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

Technology and Clinical Implementation of 4π Radiotherapy:

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Disclosure

I receive research grants from Varian Medical Systems and VisionRT

I am a founder of Celestial Medical Inc.

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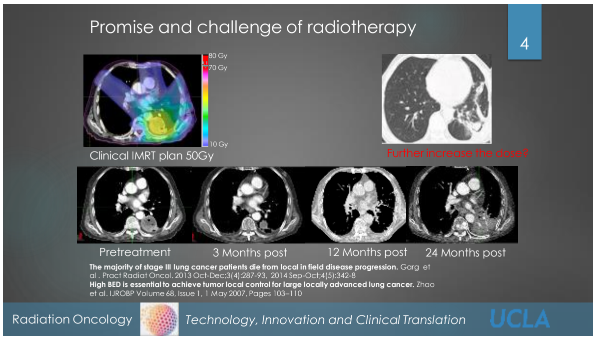
DE-SC0017057
DE-SC0017687
NIH R01CA188300

Outline

- Technical development
- Clinical implementation
- Future directions


Promise and challenge of radiotherapy
4
80 Gy
70 Gy
10 Gy
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
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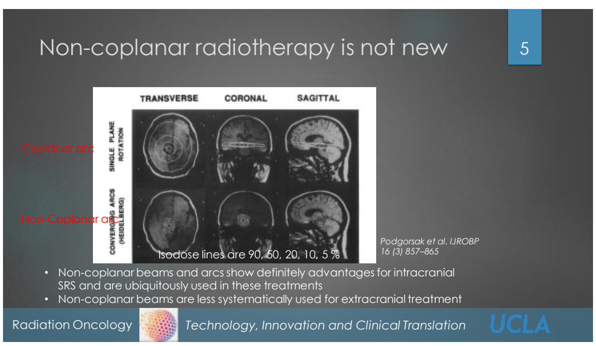
Non-coplanar radiotherapy is not new
5
TRANSVERSE
CORONAL
SAGITTAL
SINGLE PLANE ROTATION
CONVERGING ARCS (HEIDELBERG)
Coplanar arc
Non-Coplanar arc
Isodose lines are 90, 50, 20, 10, 5 %
Podgorsak et al. IJROBP 16 (3) 857–865
• Non-coplanar beams and arcs show definitely advantages for intracranial SRS and are ubiquitously used in these treatments
• Non-coplanar beams are less systematically used for extracranial treatment
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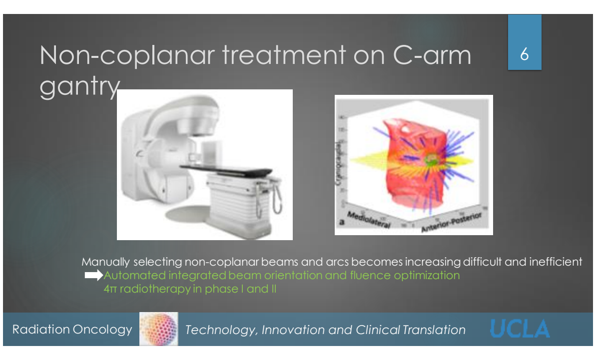
Non-coplanar treatment on C-arm gantry
6
Mediolateral
Anterior-Posterior
Manually selecting non-coplanar beams and arcs becomes increasing difficult and inefficient
Automated integrated beam orientation and fluence optimization
4π radiotherapy in phase I and II
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Phase I: Beam orientation and Fluence optimization Pricing approach and column generation

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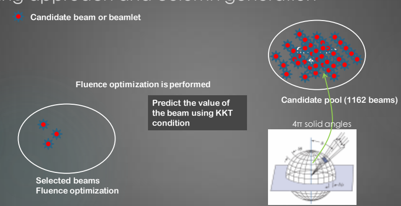

HE Romeijn, SIAM Journal on Optimization, 2005
D Nguyen, Med Phys. 2016

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Phase II: Sparsity on the structured beamlets

Jia et el. PMB 2011

Solving the group sparsity optimization problem

9

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

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)

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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)

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Proximal operator of *g*

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

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

Derivation of the proximal operator is the key to enable FISTA

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

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Convergence comparison

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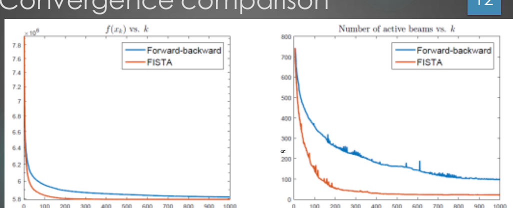
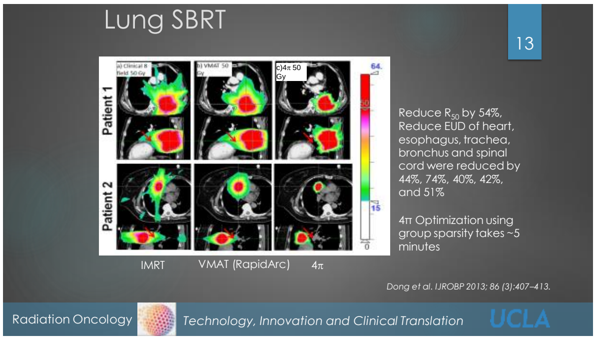


FISTA converges ~1/k² vs. Chambolle-Pock ~1/k

Chambolle-Pock does not achieve the desired beam sparsity

Solving the optimization problem in ~ 5 mins using FISTA


Lung SBRT
13
Patient 1
Patient 2
a) Clinical 8 field 50 Gy
b) VMAT 50 Gy
c)4π 50 Gy
64.
50
15
0
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.
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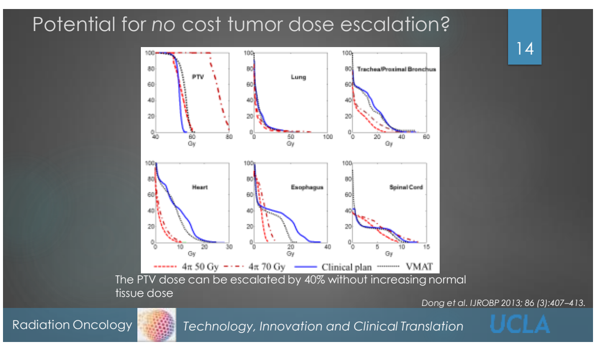
Potential for *no* cost tumor dose escalation?
14
PTV
Lung
Trachea/Proximal Bronchus
Heart
Esophagus
Spinal Cord
Gy
4π 50 Gy
4π 70 Gy
Clinical plan
VMAT
The PTV dose can be escalated by 40% without increasing normal tissue dose
Dong et al. IJROBP 2013; 86 (3):407–413.
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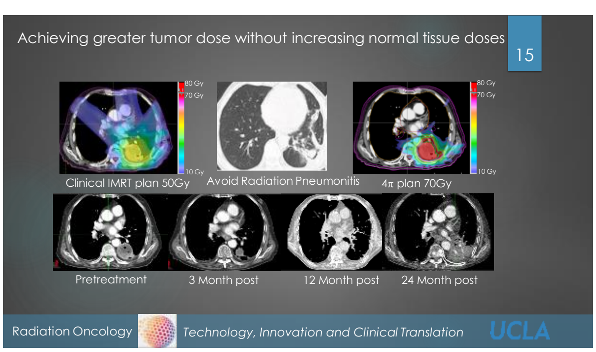
Achieving greater tumor dose without increasing normal tissue doses
15
80 Gy
70 Gy
10 Gy
Clinical IMRT plan 50Gy
Avoid Radiation Pneumonitis
4π plan 70Gy
Pretreatment
3 Month post
12 Month post
24 Month post
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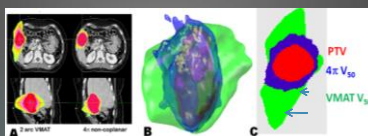
Liver cancer SBRT

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.

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

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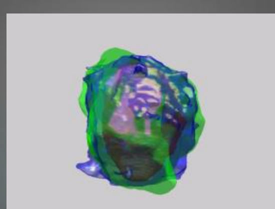

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IMRT Dose sculpting

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You have seen this……

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Compact dose distribution

19

......but not this

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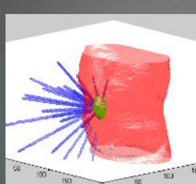
Overcoming the delivery anxiety

20



Airplane! 1980

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Collision

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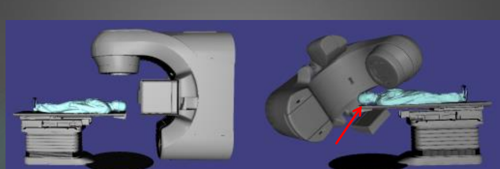

Non-coplanar beams require couch rotation (kick) that significantly increases the risk of collision that could have fatal consequences

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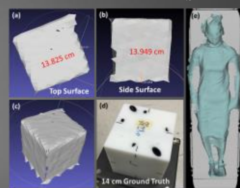
3D optical surface acquisition

- 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

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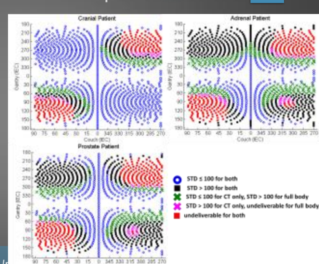
Case-specific collision maps

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



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Virtual simulation of treatment

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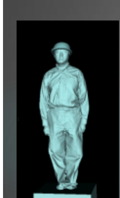
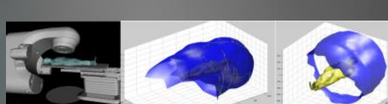


4π extracranial therapy can be non-isocentric



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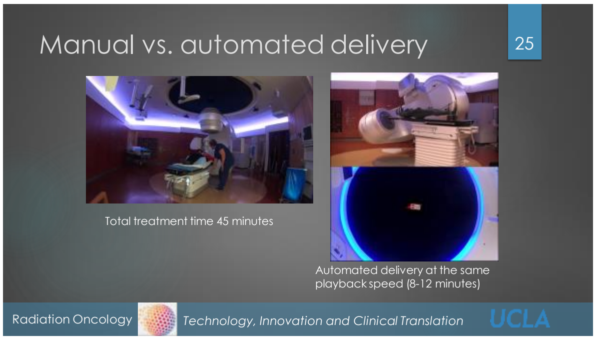
Manual vs. automated delivery
25
Total treatment time 45 minutes
Automated delivery at the same playback speed (8-12 minutes)
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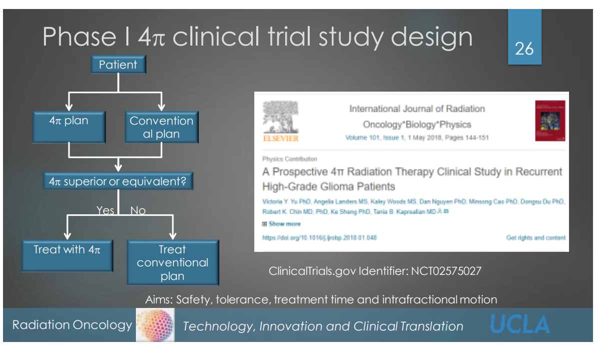
Phase I 4π clinical trial study design
26
Patient
4π plan
Conventional plan
4π superior or equivalent?
Yes
No
Treat with 4π
Treat conventional plan
International Journal of Radiation Oncology*Biology*Physics
Volume 101, Issue 1, 1 May 2018, Pages 144-151
Physics Contribution
A Prospective 4π Radiation 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
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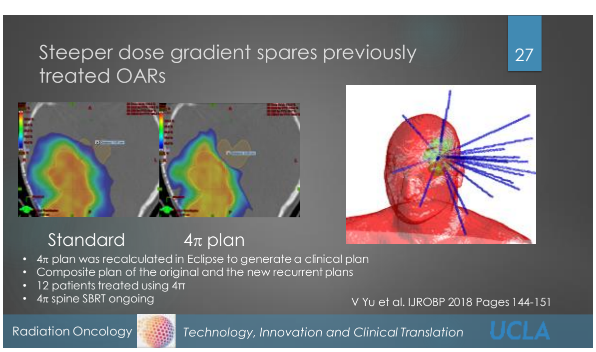
Steeper dose gradient spares previously treated OARs
27
Standard
4π plan
• 4π plan was recalculated in Eclipse to generate a clinical plan
• Composite plan of the original and the new recurrent plans
• 12 patients treated using 4π
• 4π spine SBRT ongoing
V Yu et al. IJROBP 2018 Pages 144-151
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4π prospective brain trial

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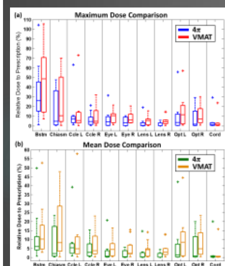

Average OAR Dose Statistics (Gy)											
		Brainstem	Chiasm	Cochlea		Eye		Lens		Optic Nerve	
				L	R	L	R	L	R	L	R
4π	Mean	3.30*	2.59*	2.33	1.45	0.94*	0.58*	0.64*	0.39*	2.03*	1.70
	Max	9.52*	5.00*	3.47	1.92	1.96	1.35*	0.87*	0.51*	2.96*	2.61
VMAT	Mean	4.37	4.69	3.05	2.04	1.62	1.52	1.30	1.30	3.10	2.19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

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Intrafractional head motion <1 mm for all treatment fractions

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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

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

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

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

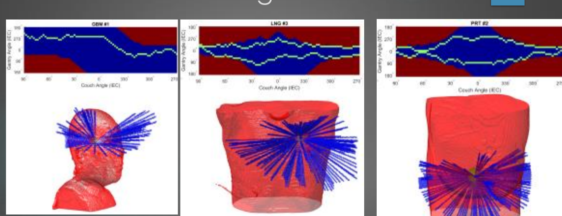
$$\sum_{b=1}^{n_b}\sum_{\alpha=1}^{n_\alpha} \underbrace{\left(g_1 \left\|D_{1_{b\alpha}} u_{b\alpha}\right\|_1 + g_2 \left\|D_{2_{b\alpha}} u_{b\alpha}\right\|_1\right)}_{\text{anisotropic TV term on } u} +$$

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

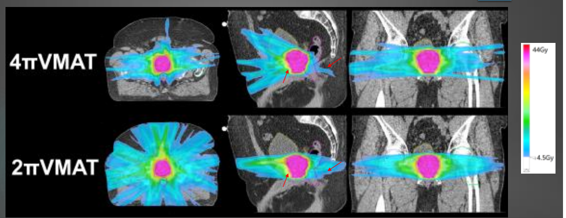
Alternating between fluence, direct aperture and beam trajectory optimization

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

Selected beam angles



Prostate: Dose



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

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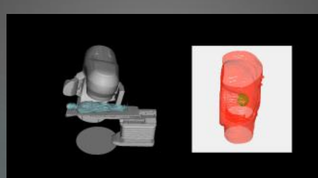
4π VMAT radiotherapy: delivery



Estimated delivery time: 5 minutes based on actual machine parameters

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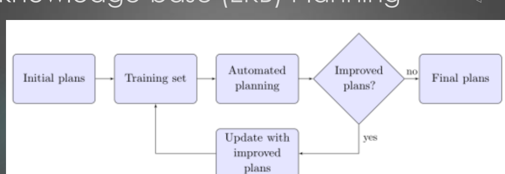
Fully automated 4π: Evolving-knowledge-base (EKB) Planning



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

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PQM Results

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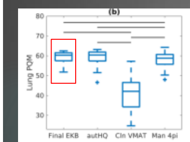

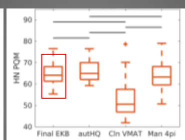

	Average PQM			
	Final EKB	autHQ	Cln VMAT	Man 4π
Lung	59.48	59.08	41.22	57.72
HN	64.50	66.31	53.78	63.49

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

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

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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.

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

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2017

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