Motion Mitigation in Spot Scanning Proton Therapy with An Automated Gating System and Voluntary Breath Holding

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Disclosures

No Conflicts of Interest

Outline

Introduction	Part 1: Commissioning & Implementation	Part 2: Dosimetric Comparisons	Part 3: Breath-hold Plan Reproducibility

• Motion Management
  ○ Spirometry System
• Gated Voluntary Breath Hold (SDX): Process Overview
	• Preparation & Patient Training
	• Initial SIM
	• Image Guidance and Treatment
		Breath Hold vs Non-Breath Hold
		• Patient Data & Analysis
		• Results:
		  ○ Liver
		  ○ Lung
			Breath Hold Plans
			• Patient Data & QACT Evaluation
			• Results:
			  ○ Target Coverage
			  ○ OAR Dose

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Varian ProBeam

5 room facility (4 gantries, 1 fixed beam)
- First treatment in February 2016
- 4 of 5 treatment rooms open and treating

- In all treatment gantries:
  - Pencil Beam Scanning (IMPT)
  - Volumetric imaging (cone beam CT)

1 Fixed beam room 4 Gantry rooms(Current clinical rooms)

Maryland Proton Treatment Center (MPTC)
University of Maryland

Siemens Definition Edge DECT
Dual Spiral Scan & TwinBeam

Siemens Aera MRI Scanner
1.5 T

Special Treatment

SDX breath-hold system
Dyn'R

- First SDX patient: March 2018
- # of SDX patients = 45
- Liver, lung, esophagus, …

Deep Thermal Therapy (DTT)
BSD-2000, Pyrexar

- First DTT patient: Oct 2018
- # of DTT patients = 20
- Pelvic and abdominal regions

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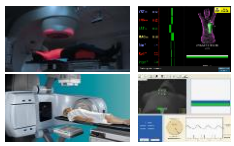
Motion Management

- **External breathing metrics** have been demonstrated useful in
  - Predicting the tumor motion
  - Reducing respiratory motion uncertainties
  - Sparing organs at risk
- **Breath-hold (BH) technique**
  - Mitigates motion of the target
  - Minimizes target margins
  - Improves normal-tissue sparing

Vedam, et al. Phys. Med. Biol. 48, 2003
Low et al. Med. Phys. 30, 2003

Motion Management

- There are different voluntary BH techniques
  - Non-spirometric (external surrogates)
    - Surface imaging (Vision RT)
    - Real-time Position Management (RPM)
    - ….



  - Spirometric (internal volumetric air flow)
    - Active Breathing Coordinator (ABC)
    - SDX with video guidance
    - ….

Motion Management

The **spirometry system** monitors the patient's breathing phase in real time.

Advantages:
- Clinical feasibility
  - Reduces tumor motion
  - Reduces treatment margins, …
- Audio-visual feedback improves reproducibility
- Gated treatment delivery
- Accurate surrogate for internal respiratory motion

Disadvantages:
- Signal drift
- Increase in the volumetric tidal flow compared to normal breathing (without spirometer)
- Uncomfortable for patients
- Gating module is not compatible for all treatment delivery systems
- Still is only a surrogate

Lu et al. Med. Phys. 32 (7), 2005
Gilbert et al. J. Appl. Physiol. 33, 1972
Askanazi et al. J. Appl. Physiol. 48, 1980

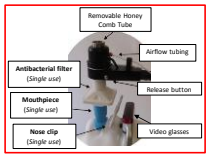
SDX System

At MPTC we use **SDX system** (Dyn'R, France)

- Voluntarily breath-hold technique

SDX System

- Airflow tube
- Filter
- Mouthpiece
- Nose clip
- Video glasses (goggle)



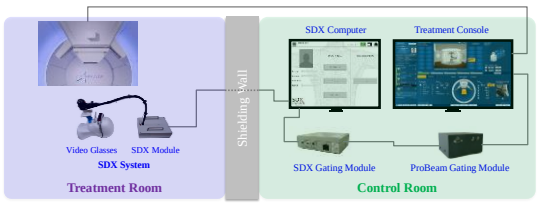
SDX – Beam connection

SDX components:

- SDX System
- SDX Computer
- SDX Gating Module

ProBeam components:

- ProBeam Gating Module
- Treatment Console
- ProBeam Nozzle



SDX Calibration & Calibration Check

Calibration Syringe

A **daily calibration/verification** must to be done on the SDX System

- Using a 3-Liter calibration syringe serving as a volumetric reference

3-Liter calibration syringe

- Check signal drift (problem of spirometry system)

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SDX Commissioning

The SDX system with automatic gating module was commissioned at MPTC

- Goal: Check the effect of breathing interruption on delivered dose
  - Point and 2D-planar dose measurements of 5 gated plans (3-4 fields per plan) with and without range shifter.

Site	Beam Delivery Type	# of Fields	Range Shifter
Esophagus	SFO	3	None
Esophagus	SFO	3	None
Lung	SFO	3	5 cm
Lung	MFO	4	5 cm
Abdomen	MFO	3	None / 2 cm

  - For each field: three measurements with 2, 3 and 5 breath-hold were done and evaluated against the one without breath-hold (reference).
    - Point dose (%difference)
    - 2D-planar dose gamma passing rate (1%/1mm)

SDX Commissioning

Results:

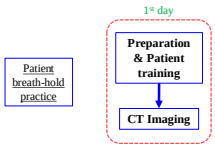
Site	Beam Delivery Type	Field ID	Range Shifter (cm)	Point Dose %Diff			Gamma Index Passing Rate % [1%/1mm]		
				2 BH	3 BH	5 BH	2 BH	3 BH	5 BH
Esophagus	SFO	1	0	0.20%	0.20%	-0.20%	100	100	99.4
		2	0	-0.20%	0.00%	0.00%	100	100	100
		3	0	-0.20%	-0.40%	0.00%	100	100	100
Esophagus	SFO	1	0	0.20%	0.20%	0.20%	98.2	98.5	98.2
		2	0	-0.20%	0.00%	0.00%	100	100	100
		3	0	0.00%	0.00%	0.00%	100	100	100
Lung	SFO	1	5	0.00%	0.00%	-0.20%	100	100	100
		2	5	0.00%	0.20%	-0.20%	100	100	100
		3	5	0.20%	0.20%	0.20%	100	100	100
Lung	MFO	1	5	0.00%	-0.10%	0.00%	100	100	100
		2	5	0.10%	0.00%	0.00%	100	100	100
		3	5	0.00%	0.00%	0.20%	98.6	97.2	97.9
		4	5	0.00%	0.00%	-0.20%	100	100	100
Abdomen	MFO	1	0	0.00%	0.00%	-0.30%	100	100	100
		2	2	0.00%	0.00%	0.00%	100	100	100
		3	0	0.00%	0.00%	-0.20%	100	100	100

Between non-breath-hold and breath-hold (reference) plans:

- The maximum percent difference of point dose measurements: 0.4%
- The lowest gamma passing rate: 97.2%

Gated Voluntary Breath Hold: Process Overview

SDX Treatment Process:



Patient instruction:

- How to breathe and hold the breath through the spirometer

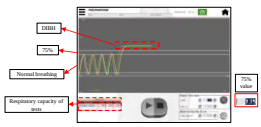
Set breath-hold level:

- Find the deepest inspiration breath-hold (DIBH)
- 70% to 80% of DIBH will be set as the breath-hold level

Preparation: Set breath-hold level and training

- Acquire 3-5 breath holds to establish the deep inspiration breath-hold level (DIBH)

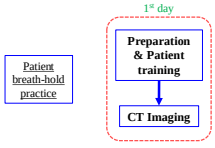
- Reduce the selected level to 75-80%
  - More comfortable
  - More reproducible
  - 75% is the default value
    - It can be adjusted



- Patient breath-hold practice (reproducibility)

Gated Voluntary Breath Hold: Process Overview

SDX Treatment Process:



Patient instruction:

- How to breathe and hold the breath through the spirometer

Set breath-hold level:

- Find the deepest inspiration breath-hold (DIBH)
- 70% to 80% of DIBH will be set as the breath-hold level

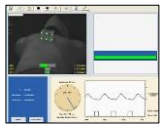
Initial CT simulation:

- SDX breath-hold system
- Normal 4D-CT (as a backup treatment)

Initial Simulation

- Imaging (CT):
  - SDX CT (manual)
    - Patient holds the breath at pre-established breath-hold level
    - The therapist starts CT scan acquisition
    - If patient goes out of breath-hold level, the therapist **Stops the imaging manually**

  - Normal 4D-CT (backup plan)



Why Did We Need a Backup Plan?

- First ProBeam center using SDX system (March 2018)
- SDX v2.06
  - Connectivity & software issues of SDX system
- One SDX device in one of the treatment rooms
  - SDX problem
  - Treatment room problem

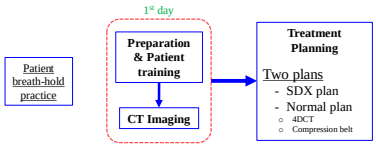
SDX v2.06

- Upgraded to v3.03 and then v3.11 (2019)
  - Much less connectivity & software issues
  - Bought the second SDX system

SDX v3.11

Gated Voluntary Breath Hold: Process Overview

SDX Treatment Process:



Treatment planning on both image sets:

- SDX plan
- Normal plan (4DCT, compression belt) as a backup plan

Physician plan evaluation

Gated Voluntary Breath Hold: Process Overview

SDX Treatment Process:

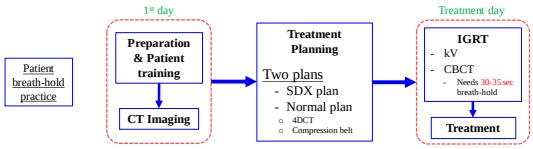


Image guidance:

- kV and CBCT images will be acquired at the pre-defined breath-hold level

Treatment:

- with the automatic gating module active and connected to the ProBeam system

Image Guidance and Treatment

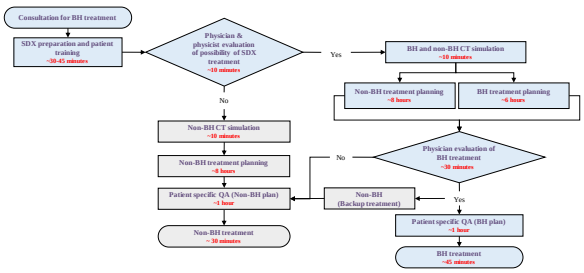
For ProBeam system:

- IGRT (manual)
  Stop the imaging manually
  – kV
  – CBCT (small FoV– full fan, ~30 secs)

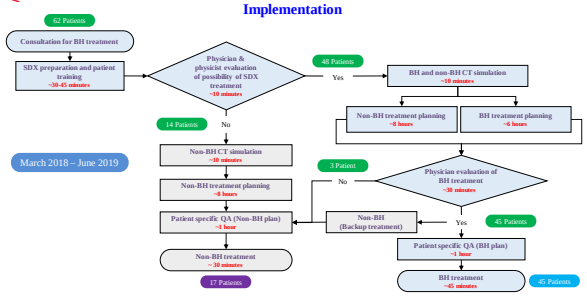
- Treatment: (automatic)
  – Automatic Gating Module **immediately stops the beam**

- Monitoring:
  – Weekly QA-CT:
  tumor response, anatomical changes

Implementation



Implementation



SDX Patients Summary

- First SDX patient: March 2018
- Total number of referred patients = **62** (until June 2019)
  - 14 patients excluded — Couldn't hold breath > 20 seconds
  - 48 patients underwent SDX simulation
    - 45 patients either treated or will be treated with SDX plans
    - For 2 patients non-breath-hold plan was chosen over the breath-hold plan
      - Higher dose to the heart due to tumor location
    - 1 patient couldn't tolerate breath-hold treatment and switched to non-breath-hold plan.

Status	Number of Patients
Treated	37
Under treatment	5
In planning phase	3

Site	Number of Patients
Liver	20
Mediastinum/Lung	14
Abdomen	5
Pancreas	3
Esophagus	3

Part 1: Summary & Recommendations

- What sites?
  - For any moving tumor due to respiratory motion
  - Patient should be able to hold breath >25 seconds (for current ProBeam system)
- The Smaller the target, the easier to implement this procedure
  - Preferably < 2 minutes delivery time per field (3-4 breath-holds)
- Ask patient to practice breath-hold before coming for initial CT and also treatment
- Make two treatment plans (SDX and normal) at the beginning
  - System reliability and limitations
- Image guidance
  - kV & CBCT (small FoV– full fan) if patient can hold the breath for 30-35 seconds
- Weekly QA-CT
  - tumor response, anatomical changes

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• Motion Management ○ Spirometry System • Gated Voluntary Breath Hold (SDX): Process Overview	• Preparation & Patient Training • Initial SIM • Image Guidance and Treatment	*Breath Hold vs Non-Breath Hold* • Patient Data & Analysis • Results: ○ Liver ○ Lung	*Breath Hold Plans* • Patient Data & QACT Evaluation • Results: ○ Target Coverage ○ OAR Dose

Breath-hold vs Non-Breath-hold Plans

Breath-hold (BH) technique
- Mitigates motion of the target
- Minimizes target margins
- Improves normal-tissue sparing

Before SDX upgrade and the second SDX system purchase
- One SDX device in one of the treatment rooms
  - SDX problem (connection and software issues)
  - Treatment room problem
- Therefore, for each patient we had a backup plan on 4DCT

Purpose:
We investigate the dosimetric comparison between breath-hold and non-breath-hold plans.

Breath-hold vs Non-Breath-hold Plans

- Twenty-seven patients treated with SDX system were used
- The breath-hold level was set to 75% of DIBH
- Clinically acceptable were created
  - Breath-hold plan (breath-hold CT)
  - Non-breath-hold plan (4D-CT)
- The dose-volume histograms (DVH) of the two plans were compared for OAR sparing
  - Mean dose: Liver, stomach, kidney, esophagus, heart
  - Max dose: Small bowel, large bowel, heart, spinal cord

Site	Number of Patients
Liver	11
Mediastinum/Lung	10
Abdomen	3
Pancreas	2
Esophagus	1

Breath-hold vs Non-Breath-hold Plans

Summary of 27 patients data

Parameter	Target or OAR
Volume (cc)	Initial Target (CTV1/ITV1)
	SFB Target (CTV2/ITV2)
Mean Dose (cGy)	Liver
	Stomach
	Kidney
	Esophagus
	Heart
V20 (%)	Lung
Max Dose (cGy)	Small Bowel
	Large Bowel
	Heart
	Spinal Cord

Breath-hold vs Non-Breath-hold Plans

Summary of 27 patients data

Parameter	Target or OAR	Breath-Hold Plan	Non-Breath-Hold Plan
Volume (cc)	Initial Target (CTV1/ITV1)	238.0 ± 251.0	344.9 ± 376.8
	SFB Target (CTV2/ITV2)	99.1 ± 121.1	145.2 ± 164.0
Mean Dose (cGy)	Liver	730.7 ± 817.8	886.1 ± 912.4
	Stomach	624.5 ± 1105.1	1039.5 ± 1717.9
	Kidney	187.2 ± 344.8	309.7 ± 444.5
	Esophagus	876.6 ± 846.2	959.8 ± 938.4
	Heart	276.0 ± 298.7	412.4 ± 460.2
V20 (%)	Lung	6.74% ± 5.79%	10.74% ± 8.73%
Max Dose (cGy)	Small Bowel	1504.2 ± 2018.7	1952.5 ± 1967.2
	Large Bowel	779.0 ± 1315.7	1938.9 ± 1988.6
	Heart	3062.4 ± 1830.6	3277.7 ± 1843.4
	Spinal Cord	1155.5 ± 1353.0	1396.5 ± 1447.8

Absolute values

Breath-hold vs Non-Breath-hold Plans

Summary of 27 patients data

Parameter	Target or OAR	Breath-Hold Plan	Non-Breath-Hold Plan	Ratio of Breath-hold Normalized to Non-Breath-Hold (%)
Volume (cc)	Initial Target (CTV1/ITV1)	238.0 ± 251.0	344.9 ± 376.8	69.72% ± 23.80%
	SFB Target (CTV2/ITV2)	99.1 ± 121.1	145.2 ± 164.0	69.22% ± 22.12%
Mean Dose (cGy)	Liver	730.7 ± 817.8	886.1 ± 912.4	71.85% ± 27.36%
	Stomach	624.5 ± 1105.1	1039.5 ± 1717.9	71.39% ± 52.07%
	Kidney	187.2 ± 344.8	309.7 ± 444.5	66.82% ± 35.79%
	Esophagus	876.6 ± 846.2	959.8 ± 938.4	90.53% ± 16.20%
	Heart	276.0 ± 298.7	412.4 ± 460.2	75.27% ± 23.43%
V20 (%)	Lung	6.74% ± 5.79%	10.74% ± 8.73%	76.79% ± 56.33%
Max Dose (cGy)	Small Bowel	1504.2 ± 2018.7	1952.5 ± 1967.2	81.41% ± 44.25%
	Large Bowel	779.0 ± 1315.7	1938.9 ± 1988.6	58.26% ± 39.96%
	Heart	3062.4 ± 1830.6	3277.7 ± 1843.4	93.99% ± 16.18%
	Spinal Cord	1155.5 ± 1353.0	1396.5 ± 1447.8	83.82% ± 51.41%

Absolute values Normalized values

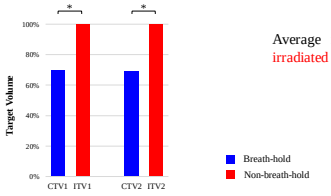
Breath-hold vs Non-Breath-hold Plans

Summary of 27 patients data

Parameter	Target or OAR	Breath-Hold Plan	Non-Breath-Hold Plan	Ratio of Breath-hold Normalized to Non-Breath-Hold (%)	p-value	Number of Patients
Volume (cc)	Initial Target (CTV1/ITV1)	238.0 ± 251.0	344.9 ± 376.8	69.72% ± 23.80%	<0.05	27
	SFB Target (CTV2/ITV2)	99.1 ± 121.1	145.2 ± 164.0	69.22% ± 22.12%	<0.05	11
Mean Dose (cGy)	Liver	730.7 ± 817.8	886.1 ± 912.4	71.85% ± 27.36%	<0.05	21
	Stomach	624.5 ± 1105.1	1039.5 ± 1717.9	71.39% ± 52.07%	0.06	15
	Kidney	187.2 ± 344.8	309.7 ± 444.5	66.82% ± 35.79%	<0.05	16
	Esophagus	876.6 ± 846.2	959.8 ± 938.4	90.53% ± 16.20%	0.06	21
	Heart	276.0 ± 298.7	412.4 ± 460.2	75.27% ± 23.43%	<0.05	24
V20 (%)	Lung	6.74% ± 5.79%	10.74% ± 8.73%	76.79% ± 56.33%	<0.05	20
Max Dose (cGy)	Small Bowel	1504.2 ± 2018.7	1952.5 ± 1967.2	81.41% ± 44.25%	0.17	13
	Large Bowel	779.0 ± 1315.7	1938.9 ± 1988.6	58.26% ± 39.96%	<0.05	12
	Heart	3062.4 ± 1830.6	3277.7 ± 1843.4	93.99% ± 16.18%	0.06	24
	Spinal Cord	1155.5 ± 1353.0	1396.5 ± 1447.8	83.82% ± 51.41%	<0.05	26

Breath-hold vs Non-Breath-hold Plans

Ratio of Breath-hold Normalized to Non-Breath-Hold (%)



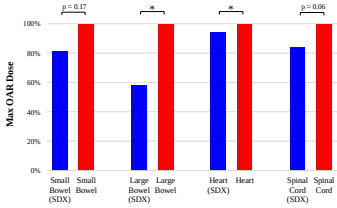
Average reduction of 30% in the irradiated volume with SDX

* p < 0.05

27 patients 11 patients

Breath-hold vs Non-Breath-hold Plans

Ratio of Breath-hold Normalized to Non-Breath-Hold (%)



Average max dose reduction with SDX:

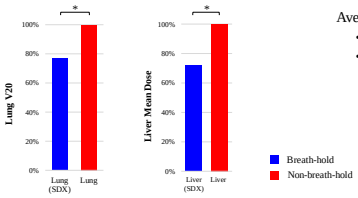
- Small Bowel: 20%
- Large Bowel: 42%
- Heart: 5%
- Spinal cord: 18%

* p < 0.05

13 patients 12 patients 24 patients 26 patients

Breath-hold vs Non-Breath-hold Plans

Ratio of Breath-hold Normalized to Non-Breath-Hold (%)



Average reduction with SDX:

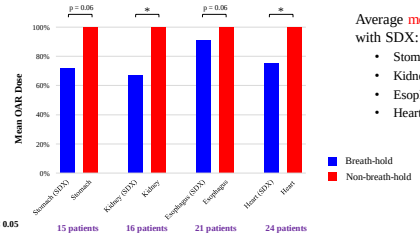
- Lung V20: 25%
- Liver Mean dose: 30%

* $p < 0.05$

20 patients 21 patients

Breath-hold vs Non-Breath-hold Plans

Ratio of Breath-hold Normalized to Non-Breath-Hold (%)



Average mean dose reduction with SDX:

- Stomach: 28%
- Kidney: 32%
- Esophagus: 10%
- Heart: 25%

* $p < 0.05$

15 patients 16 patients 21 patients 24 patients

Breath-hold vs Non-Breath-hold Plans

Ratio of Breath-hold Normalized to Non-Breath-Hold (%)

- Liver group (11 patients)
- Mediastinum/lung group (10 patients)

Site	Number of Patients
Liver	11
Mediastinum/Lung	10
Abdomen	3
Pancreas	2
Esophagus	1

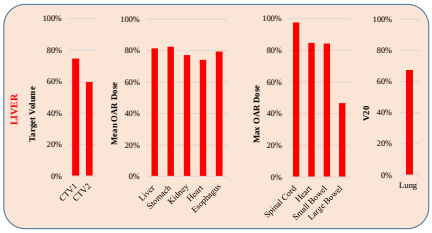
Breath-hold vs Non-Breath-hold Plans

Liver group (11 patients)

Ratio of Breath-hold Normalized to Non-Breath-Hold (%)

Reduction:

- Target Volume ~25-40%
- Mean OAR Dose ~ 20%
- Max OAR Dose ~ 5-50%
- Lung V20 ~ 35%



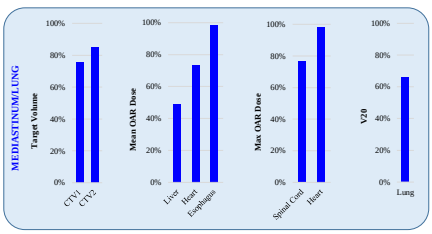
Breath-hold vs Non-Breath-hold Plans

Mediastinum/lung group (10 patients)

Ratio of Breath-hold Normalized to Non-Breath-Hold (%)

Reduction:

- Target Volume ~15-25%
- Mean OAR Dose ~ 5-50%
- Max OAR Dose ~ 5-25%
- Lung V20 ~ 35%



Part 2: Conclusions

- Breath-hold plans can significantly reduce the treated target volume to ~70-80%.
  - Liver group: 60-75%
  - Mediastinum/lung group: 75-85%
- For organs most affected by respiratory motion (lung and liver), BH technique consistently reduced dose by 20-25%
- For other OARs, BH plans resulted in lower
  - Mean dose by as much as 10-35%.
  - Max dose by as much as 5-40%.

Introduction	Part 1: Commissioning & Implementation	Part 2: Dosimetric Comparisons	Part 3: Breath-hold Plan Reproducibility
• Motion Management ○ Spirometry System • Gated Voluntary Breath Hold (SDX): Process Overview	• Preparation & Patient Training • Initial SIM • Image Guidance and Treatment	*Breath Hold vs Non-Breath Hold* • Patient Data & Analysis • Results: ○ Liver ○ Lung	*Breath Hold Plans* • Patient Data & QACT Evaluation • Results: ○ Target Coverage ○ OAR Dose

Breath-hold Plan Reproducibility

Breath-hold (BH) technique
- Mitigates motion of the target
- Minimizes target margins
- Improves normal-tissue sparing

Do we need to monitor the reproducibility of the plan?

Can we use the same plan for the whole course of treatments?

Our recommendation for SDX plans:

Weekly QA-CT

Tumor response, anatomical changes

Assessing the reproducibility of SDX plans

QACT Patients Summary

We use 5mm robust evaluation for SDX plans.

- Reproducibility of the breath-hold plans were assessed by
  - Using QACT scans for each patient
  - Re-calculating the initial treatment plan on the QACT scans.

QACT of SDX patients	
Number of Patients	30
Total Number of QACTs	62

Site	Number of Patients
Liver	14
Mediastinum/Lung	10
Abdomen	2
Pancreas	3
Esophagus	1

Purpose:

We investigate the reproducibility of breath-hold plans using frequent quality assurance CT scans (QACTs).

QACT Evaluation

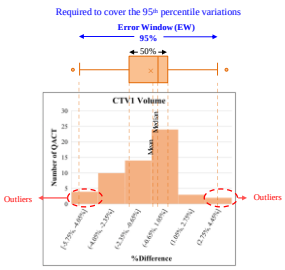
At MPTC, decision for replan or repeat of QACT based on:

- Target V95% decreased by more than 5% of the initial plan, or
- Dose to critical organs at risk (OARs) increased significantly (physician decision)

To evaluate the reproducibility of BH plan, we looked at

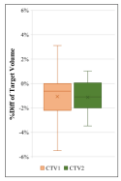
- DVH variations of QACT plans with respect to the initial CT plan
- Errors reported as percent difference (for target) and absolute dose difference (for OARs) with respect to initial plan
- Error window (EW) required to cover the 95th percentile variations

Target Volume



Volume:
CTV1 → EW ~ 8.6%
(initial plan, 28 patients)

CTV2 → EW ~ 4.5%
(boost plan, 9 patients)



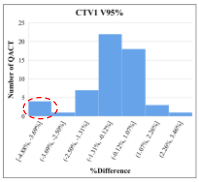
Target Coverage

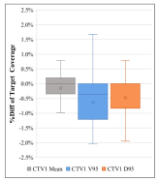
V95, D95, and Mean Dose

Variation in target coverage (V95) was < 5%

Mean dose → EW ~ 1.8%

V95% → EW ~ 3.7%





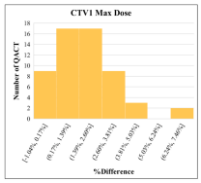
Two replans due to **change in target coverage and OAR dose** as a result of anatomical changes

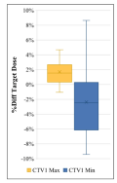
Target Coverage

Maximum and Minimum Dose

CTV1 Max dose → EW ~ 5.7%

CTV1 Min dose → EW ~ 18.1%





Larger variations observed in maximum and minimum doses

OAR Dose

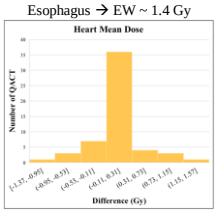
Mean Dose

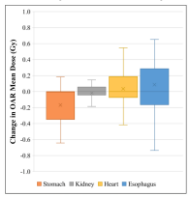
Heart → EW ~ 1.0 Gy

Esophagus → EW ~ 1.4 Gy

Stomach → EW ~ 0.8 Gy

Kidney → EW ~ 0.3 Gy





OAR Dose

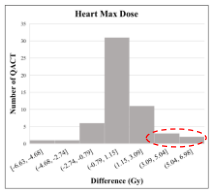
Max Dose

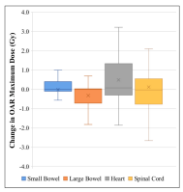
Heart → EW ~ 5.1 Gy

Spinal Cord → EW ~ 4.8 Gy

Small Bowel → EW ~ 1.6 Gy

Large Bowel → EW ~ 2.5 Gy



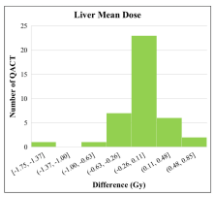


Two replans due to **significant change in heart dose** as a result of anatomical changes

OAR Dose

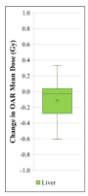
Lung and Liver

Variation comparable to other organs despite associated respiratory motion



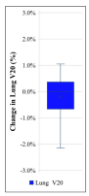
Liver Mean Dose:

EW ~ 0.9 Gy



Lung V20:

EW ~ 3.2%



Part 3: Summary & Conclusions

- Out of 30 patient plans:
  - We had 4 replans due to tumor volume and/or anatomical changes
- Breath-hold technique can manage respiratory motion
  - Lung V20 and liver mean dose are comparable to other organs
- In the absence of anatomical changes, coverage and OAR doses were reproducible within clinically acceptable margins
- Using 5 mm robust evaluation gives fairly reproducible plan
- Small variations in the target coverage (V95%)
- Larger variations observed in maximum and minimum doses for the target and OARs

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