.D., Heidi N Yeung, M.D., Lorene M Nelson, Ph.D., Albert C Koong, M.D. Ph.D. (2012)

# Accuracy and sources of uncertainties

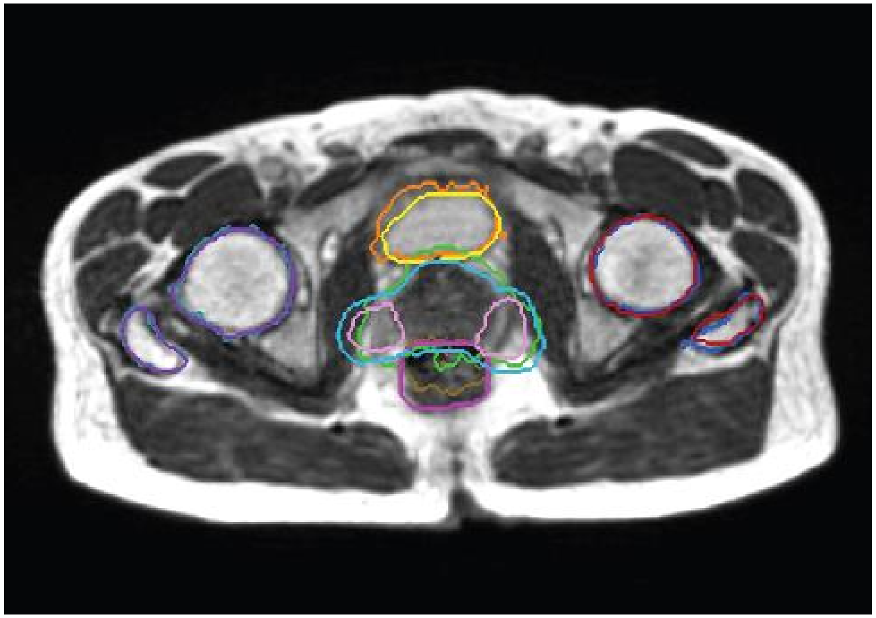
- Accuracy of auto-deformed contours depends on the accuracy of the deformable registration:
  - Image quality (noise and motion artifacts)
  - Original contour definition
    - Contours defined based on geometric boundaries (GTV vs. ITV)
  - Magnitude of change: If there is a large change in a specific organ, auto-deformation may not be able to capture that (Bladder filling)





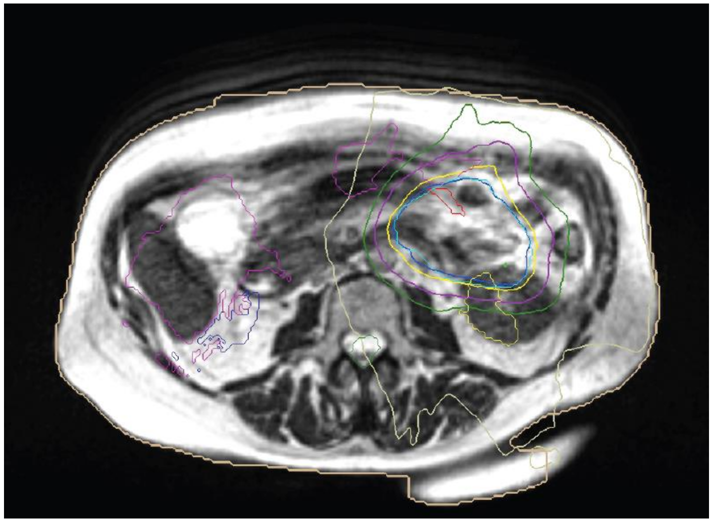
# Accuracy and sources of uncertainties

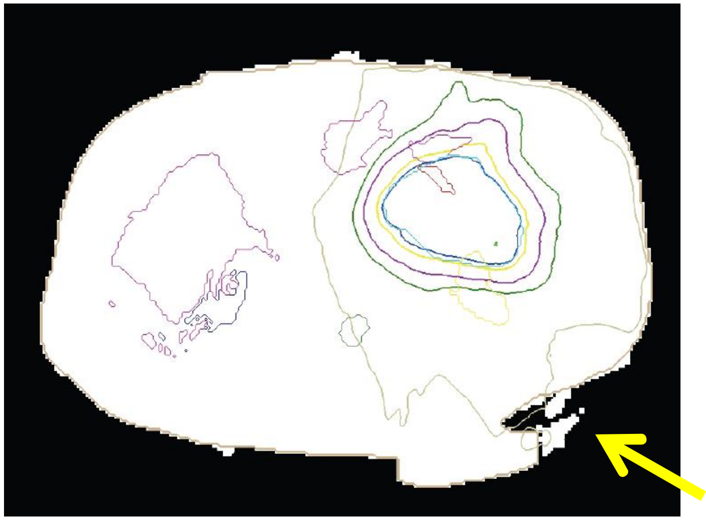
- Quality of the re-optimized plan is dependent on the accuracy of the contours used in re-optimization
- Proximity of the location of error in the OAR contour to the target is also a significant factor
  - If a max dose on an OAR is of concern, only the region near the target needs to be very accurate



# Accuracy and sources of uncertainties

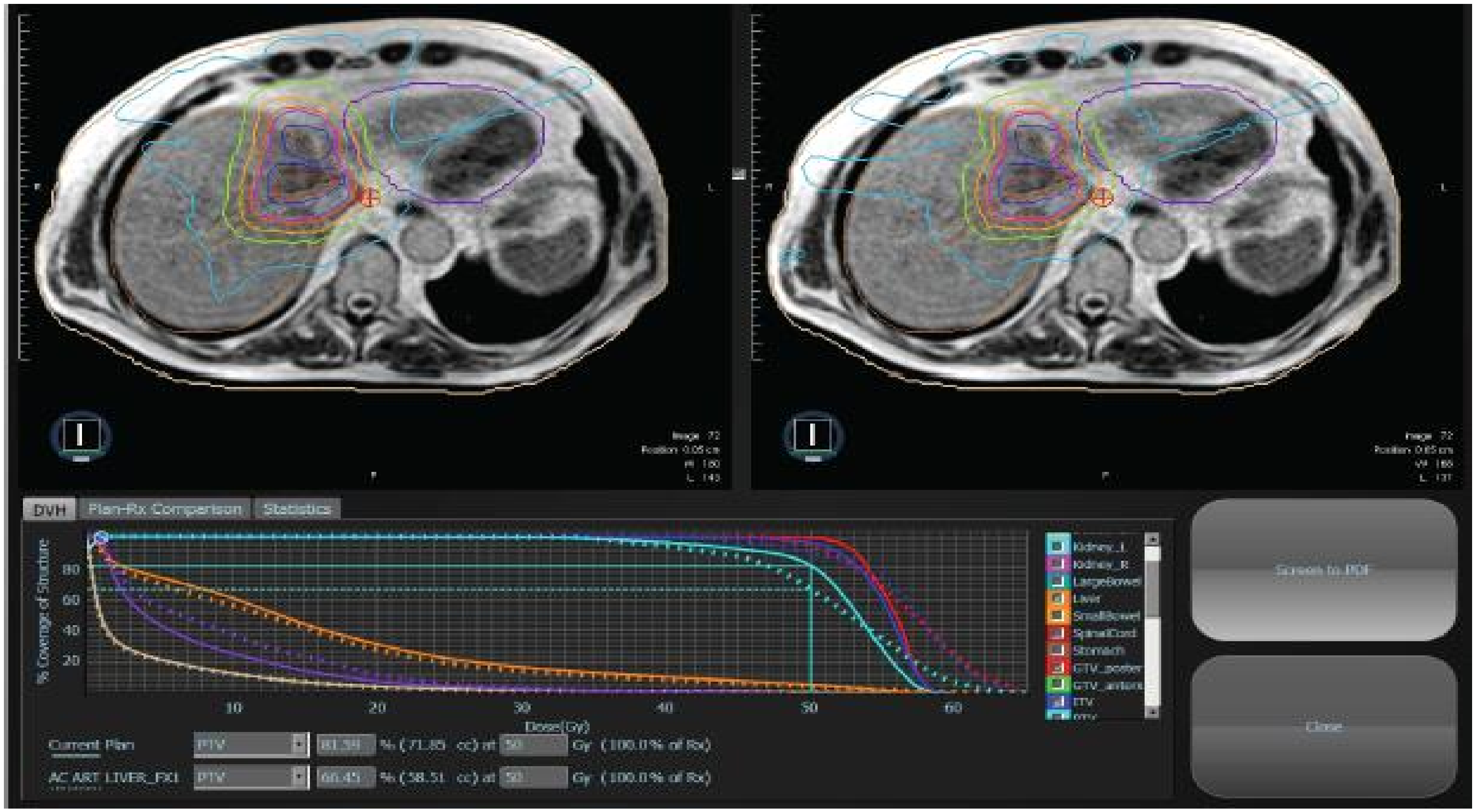
- Errors in electron density
  - Most significant if there is tissue in the path of the beam that is not accounted for – Can be improved by better patient setup
  - Errors in boundaries inside the patient were found to have insignificant impact on dose
  - All deviations larger than 1 cm across will be manually modified





# Accuracy and sources of uncertainties

- Selection of a good set of initial optimization parameters impacts the quality of the reoptimized plan



Compared to the standard IMRT process, which of the following failure modes is most likely to cause a treatment error in an adaptive process

20% 1. Errors in density

20% 2. Errors in contouring

20% 3. Insufficient plan quality review

20% 4. Isocenter accuracy

20% 5. Errors in fusion

10

# Compared to the standard IMRT process, which of the following failure modes is most likely to cause a treatment error in an adaptive process

1. Errors in density
2. Errors in contouring
3. Insufficient plan quality review
4. Isocenter accuracy
5. Errors in fusion

Noel, C. Process-based quality management for clinical implementation of adaptive radiotherapy. MedPhys 41(8).

# Discussion

- Online treatment adaptation is clinically possible
  - 14 patients evaluated, 11 have been adapted one or more fractions
  - Total of 25 adaptive fractions since Sept 2014

- The process and the tools available are not perfect and need improvement in speed, accuracy, and automation

- This is certainly not a vendor specific process. The tools are there and they just need to be put together.

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# Thank You !