IMPT for lung cancer: Physics Consideration

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• 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 $\geq 40$ 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

- Significant increase in late rectal complications when more than 25% of rectum received 70 Gy above.
Experience and learning curve matters

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

Solid: PSPT, dashed IMRT | Solid: 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

- 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
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

“PTV” is not a good concept for IMPT

- Better PTV coverage (dashed line) does not necessarily 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

PSPT

IMPT

Volume (%)

Dose (Gy)

GTV  CTV  Brainstem  Left temporal lobe  Optic chiasm  Right optic nerve
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.

It is not recommended based on motion analysss.

Hope we can put her on trial. Thanks.
4D Interplay/dynamic Dose

IMPT treatment plan

4D Interplay Dose Simulator

Dose Distribution

Images and deform vectors

Breathing Pattern
Time Stamps in the Spot Scanning

For MU>0.04, spot is repainted

- Beam on max 10 ms for max MU 0.04
- Beam off 3 ms
- Pulse max 4.4 s (hundreds of beam on/off)
- Pulse off 2.1 s
- Energy switch 2.1 s
- Map scan of each spot to a resp. phase

Random respiratory phase at beginning of a field or fraction
“1FX dynamic dose” as a surrogate to evaluate the robustness of the plan against interplay effects.

- Patient 4:
  - Volume: 358.24 cc
  - Motion: 0.46 cm

- Patient 5:
  - 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

• Reduce the max MU for each spot → Effectively increase number of isolayer repainting and treatment delivery time
Reduce the max MU for each spot: iso-layer repainting

• 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

- 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
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.
Physicist’s recommendation and physician’s response

- 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
New plan and new QA

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

The analysis of the Mosaic-like measurements for the MFORB new 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.

<table>
<thead>
<tr>
<th>Field 1</th>
<th>Field 2</th>
<th>Field 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1%</td>
<td>0.8%</td>
<td>1.1%</td>
</tr>
<tr>
<td>99.55%</td>
<td>100.00%</td>
<td>100.00%</td>
</tr>
<tr>
<td>94.02%</td>
<td>99.98%</td>
<td>98.66%</td>
</tr>
</tbody>
</table>

-Matt
Current “QA” workflow to check the accuracy of the dose calculation

Plan rejected

Agree?

No

Yes
Propose workflow to address some “accuracy” issue

2nd Check

Plan rejected

Agree?

Yes

HPlusQA

Plan rejected

No

Agree?

Yes
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

• 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 …
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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, indeed suffered from acute rectal toxicity. In the respective IMRT plan, only 16.6% of the rectal volume received 70 Gy more.
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

No EA

ACS: Tx mode

EA

ACS: Physics mode