AAPM 2018 JUL 29–AUG 2
BEYOND THE FUTURE!
60TH ANNUAL MEETING & EXHIBITION | NASHVILLE, TN

Technology and Clinical Implementation of 4π Radiotherapy:

KE SHENG, PH.D., DABR, FAAPM
UNIVERSITY OF CALIFORNIA, LOS ANGELES
UCLA

Disclosure

I receive research grants from Varian Medical Systems and VisionRT

I am a founder of Celestial Medical Inc.

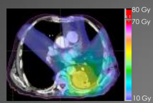
Funding source:
NIH R21EB025269
NIH U19AI067769
NIH R43CA183390
NIH R44CA183390
DE-SC0017057
DE-SC0017687
NIH R01CA188300

Outline

- Technical development
- Clinical implementation
- Future directions

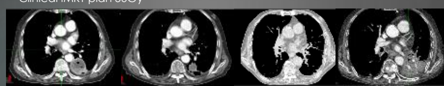
Promise and challenge of radiotherapy

4



Clinical IMRT plan 50Gy

Further increase the dose?



Pretreatment | 3 Months post | 12 Months post | 24 Months post

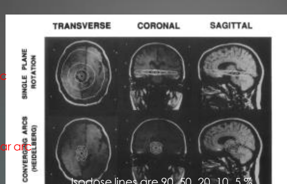
The majority of stage III lung cancer patients die from local in field disease progression. Garg et al . Pract Radiat Oncol. 2013 Oct-Dec;3(4):287-93, 2014 Sep-Oct;4(5):342-8
High BED is essential to achieve tumor local control for large locally advanced lung cancer. Zhao et al. IJROBP Volume 68, Issue 1, 1 May 2007, Pages 103–110

Non-coplanar radiotherapy is not new

5

Coplanar arc

Non-Coplanar arc



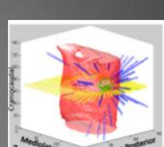
Isodose lines are 90, 50, 20, 10, 5 %

Podgorsak et al. IJROBP 16 (3) 857–865

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

Non-coplanar treatment on C-arm gantry

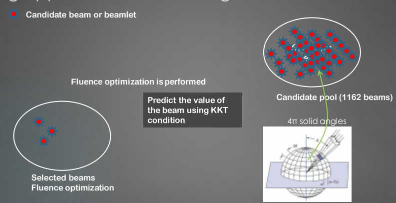
6



Manually selecting non-coplanar beams and arcs becomes increasing difficult and inefficient
➡ Automated integrated beam orientation and fluence optimization
4π radiotherapy in phase I and II

Phase I: Beam orientation and Fluence optimization
Pricing approach and column generation

7



HE Romeijn, SIAM Journal on Optimization, 2005
D Nguyen, Med Phys. 2016

Radiation Oncology *Technology, Innovation and Clinical Translation* UCLA

Phase II: Sparsity on the structured beamlets

Encouraging sparsity on the beamlets

Encouraging sparsity on the structured beams

8

Jia et al. PMB 2011

Solving the group sparsity optimization problem

9

$$\begin{aligned} \underset{x}{\text{minimize}} \quad & \underbrace{\frac{1}{2}\|(\ell - A_0 x)_+\|_2^2}_{\text{PTV}} + \underbrace{\sum_{i=0}^{N} \frac{\alpha_i}{2}\|(A_i x - d_i)_+\|_2^2 + \frac{\beta_i}{2}\|A_i x\|_2^2}_{\text{OARs}} + \underbrace{\gamma\|Dx\|_1^{(\mu)}}_{\text{smoothness}} + \underbrace{\sum_{b=1}^{B} w_b\|x_b\|_2}_{\text{group sparsity}} \quad (1) \\ \text{subject to} \quad & x \geq 0. \end{aligned}$$

Fast Iterative Shrinkage-Thresholding Algorithm (FISTA)

$$\underset{x \in \mathbb{R}^n}{\text{minimize}} \; f(x) + g(x),$$

$$f(x) = \frac{1}{2}\|(\ell - A_0 x)_+\|_2^2 + \sum_{i=0}^{N} \frac{\alpha_i}{2}\|(A_i x - d_i)_+\|_2^2 + \frac{\beta_i}{2}\|A_i x\|_2^2 + \gamma\|Dx\|_1^{(\mu)}$$

$$g(x) = \begin{cases} \sum_{b=1}^{B} w_b\|x_b\|_2 & \text{if } x \geq 0, \\ \infty & \text{otherwise.} \end{cases}$$

O'Connor et al. PMB 2018 63(4)

Radiation Oncology *Technology, Innovation and Clinical Translation* UCLA

Gradient of *f*

10

$$f(x) = \frac{1}{2}\|(\ell - A_0 x)_+\|_2^2 + \sum_{i=0}^{N} \frac{\alpha_i}{2}\|(A_i x - d_i)_+\|_2^2 + \frac{\beta_i}{2}\|A_i x\|_2^2 + \gamma\|Dx\|_1^{(\mu)}$$

$$\nabla f(x) = -A_0^T(\ell - A_0 x)_+ + \sum_{i=0}^{N} \alpha_i A_i^T (A_i x - d_i)_+ + \beta_i A_i^T A_i x + \frac{\gamma}{\mu} D^T P_{[-\mu,\mu]}(Dx).$$

O'Connor et al. PMB 2018 63(4)

Radiation Oncology Technology, Innovation and Clinical Translation UCLA

Proximal operator of *g*

11

$$\text{prox}_{tg}(x) = \begin{bmatrix} \text{prox}_{tg_1}(x_1) \\ \text{prox}_{tg_2}(x_2) \\ \vdots \\ \text{prox}_{tg_B}(x_B) \end{bmatrix}, \qquad \text{prox}_{tg_b}(x_b) = \text{prox}_{tw_b\|\cdot\|_2}(\max(x_b, 0)).$$

$$\text{prox}_{tw_b\|\cdot\|_2}(y) = y - Py,$$

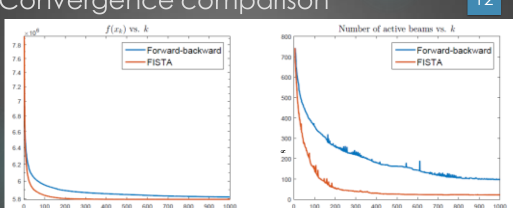
Derivation of the proximal operator is the key to enable FISTA

O'Connor et al. PMB 2018 63(4)

Radiation Oncology Technology, Innovation and Clinical Translation UCLA

Convergence comparison

12



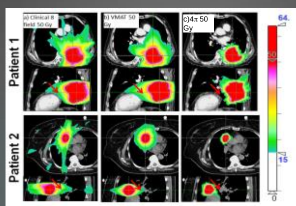
FISTA converges ~1/k² vs. Chambolle-Pock ~1/k

Chambolle-Pock does not achieve the desired beam sparsity

Solving the optimization problem in ~ 5 mins using FISTA

Lung SBRT

13



IMRT VMAT (RapidArc) 4π

Reduce R_{50} by 54%, Reduce EUD of heart, esophagus, trachea, bronchus and spinal cord were reduced by 44%, 74%, 40%, 42%, and 51%

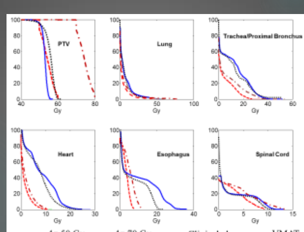
4π Optimization using group sparsity takes ~5 minutes

Dong et al. IJROBP 2013; 86 (3):407–413.

Radiation Oncology *Technology, Innovation and Clinical Translation* UCLA

Potential for *no* cost tumor dose escalation?

14



The PTV dose can be escalated by 40% without increasing normal tissue dose

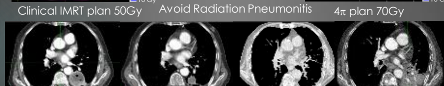
Dong et al. IJROBP 2013; 86 (3):407–413.

Radiation Oncology *Technology, Innovation and Clinical Translation* UCLA

Achieving greater tumor dose without increasing normal tissue doses

15

Clinical IMRT plan 50Gy Avoid Radiation Pneumonitis 4π plan 70Gy

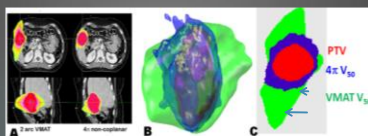


Pretreatment 3 Month post 12 Month post 24 Month post

Radiation Oncology *Technology, Innovation and Clinical Translation* UCLA

Liver cancer SBRT

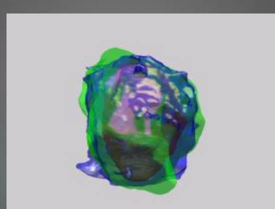
Minimum isodose 50%



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

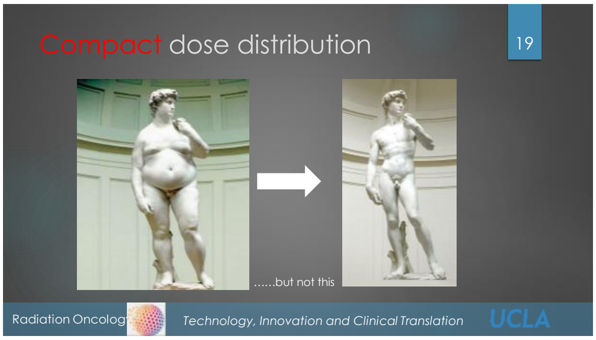
Dong, P et al, Int J Radiat Oncol Biol Phys, 2013. 85(5): p. 1360-1366.

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

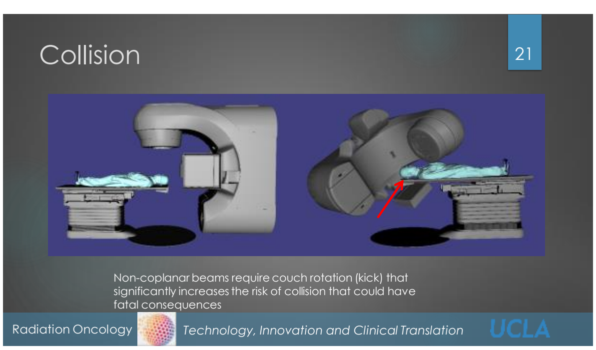


IMRT Dose sculpting

You have seen this......

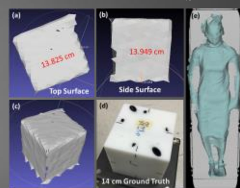

Compact dose distribution
19
......but not this
Radiation Oncology
Technology, Innovation and Clinical Translation
UCLA


Overcoming the delivery anxiety
20
Airplane! 1980
Radiation Oncology
Technology, Innovation and Clinical Translation
UCLA


Collision
21
Non-coplanar beams require couch rotation (kick) that significantly increases the risk of collision that could have fatal consequences
Radiation Oncology
Technology, Innovation and Clinical Translation
UCLA

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 cubical phantom
  - <2mm discrepancy
- Patient and phantom surfaces acquired immediately after CT simulation to ensure consistent setup

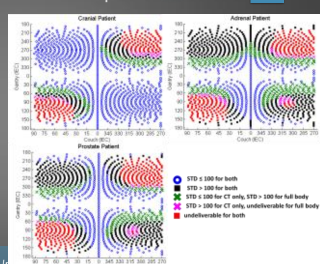


V. Yu et al. AAPM 2018 SU-L-KDBRA1-5

Radiation Oncology Technology, Innovation and Clinical Translation UCLA

Case-specific collision maps

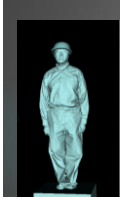
- Minimum achievable source to target distances for 1162 evenly spaced candidate beams
  - Programmatic exhaustive search



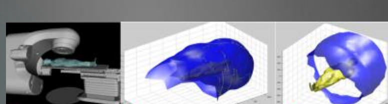
Radiation Oncology Technology, I

Virtual simulation of treatment

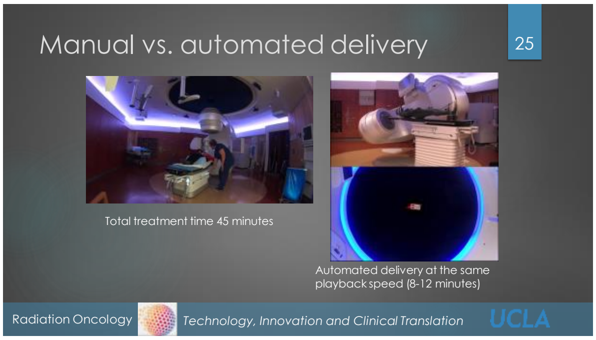
24

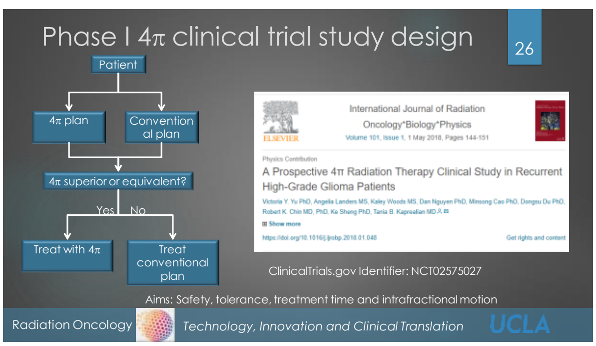


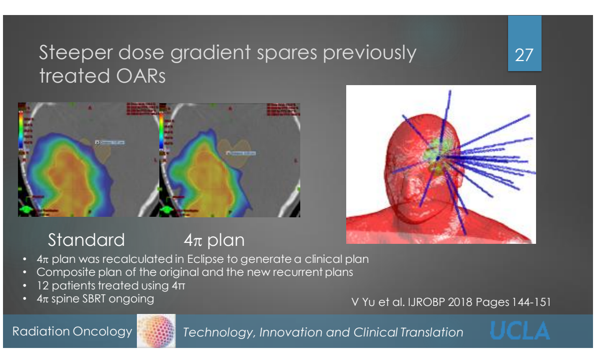
4π extracranial therapy can be non-isocentric



Radiation Oncology Technology, Innovation and Clinical Translation UCLA

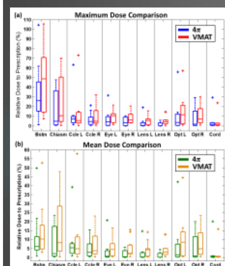

Manual vs. automated delivery
25
Total treatment time 45 minutes
Automated delivery at the same playback speed (8-12 minutes)
Radiation Oncology
Technology, Innovation and Clinical Translation
UCLA


Phase I 4π clinical trial study design
26
Patient
4π plan
Conventional plan
4π superior or equivalent?
Yes
No
Treat with 4π
Treat conventional plan
ELSEVIER
International Journal of Radiation Oncology*Biology*Physics
Volume 101, Issue 1, 1 May 2018, Pages 144-151
Physics Contribution
A Prospective 4π Radiation Therapy Clinical Study in Recurrent High-Grade Glioma Patients
Victoria Y. Yu PhD, Angelia Landers MS, Kaley Woods MS, Dan Nguyen PhD, Minsong Cao PhD, Dongsu Du PhD, Robert K. Chin MD, PhD, Ke Sheng PhD, Tania B. Kaprealian MD
Show more
https://doi.org/10.1016/j.ijrobp.2018.01.048
Get rights and content
ClinicalTrials.gov Identifier: NCT02575027
Aims: Safety, tolerance, treatment time and intrafractional motion
Radiation Oncology
Technology, Innovation and Clinical Translation
UCLA


Steeper dose gradient spares previously treated OARs
27
Standard
4π plan
• 4π plan was recalculated in Eclipse to generate a clinical plan
• Composite plan of the original and the new recurrent plans
• 12 patients treated using 4π
• 4π spine SBRT ongoing
V Yu et al. IJROBP 2018 Pages 144-151
Radiation Oncology
Technology, Innovation and Clinical Translation
UCLA

4π prospective brain trial

28



Average OAR Dose Statistics (Gy)											
		Brainstem	Chiasm	Cochlea		Eye		Lens		Optic Nerve	
				L	R	L	R	L	R	L	R
4π	Mean	3.30*	2.59*	2.33	1.45	0.94*	0.58*	0.64*	0.39*	2.03*	1.70
	Max	9.52*	5.00*	3.47	1.92	1.96	1.35*	0.87*	0.51*	2.96*	2.61
VMAT	Mean	4.37	4.69	3.05	2.04	1.62	1.52	1.30	1.30	3.10	2.19
	Max	13.01	7.04	3.81	2.79	2.59	2.42	1.59	1.61	4.30	3.02

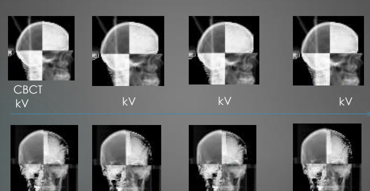
Treatment Duration Tolerability	Nausea	Dizziness	Pain
8.625	0	0.66	1.07

Patient self reported discomfort in a scale of 0-10

V Yu et al. IJROBP 2018 Pages 144-151

Intrafractional motion monitoring

29



Intrafractional head motion <1 mm for all treatment fractions

Radiation Oncology *Technology, Innovation and Clinical Translation* UCLA

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

$$\underset{\{f_{b\alpha}, c_{b\alpha}, u_{b\alpha}\}_{b,\alpha=1}^{n_b,n_\alpha}}{\textit{minimize}} \underbrace{\frac{1}{2}\left\| W\left(\left(\sum_{b=1}^{n_b}\sum_{\alpha=1}^{n_\alpha} A_{b\alpha} f_{b\alpha}\right) - d\right)\right\|_2^2}_{\textit{fidelity term}} +$$

$$\sum_{b=1}^{n_b}\sum_{\alpha=1}^{n_\alpha} \underbrace{\left(\lambda_1 \left\|D_{1_{b\alpha}} f_{b\alpha}\right\|_1 + \lambda_2 \left\|D_{2_{b\alpha}} f_{b\alpha}\right\|_1\right)}_{\textit{anisotropic TV term on } f} +$$

$$\frac{1}{2}\sum_{b=1}^{n_b}\sum_{\alpha=1}^{n_\alpha} \underbrace{\left(\gamma_1 \left\|\sqrt{diag(u_{b\alpha})}(f_{b\alpha} - c_{b\alpha})\right\|_2^2 + \gamma_2 \left\|\sqrt{diag(1 - u_{b\alpha})} f_{b\alpha}\right\|_2^2\right)}_{\textit{single segment term}} +$$

$$\sum_{b=1}^{n_b}\sum_{\alpha=1}^{n_\alpha} \underbrace{\left(g_1 \left\|D_{1_{b\alpha}} u_{b\alpha}\right\|_1 + g_2 \left\|D_{2_{b\alpha}} u_{b\alpha}\right\|_1\right)}_{\textit{anisotropic TV term on } u} +$$

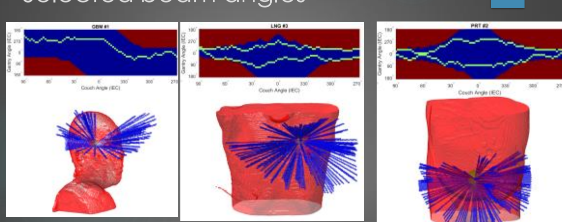
$$\sum_{b=1}^{n_b}\sum_{\alpha=1}^{n_\alpha} \underbrace{\gamma_3 G_{b\alpha}\|f_{b\alpha}\|_2 + \gamma_4 G_{b\alpha}(1 - P_{b\alpha})\|f_{b\alpha}\|_2}_{\textit{group sparsity term}} + \underbrace{g_3 \|D_P u\|_1}_{\textit{aperture continuity term}}$$

Alternating between fluence, direct aperture and beam trajectory optimization

Lyu et al. AAPM 2018 TH-AB-KDBRA1-1
Lyu et al. PMB 2018

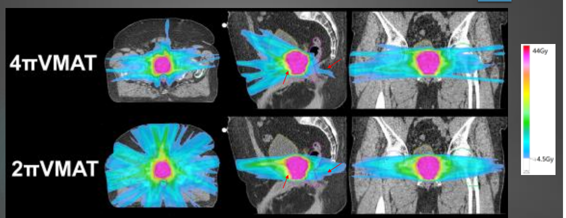
Radiation Oncology *Technology, Innovation and Clinical Translation* UCLA

Selected beam angles



Radiation Oncology *Technology, Innovation and Clinical Translation* UCLA

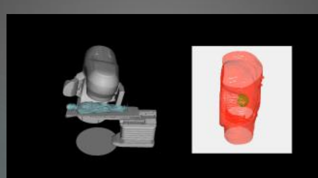
Prostate: Dose



Lyu et al. AAPM 2018 TH-AB-KDBRA1-1
Lyu et al. PMB 2018

Radiation Oncology *Technology, Innovation and Clinical Translation* UCLA

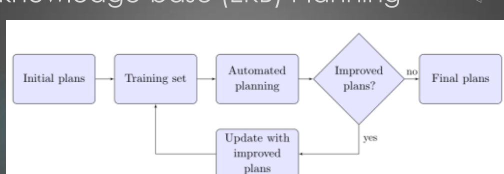
4π VMAT radiotherapy: delivery



Estimated delivery time: 5 minutes based on actual machine parameters

Radiation Oncology *Technology, Innovation and Clinical Translation* UCLA

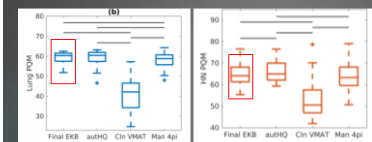
Fully automated 4π: Evolving-knowledge-base (EKB) Planning



Landers et al. AAPM 2018 MO-AB-KDBRA1-3

Radiation Oncology *Technology, Innovation and Clinical Translation* UCLA

PQM Results



	Average PQM			
	Final EKB	autHQ	Cln VMAT	Man 4π
Lung	59.48	59.08	41.22	57.72
HN	64.50	66.31	53.78	63.49

Fully automated EKB 4π plans match the quality of manual 4π plans

Landers et al. AAPM 2018 MO-AB-KDBRA1-3

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.

http://shenglab.dgsom.ucla.edu/

2017

2018