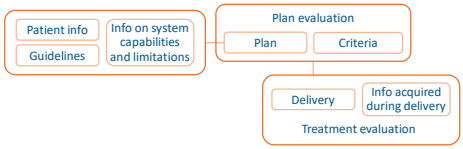
UFHealth PROTON THERAPY INSTITUTE

PROTON TREATMENT PLANNING IN THE PRESENCE OF UNCERTAINTIES

STELLA FLAMPOURI

AAPM 2018

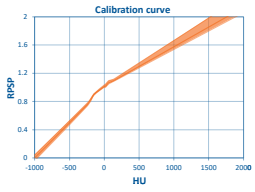
Radiotherapy workflow



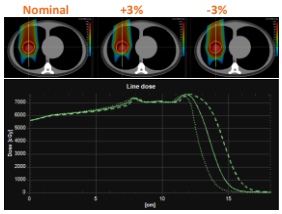
Treatment plan robustness is the ability to retain objectives under the influence of uncertainties

Proton range calculation uncertainties - Estimation

- Proton range in tissue calculated with ambiguous HU – RPS translation



Proton range calculation uncertainties - Remedies

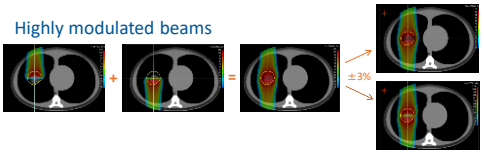


Robustness increase with

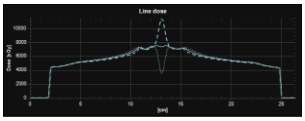
- Margins along each beam
- Multiple beams
- Beam orientation selection

Proton range calculation uncertainties – Remaining issues

Highly modulated beams



- No geometric margin can fix this
- Modulation reduction helps
  IMPT → limited modulation → SFUD



Intervening tissue variations

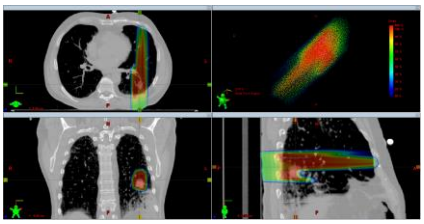
- Proton range depends on tissue *composition* and ***density***
- Any tissue variation in proton path
  → range changes
  → dose distribution variation
- Setup errors
  Intra-fractional motions and deformations
  Inter-fractional anatomical changes
  } range uncertainty

Intervening tissue variations - Estimation

- Setup errors – isocenter shifts

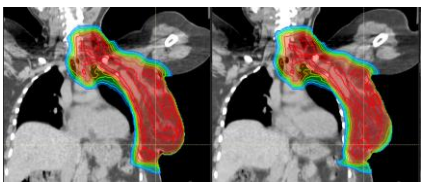
Intervening tissue variations - Estimation

- Setup errors
- Intra-fractional motion and deformation



Intervening tissue variations - Estimation

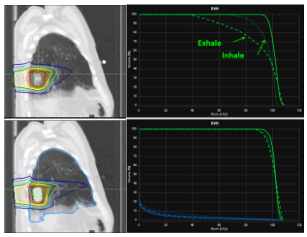
- Setup errors
- Intra-fractional motion and deformation
- Inter-fractional anatomical variations



Intervening tissue variations - Remedies

Robustness increase with

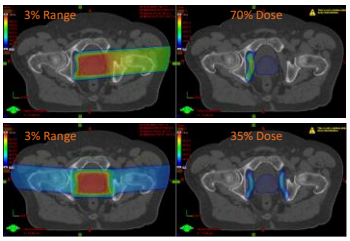
- Margin along beam



Intervening tissue variations - Remedies

Robustness increase with

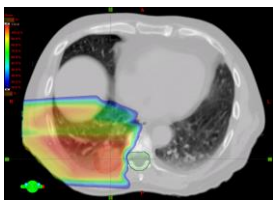
- Margin along beam
- Multiple beams



Intervening tissue variations - Remedies

Robustness increase with

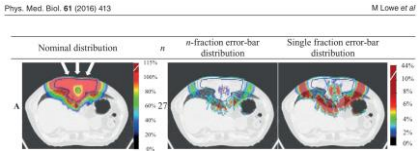
- Margin along beam
- Multiple beams
- Beam orientation selection



Intervening tissue variations - Remedies

Robustness increase with

- Margin along beam
- Multiple beams
- Beam orientation selection
- Fractionation



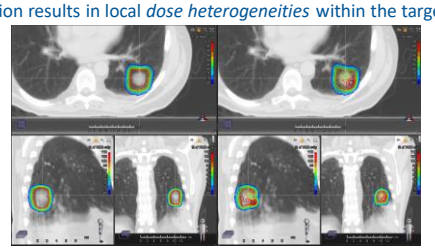
Intervening tissue variations - Remedies

Robustness increase with

- Margin along beam
- Multiple beams
- Beam orientation selection
- Fractionation
- *Plan verification and adaptation schemes*

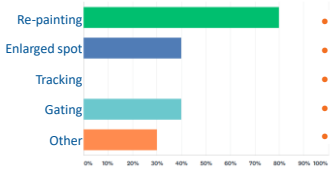
Interplay - Estimation

- Interference of dynamic pencil beam delivery with the target motion results in local *dose heterogeneities* within the target



Interplay - Remedies

Do you use any of the following to reduce interplay effect?

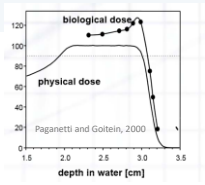


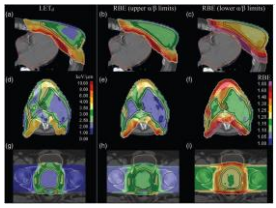
- Fractionation
- Motion reduction
- Motion limits for PBS treatments
- Multiple fields
- Combinations of the above

Survey on PBS robustness: June/July 2018, answered by 11/20 US proton centers with PBS

RBE variability - Estimation

- Clinically used proton RBE = 1.1 but





Acta Oncol 2017 Jun;56(6):769-77

Incorporation of relative biological effectiveness uncertainties into proton plan robustness evaluation

RBE variability - Remedies

- Empirical methods to spare organs behind distal fall off
  - Multiple beams
  - Beam direction
  - Reduced physical dose limits

Pediatric Brainstem

Metric	Goal	Max Dose
$D_{0.1cc}$	56.6 Gy*	58 Gy*
$D_{10\%}$	55.4 Gy*	56 Gy*
$D_{50\%}$	52.4 Gy*	54 Gy*

* RBE = 1.1

- LET-weighted dose calculation and optimization

RBE variability - Remedies

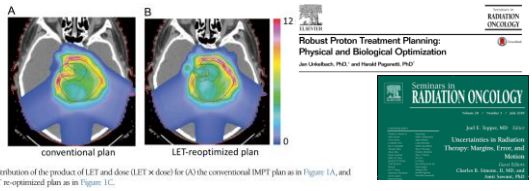


Figure 3 Distribution of the product of LET and dose (LET × dose) for (A) the conventional IMPT plan as in Figure 1A, and (B) the LET re-optimized plan as in Figure 1C.

- LET-weighted dose calculation and optimization

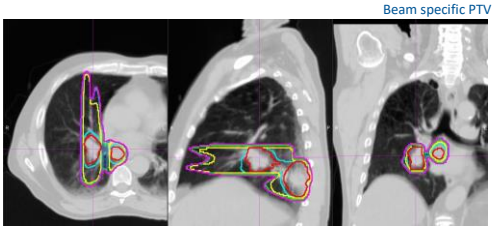
Clinical practice

Which uncertainties are usually accounted for in treatment planning at your clinic?

ANSWER CHOICES	RESPONSES
Range calculation uncertainties	100.00%
Setup errors	100.00%
Intra-fractional anatomical variations (excluding interplay)	72.73%
Interplay effects between moving anatomy and scanning beam	36.36%
Inter-fractional anatomical variations (limited to variation in target position relative to other tissues, not severe changes)	36.36%
Variable RBE	36.36%
Other (please specify)	9.09%
Total Respondents: 11	

Uncertainties and PTVs

Beam specific PTV



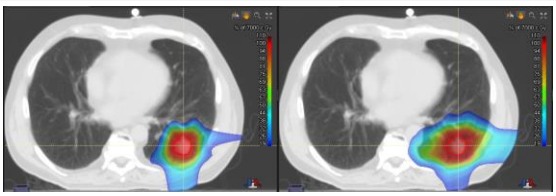
Reminder

- The goal is not to treat more but to treat better

Solution – Robust optimization

- Incorporation of error scenarios in optimization
- Common error scenarios:
  - range uncertainty
  - isocenter shifts
  - multiple CT sets
- Optimization approaches
  - Probabilistic
  - Worst-case
- Robust objectives and constraints for targets and OARs

Robust optimization



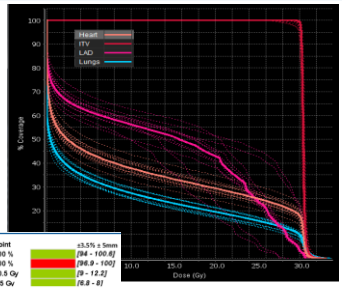
Target coverage
static anatomy

Target coverage
±3.5% range uncertainty
±5 mm isocenter shifts (x, y or z)
Inhale / Exhale / AVG

Robust optimization – Current limitations

- Worst-case of few uncertainties included
- Difficult implementation of probabilistic simulations
- No interplay included
- Difficult to distinguish between random and systematic errors
- Optimization is slow
- Difficult to evaluate

Robust optimization – Evaluation



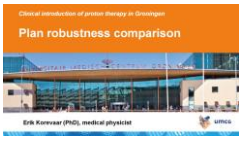
Structure	DVHpoint	Goals	Point	±3.5% ± 5mm
ITV	Relative dose at 99% volume	100 %	100 %	[94 - 100.6]
ITV	Relative volume at 99% dose	99.9	100 %	[96.9 - 100]
Heart	Mean absolute dose	15, 20 Gy	10.5 Gy	[9 - 12.2]
Lungs	Mean absolute dose	14, 18 Gy	7.5 Gy	[6.8 - 8]

Photon – Proton comparison

Equivalent scenarios
- setup for photons
- setup and range for protons

Calibration of old criteria with new for photons

Compare plans with the same metric



Towards a Clinical Decision Support System for External Beam Radiation Oncology Prostate Cancer Patients: Proton vs. Photon Radiotherapy? A Radiobiological Study of Robustness and Stability.

What is missing

- Robust optimization: fast MC, 4D, biological planning
- Robustness evaluation: Standard tools in commercial TPS
- Methods to score and compare plan quality that includes robustness to facilitate clinical decision making

ΕΝ ΟΙΔΑ ΟΤΙ ΟΥΔΕΝ ΟΙΔΑ 

PBS Proton Treatment Plan Robustness Questionnaire

Friday, July 27, 2018

Powered by SurveyMonkey

11

Total Responses

Date Created: Monday, March 12, 2018

Complete Responses: 11

Powered by SurveyMonkey

Q1: Institution

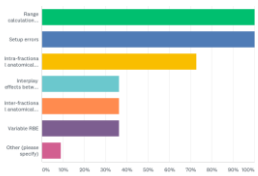
Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Maryland Proton Treatment Center	9.09%	1
Mayo Clinic Proton Beam Therapy AZ	9.09%	1
Mayo Clinic Proton Beam Therapy MN	9.09%	1
MGH Francis H. Burr Proton Beam Therapy Center	9.09%	1
Miami Cancer Institute	9.09%	1
Northwestern Medicine Chicago Proton Center	9.09%	1
Procure Proton Therapy Center NJ	9.09%	1
Provision CARES Center for Proton Therapy	9.09%	1
Texas Center for Proton Therapy	9.09%	1
University of Florida Health Proton Therapy Institute	9.09%	1
University of Pennsylvania Roberts Proton Therapy Center	9.09%	1

Powered by SurveyMonkey

Q4: Which uncertainties are usually accounted for in treatment planning at your clinic?

Answered: 11 Skipped: 0



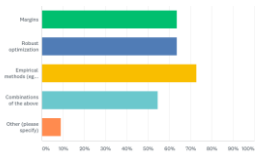
ANSWER CHOICES	RESPONSES	
Range calculation uncertainties	100.00%	11
Setup errors	100.00%	11
Intra-fractional anatomical variations (excluding interplay)	72.73%	8
Interplay effects between moving anatomy and scanning beam	36.36%	4
Inter-fractional anatomical variations (limited to variation in target position relative to other tissues, not severe changes)	36.36%	4
Variable RBE	36.36%	4
Other (please specify)	9.09%	1
Total Respondents: 11		

Other (please specify) We have introduced a 4D calculator, but at this time it is not widely used

Powered by SurveyMonkey

Q5: How are these uncertainties usually accounted for?

Answered: 11 Skipped: 0



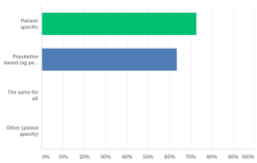
ANSWER CHOICES	RESPONSES	
Margins	63.64%	7
Robust optimization	63.64%	7
Empirical methods (eg multiple fields)	72.73%	8
Combinations of the above	54.55%	6
Other (please specify)	9.09%	1
Total Respondents: 11		

Other (please specify) Intrinsic robustness of large spot size

Powered by SurveyMonkey

Q6: Your approach for achieving and evaluating robustness is

Answered: 11 Skipped: 0

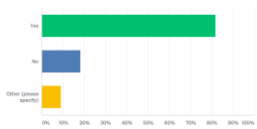


ANSWER CHOICES	RESPONSES	
Patient specific	72.73%	8
Population based (eg per treatment site)	63.64%	7
The same for all	0.00%	0
Other (please specify)	0.00%	0
Total Respondents: 11		

Powered by SurveyMonkey

Q7: Do you use SFUD or reduced modulation IMPT to increase plan robustness (eg specifying minimum isodose line for each field cover the target)?

Answered: 11 Skipped: 0



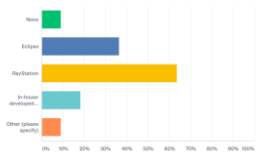
ANSWER CHOICES	RESPONSES	
Yes	81.82%	9
No	18.18%	2
Other (please specify)	9.09%	1
Total Respondents: 11		

Other (please specify) If SFO can be used then that is the first method.

Powered by SurveyMonkey

Q8: What software do you use for robust optimization?

Answered: 11 Skipped: 0

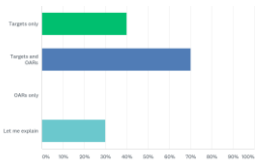


ANSWER CHOICES	RESPONSES	
None	9.09%	1
Eclipse	36.36%	4
RayStation	63.64%	7
In-house developed software	18.18%	2
Other (please specify)	9.09%	1
Total Respondents: 11		

Other (please specify)	We just introduced our in house method that includes biologic and robustness along with Monte Carlo calc during optimization.

Q9: Do you use robust objectives/constraints for

Answered: 10 Skipped: 1

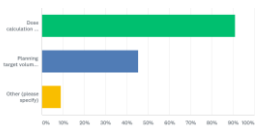


ANSWER CHOICES	RESPONSES	
Targets only	40.00%	4
Targets and OARs	70.00%	7
OARs only	0.00%	0
Let me explain	30.00%	3
Total Respondents: 10		

Let me explain	Sometimes targets only, sometimes targets and OARs
	Targets and select OARs, not all OARs
	Usually, margins and SFUD are used, sometimes robust for targets and OARs

Q10: How do you evaluate plan robustness to uncertainties?

Answered: 11 Skipped: 0

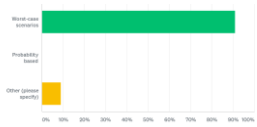


ANSWER CHOICES	RESPONSES	
Dose calculation of error scenarios	90.91%	10
Planning target volume coverage	45.45%	5
Other (please specify)	9.09%	1
Total Respondents: 11		

Other (please specify)	PTV for prostate, CTV coverage in scenarios for other sites.

Q11: Are the error scenarios

Answered: 11 Skipped: 0



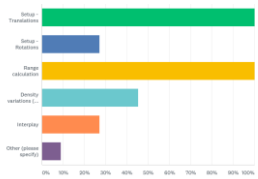
ANSWER CHOICES	RESPONSES	
Worst-case scenarios	90.91%	10
Probability based	0.00%	0
Other (please specify)	9.09%	1
Total Respondents: 11		

Other (please specify)	Each senario is independent, i.e. +x, -x, etc.

Powered by SurveyMonkey

Q12: For the error scenario calculation, which type of errors do you include?

Answered: 11 Skipped: 0



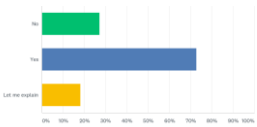
ANSWER CHOICES	RESPONSES	
Setup - Translations	100.00%	11
Setup - Rotations	27.27%	3
Range calculation	100.00%	11
Density variations (eg multiple CT sets)	45.45%	5
Interplay	27.27%	3
Other (please specify)	9.09%	1
Total Respondents: 11		

Other (please specify)	All get translation and range; for certain cases multiple CT sets are used, and certain cases we look at rotations, Interplay is just being indroduced.

Powered by SurveyMonkey

Q13: Is robustness performed and evaluated for every plan?

Answered: 11 Skipped: 0



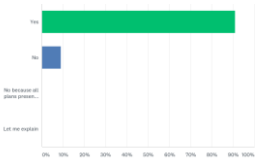
ANSWER CHOICES	RESPONSES	
No	27.27%	3
Yes	72.73%	8
Let me explain	18.18%	2
Total Respondents: 11		

Let me explain	Population-based
	For all PBS plans

Powered by SurveyMonkey

Q14: Is robustness considered during plan evaluation and selection?

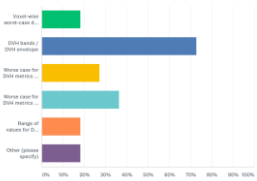
Answered: 11 Skipped: 0



ANSWER CHOICES	RESPONSES	
Yes	90.91%	10
No	9.09%	1
No because all plans presented are robust	0.00%	0
Let me explain	0.00%	0
Total Respondents: 11		

Q15: How do you present the results of robustness evaluation?

Answered: 11 Skipped: 0

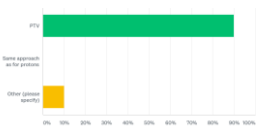


ANSWER CHOICES	RESPONSES	
Voxel-wise worst-case dose distribution	18.18%	2
DVH bands / DVH envelope	72.73%	8
Worse case for DVH metrics - Target coverage only	27.27%	3
Worse case for DVH metrics - Target coverage and OAR dose	36.36%	4
Range of values for DVH metrics	18.18%	2
Other (please specify)	18.18%	2
Total Respondents: 11		

Other (please specify)	Also look at the dose distribution of the robust scenarios for certain cases Evaluated by physics, presented only on request.

Q16: If your clinic also has conventional radiation, how do you deal with the uncertainties there?

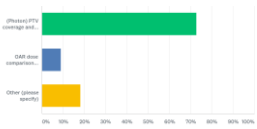
Answered: 10 Skipped: 1



ANSWER CHOICES	RESPONSES	
PTV	90.00%	9
Same approach as for protons	0.00%	0
Other (please specify)	10.00%	1
Total Respondents: 10		

Q17: How do you do deal with uncertainties and robustness for inter-modality plan comparisons?

Answered: 11 Skipped: 0



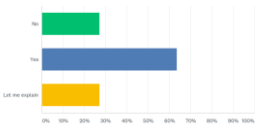
ANSWER CHOICES	RESPONSES	
(Photon) PTV coverage and OAR dose	72.73%	8
OAR dose comparison only, assuming that plans are equally robust	9.09%	1
Other (please specify)	18.18%	2
Total Respondents: 11		

Other (please specify)	photon robustness and proton one independently
	No intermodality plans, proton only.

Powered by SurveyMonkey

Q18: Do you compensate for range calculation errors with a margin?

Answered: 11 Skipped: 0



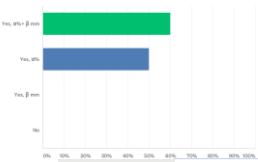
ANSWER CHOICES	RESPONSES	
No	27.27%	3
Yes	63.64%	7
Let me explain	27.27%	3
Total Respondents: 11		

Let me explain	Robust optimization
	Some times
	intrinsic robustness of large spot

Powered by SurveyMonkey

Q19: Do you use a recipe for this margin?

Answered: 10 Skipped: 1



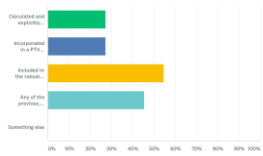
ANSWER CHOICES	RESPONSES	
Yes, α%+ β mm	60.00%	6
Yes, α%	50.00%	5
Yes, β mm	0.00%	0
No	0.00%	0
Total Respondents: 10		

Formula/values used	3.5% for PBS, 2.5% + 2mm for App/Comp based
	2.5%+1.5mm
	Variable; 3%+1mm; 2.3%+3mm (H&N/Brain)
	typically 3% but depends if there is hardware and other factors, somtimes 5%
	2.5, 1
	uniform scanning: 2.5%+2mm; PBS 3.5%

Powered by SurveyMonkey

Q20: How is this margin applied?

Answered: 11 Skipped: 0

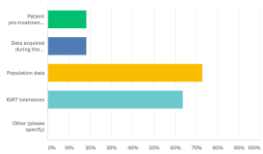


ANSWER CHOICES	RESPONSES	
Calculated and explicitly applied on each beam	27.27%	3
Incorporated in a PTV expansion	27.27%	3
Included in the robust optimization	54.55%	6
Any of the previous, depending on the site	45.45%	5
Something else	0.00%	0
Total Respondents: 11		

Powered by SurveyMonkey

Q21: How do you estimate setup errors?

Answered: 11 Skipped: 0

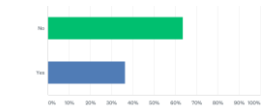


ANSWER CHOICES	RESPONSES	
Patient pre-treatment data	18.18%	2
Data acquired during the course of treatment	18.18%	2
Population data	72.73%	8
IGRT tolerances	63.64%	7
Other (please specify)	0.00%	0
Total Respondents: 11		

Powered by SurveyMonkey

Q22: Do you take into account the effect of fractionation in determining your random setup errors?

Answered: 11 Skipped: 0

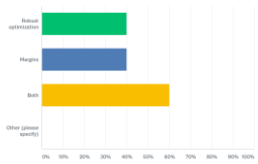


ANSWER CHOICES	RESPONSES	
No	63.64%	7
Yes	36.36%	4
Total Respondents: 11		

Powered by SurveyMonkey

Q23: How do you compensate for setup errors?

Answered: 10 Skipped: 1

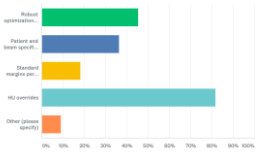


ANSWER CHOICES	RESPONSES	
Robust optimization	40.00%	4
Margins	40.00%	4
Both	60.00%	6
Other (please specify)	0.00%	0
Total Respondents: 10		

Powered by SurveyMonkey

Q24: How do you compensate for intra-fractional density variations?

Answered: 11 Skipped: 0



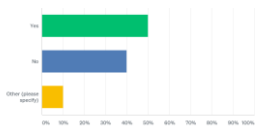
ANSWER CHOICES	RESPONSES	
Robust optimization - multiple images	45.45%	5
Patient and beam specific margins	36.36%	4
Standard margins per site	18.18%	2
HU overrides	81.82%	9
Other (please specify)	9.09%	1
Total Respondents: 11		

Other (please specify) not optimization, but verify plan on multiple images

Powered by SurveyMonkey

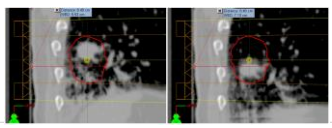
Q25: Do you calculate motion along the beams in WEPL (water equivalent pathlength)?

Answered: 10 Skipped: 1



ANSWER CHOICES	RESPONSES	
Yes	50.00%	5
No	40.00%	4
Other (please specify)	10.00%	1
Total Respondents: 10		

Other (please specify) I do not understand the question.

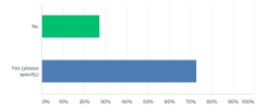


I meant the max difference in WEPL along the beam from the surface to the distal edge of the target during a breathing cycle. Stella

Powered by SurveyMonkey

Q26: Do you have limits of the observed motion above which PBS is not used?

Answered: 11 Skipped: 0



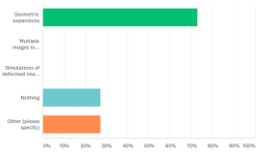
ANSWER CHOICES	RESPONSES	
No	27.27%	3
Yes (please specify)	72.73%	8
Total Respondents: 11		

Specify	0.5cm of target motion
	1cm but there are exceptions if motion management is heavily managed
	we use gating or breahold to reduce motion to below 1cm and include repaint
	less then 1.5 cm
	Breath hold is used in these cases
	1 cm limit
	5-10 mm
	1 cm

Powered by SurveyMonkey

Q27: How do you compensate for inter-fractional density variations? (for example relative prostate-to-bone position, not severe anatomical changes)

Answered: 11 Skipped: 0



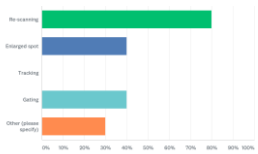
ANSWER CHOICES	RESPONSES	
Geometric expansions	72.73%	8
Multiple images in robust optimization	0.00%	0
Simulations of deformed images and/or contours in robust optimization	0.00%	0
Nothing	27.27%	3
Other (please specify)	27.27%	3
Total Respondents: 11		

Specify	re CT and dose assessment
	restrict motion between soft tissue and bone
	Robust evaluations

Powered by SurveyMonkey

Q28: For PBS, do you use any of the following to reduce interplay effect?

Answered: 10 Skipped: 1



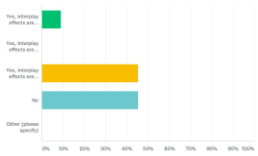
ANSWER CHOICES	RESPONSES	
Re-scanning	80.00%	8
Enlarged spot	40.00%	4
Tracking	0.00%	0
Gating	40.00%	4
Other (please specify)	30.00%	3
Total Respondents: 10		

Other (please specify)	We have a large spot but we do not treat moving targets yet
	multible beam angles
	Breath hold

Powered by SurveyMonkey

Q29: Do you have available tools to calculate interplay?

Answered: 11 Skipped: 0

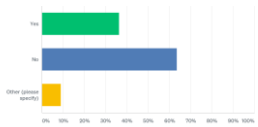


ANSWER CHOICES	RESPONSES	
Yes, interplay effects are calculated for all patients with breathing motion	9.09%	1
Yes, interplay effects are calculated for specific target size/position/motion groups	0.00%	0
Yes, interplay effects are calculated occasionally	45.45%	5
No	45.45%	5
Other (please specify)	0.00%	0
Total Respondents: 11		

Powered by SurveyMonkey

Q30: Does lack of interplay calculation tools prevent you for treating patients?

Answered: 11 Skipped: 0



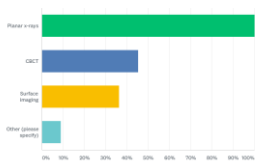
ANSWER CHOICES	RESPONSES	
Yes	36.36%	4
No	63.64%	7
Other (please specify)	9.09%	1
Total Respondents: 11		

Other (please specify)	if it is outside our comfort zone and if we did not have interplay calcuation then yes it would prevent treatment of some patients

Powered by SurveyMonkey

Q31: What image guidance do you use for treatment?

Answered: 11 Skipped: 0



ANSWER CHOICES	RESPONSES	
Planar x-rays	100.00%	11
CBCT	45.45%	5
Surface imaging	36.36%	4
Other (please specify)	9.09%	1
Total Respondents: 11		

Other (please specify)	CT on Rails

Powered by SurveyMonkey

Q32: If you are using a target surrogate for registration, what is it? (ie fiducial markers, bone, etc

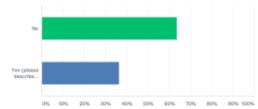
Answered: 8 Skipped: 3

Responses	For planer x-rays fiducials and bone depending the tx site
	Fiducial markers, wire on scars, bony anatomy
	sometimes bones, sometimes markers
	fiducial, bone
	Markers
	fiducials in prostate, bone elsewhere
	implanted marker, surgical clips, calcifications
	fiducial, bone

Powered by SurveyMonkey

Q33: Do you monitor motion during irradiation?

Answered: 11 Skipped: 0



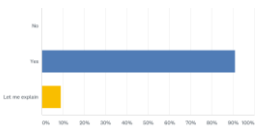
ANSWER CHOICES	RESPONSES	
No	63.64%	7
Yes (please describe briefly your method)	36.36%	4
Total Respondents: 11		

Yes (please describe briefly your method)	surface imaging
	Anzai laser interferometer, which functions like a RPM
	surface imaging
	RPM

Powered by SurveyMonkey

Q34: Do you verify the dose distribution with QA CTs acquired throughout treatment?

Answered: 11 Skipped: 0



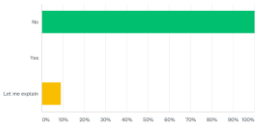
ANSWER CHOICES	RESPONSES	
No	0.00%	0
Yes	90.91%	10
Let me explain	9.09%	1
Total Respondents: 11		

Let me explain	Population-based

Powered by SurveyMonkey

Q35: Do you use CBCT-based virtual CTs to calculate dose and/or adapt plans?

Answered: 11 Skipped: 0



ANSWER CHOICES	RESPONSES	
No	100.00%	11
Yes	0.00%	0
Let me explain	9.09%	1
Total Respondents: 11		

Let me explain In research phase to caclulate vCT

Powered by SurveyMonkey

Q36: What percentage of your patients do you think have modifications to their plans?

Answered: 9 Skipped: 1

Responses
30%
45
25%
22%, 31% of non-prostate
40 to 50%
10
10
20
30%
5-15%

Powered by SurveyMonkey

Q37: What tools do you think you are missing for efficient robust treatment planning?

Answered: 7 Skipped: 4

Responses
Faster calculation and optimization times. Better tools to present robustness data to physicians.
Interplay calculator, fast error scenario calculator
Doing worst case optimization is suboptimal, can miss certain things. Multi-image and 4D optimization including robustness is needed. Having robust biological planning is also needed.
RS7 is coming out with deformed target contour for robust optimization. After that, I think we need in-room Proton CT to deal with uncertainty once and for all.
Currently, we evaluate scenarios independently after optimization. It would be ideal if dose information from robust optimization was saved and displayed. We look forward to using the new tools when we upgrade to RS8a.
Automated analysis
Fast Monte Carlo. Would like to avoid the "garbage-in-garbage-out" effect.

Powered by SurveyMonkey

Q38: Do you have something to add?

Answered: 2 Skipped: 9

Responses	It would be nice to see "PTV" concept totally gone from proton and photon therapy and use of robust optimization be mainstream.
	These surveys are a great idea. This is the second one I have filled out so far. Have you published any results yet?

I like them too. I am afraid though that people are tired of them. I think it would be difficult to publish this with so few responses. Stella