Technology and Clinical Implementation of $4\pi$ Radiotherapy:
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Outline
• Technical development
• Clinical implementation
• Future directions

High BED is essential to achieve tumor local control for large locally advanced lung cancer. Zhao et al. IJROBP Volume 68, Issue 1, 1 May 2007, Pages 103–110.

Non-coplanar radiotherapy is not new

• Non-coplanar beams and arcs show definite advantages for intracranial SRS and are ubiquitously used in these treatments
• Non-coplanar beams are less systematically used for extracranial treatment

Manually selecting non-coplanar beams and arcs becomes increasingly difficult and inefficient as the complexity of treatment planning and intensity modulation increases. Automation of beam orientation and fluence optimization is essential in phase I and II radiotherapy.
Phase I: Beam orientation and fluence optimization
Pricing approach and column generation

Candidate beam or beamlet

Fluence optimization is performed

Predict the value of the objective using KKT conditions

Candidate pool (1162 beams)

Phase II: Sparsity on the structured beamlets

Encouraging sparsity on the beams

Encouraging sparsity on the structured beams

Solving the group sparsity optimization problem

\[ \min_{x} \frac{1}{2} \| F - Ax \|_2^2 + \sum_{i=1}^{N} \left( \frac{1}{2} \| A_{i} x_{i} - y_{i} \|_2^2 + \frac{\mu}{2} \| x_{i} \|_{2,1} \right) \]

\[ f(x) = \frac{1}{2} \| F - Ax \|_2^2 + \sum_{i=1}^{N} \frac{1}{2} \| A_{i} x_{i} - y_{i} \|_2^2 + \frac{\mu}{2} \| x_{i} \|_{2,1} \]

\[ g(x) = \begin{cases} \sum_{i=1}^{N} \| x_{i} \|_{2,1} & \text{if } x \geq 0, \\ \infty & \text{otherwise.} \end{cases} \]
Gradient of $f$

$$f(x) = \frac{1}{2} \| (I - Ax) \|_2^2 + \sum_{i=1}^{n} \frac{\alpha_i}{2} \| Ax - d_i \|_2^2 + \frac{\alpha_i}{2} \| Ax \|_2^2 - \| D x \|_0^0$$

$$\nabla f(x) = -A^T (I - Ax)_+ + \sum_{i=1}^{n} \alpha_i A^T (Ax - d_i)_+ + \beta A^T A x + \frac{\beta}{\mu} D^T P_{\mu \alpha}(D x).$$

Proximal operator of $g$

$$\text{prox}_g(y) = \begin{bmatrix} \text{prox}_{\mu \alpha}(x_1) \\ \text{prox}_{\mu \alpha}(x_2) \\ \vdots \\ \text{prox}_{\mu \alpha}(x_p) \end{bmatrix}, \quad \text{prox}_{\mu \alpha}(x) = \text{prox}_{\mu \alpha}(\| x \|_2, 0).$$

Derivation of the proximal operator is the key to enable FISTA

Convergence comparison

FISTA converges $\sim 1/k^2$ vs. Chambolle-Pock $\sim 1/k$. Chambolle-Pock does not achieve the desired beam sparsity.

Solving the optimization problem in ~ 5 mins using FISTA.
Reduce R50 by 54%, increase EUD of heart, esophagus, trachea, bronchus, and spinal cord were reduced by 44%, 74%, 6%, 42%, and 51%

Optimization using group sparsity takes ~5 minutes

Potential for no cost tumor dose escalation?

Clinical IMRT plan 50Gy

Achieving greater tumor dose without increasing normal tissue doses

Avoid Radiation Pneumonitis
Liver cancer SBRT

The mean normal liver volume receiving <15 Gy was increased by 51 cc (range 21 - 107 cc) with a 31% reduction of the mean normal liver dose.

3D isodose cloud comparison between non-coplanar 4π and coplanar plans

IMRT Dose sculpting

You have seen this......
Compact dose distribution

...but not this

Non-coplanar beams require couch rotation (kick) that significantly increases the risk of collision that could have fatal consequences.
3D optical surface acquisition

- Two pairs of wall-mounted 3D stereo cameras in CT simulation room
- Low-pass filters to reduce sensitivity to room lighting
- Surface accuracy verified by scanning cubic phantom
- <2mm discrepancy
- Patient and phantom surfaces acquired immediately after CT simulation to ensure consistent setup

Case-specific collision maps

- Minimum achievable source to target distances for 1162 evenly spaced candidate beams
- Programmatic exhaustive search

Virtual simulation of treatment

4x extracranial therapy can be non-isocentric
**Manual vs. automated delivery**

- Total treatment time: 45 minutes
- Automated delivery of the same playback speed (8-12 minutes)

**Phase I 4π clinical trial study design**

- Patient
  - 4π plan
  - Conventional plan
  - 4π superior or equivalent?
    - Yes
    - No
  - Treat with 4π
  - Treat conventional plan

Aims: Safety, tolerance, treatment time and intrafractional motion

**Steeper dose gradient spares previously treated OARs**

- Standard
  - 4π plan
  - 4π plan was recalculated in Eclipse to generate a clinical plan
  - Composite plan of the original and the new recurrent plan
  - 12 patients treated using 4π
  - 4π spine SBRT ongoing

ClinicalTrials.gov Identifier: NCT02575027

V Yu et al. IJROBP 2018 Pages 144-151
4π prospective brain trial

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Average OAR Dose Statistics (Gy)

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<th>Brainstem</th>
<th>Chiasm</th>
<th>Cochlea</th>
<th>Eye</th>
<th>Lens</th>
<th>Optic Nerve</th>
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<th>R</th>
<th>L</th>
<th>R</th>
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<td>Max</td>
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VMAT

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Patient self-reported discomfort in a scale of 0-10

Intrafractional motion monitoring

Intrafractional head motion <1 mm for all treatment fractions

Future development of 4π radiotherapy

- 4π VMAT
- Fully automated evolving knowledge base (EKB) 4π treatment planning and delivery
4π VMAT
• 4π VMAT is a way to further accelerate 4π IMRT
• A simple way to create non-coplanar VMAT is by generating static beams first and then connect them with arcs
• However, these arcs are not dosimetrically desirable.
• Need to include arc trajectory selection in optimization

4π VMAT radiotherapy: cost function

\[
\begin{align*}
\text{minimize} & \quad \Phi = \sum_{i=1}^{\text{Total Beams}} \left[ (\alpha_i + \beta_i)(\text{Fluence}_{\text{Ref}} - \text{Fluence}_{\text{Plan}}) + (\gamma_i + \delta_i)(\text{Direct Aperture}_{\text{Ref}} - \text{Direct Aperture}_{\text{Plan}}) \right] \\
& \quad + \sum_{i=1}^{\text{Cost Segments}} \left[ (\epsilon_i + \zeta_i)(\text{Segment Cost}_{\text{Ref}} - \text{Segment Cost}_{\text{Plan}}) \right] \\
& \quad + \sum_{i=1}^{\text{AP Segments}} \left[ (\eta_i + \iota_i)(\text{Aperture Cost}_{\text{Ref}} - \text{Aperture Cost}_{\text{Plan}}) \right]
\end{align*}
\]

Selected beam angles
Prostate: Dose

4π VMAT

2π VMAT

Radiation Oncology Technology, Innovation and Clinical Translation UCLA

4π VMAT radiotherapy: delivery

Estimated delivery time: 5 minutes based on actual machine parameters

Radiation Oncology Technology, Innovation and Clinical Translation UCLA

Fully automated 4π: Evolving-knowledge-base (EKB) Planning

Initial plan → Training set → Automated planning → Improved plan? → Final plan

Update with improved plan

Radiation Oncology Technology, Innovation and Clinical Translation UCLA
Conclusion

- 4π radiotherapy optimally uses the enhanced beam geometry freedom to create highly compact dose distribution.
- The path to overcoming the computational challenge of 4π IMRT and VMAT treatment planning has been elucidated.
- The feasibility of delivering optimized 4π treatment has been shown in an early phase clinical trial.
- Extending 4π to extracranial sites may be calling for a new hardware architecture.