Non-Coplanar Spatially Fractionated Radiation Therapy (SFRT) for Complex Thoracic Lesions: Using MapRT to Improve SFRT Efficacy and OAR Dose Reduction

Dr. Benjamin P. Ziemer BS^3 MS PhD DABR

- **Background & Disclosures**
- Features / Rationale of High Dose Treatments
- Spatial Fractionation Radiation Therapy (SFRT):
  techniques, motivation, results
- CHLA SFRT Case Studies

Dr. Benjamin P. Ziemer BS^3 MS PhD DABP

Children's Hospital LOS ANGELES

Background:

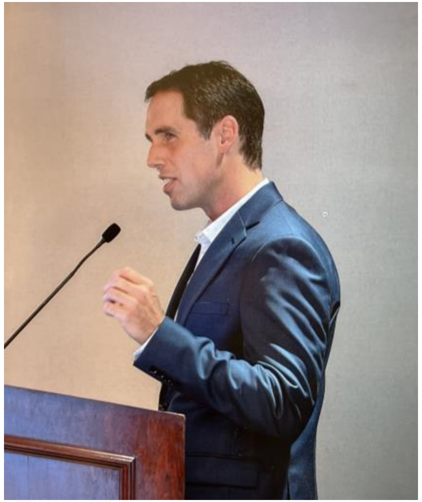
University of Wisconsin Madison
- BS in Chemistry, Mathematics, Physics

University of California Irvine
- MS / PhD in Experimental Particle Physics
- Postdoc in Imaging Medical Physics

University of California San Diego
- Postdoc in Therapeutic Medical Physics

University of California San Francisco
- Residency in Therapeutic Medical Physics
- *Assistant Professor: CNS / SRS Specialty*

University of Southern California
- ***Lead Physicist at Children's Hospital Los Angeles***
- ***Assistant Professor at USC***



Disclosures:

- ***travel and lodging were provided by VisionRT***
- ***a selective review of the literature is present***

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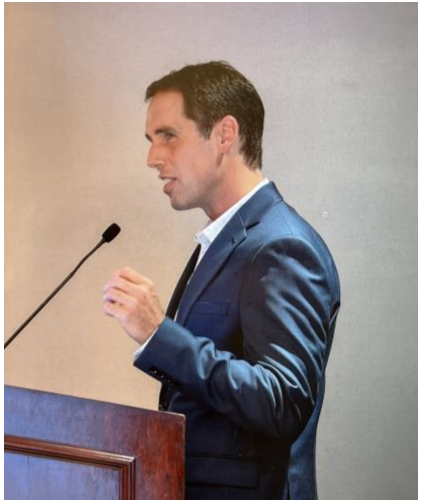

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Dose escalation improves outcomes in numerous cancer histologies

Children's Hospital LOS ANGELES

June 14, 2018

Effect of Standard vs Dose-Escalated Radiation Therapy for Patients With Intermediate-Risk Prostate Cancer

The NRG Oncology RTOG 0126 Randomized Clinical Trial

Jeff M. Michalski, MD, MBA[1]; Jennifer Moughan, MS[2]; James Purdy, PhD[3]; et al

» Author Affiliations | Article Information

JAMA Oncol. 2018;4(6):e180039. doi:10.1001/jamaoncol.2018.0039

Clinical Investigation

Focal Radiation Therapy Dose Escalation Improves Overall Survival in Locally Advanced Pancreatic Cancer Patients Receiving Induction Chemotherapy and Consolidative Chemoradiation

CrossMark

Sunil Krishnan, MD,* Awalpreet S. Chadha, MD,* Yelin Suh, PhD,† Hsiang-Chun Chen, PhD,‡ Arvind Rao, PhD,§ Prajnan Das, MD,* Bruce D. Minsky, MD,* Usama Mahmood, MD,* Marc E. Delclos, MD,* Gabriel O. Sawakuchi, PhD,†,‖ Sam Beddar, PhD,† Matthew H. Katz, MD,¶ Jason B. Fleming, MD,¶ Milind M. Javle, MD,# Gauri R. Varadhachary, MD,# Robert A. Wolff, MD,# and Christopher H. Crane, MD*

**Departments of Radiation Oncology and †Radiation Physics, The University of Texas, Houston, Texas; ‡Departments of Biostatistics and §Bioinformatics and Computational Biology, MD Anderson Cancer Center, Houston, Texas; ‖Graduate School of Biomedical Sciences, The University of Texas, Houston, Texas; and ¶Departments of Surgical Oncology and #Gastrointestinal Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas*

Received May 26, 2015, and

CLINICAL INVESTIGATION **Liver**

DOSE-ESCALATION STUDY OF SINGLE-FRACTION STEREOTACTIC BODY RADIOTHERAPY FOR LIVER MALIGNANCIES

Karyn A. Goodman, M.D.,* Ellen A. Wiegner, M.D.,† Katherine E. Maturen, M.D.,‡ Zhigang Zhang, Ph.D.,§ Qianxing Mo, Ph.D.,§ George Yang, M.D.,¶ Iris C. Gibbs, M.D.,† George A. Fisher, M.D., Ph.D.,‖ and Albert C. Koong, M.D., Ph.D.†

*Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY; Departments of †Radiation Oncology and ‡Radiology, Stanford University, Stanford, CA; §Departments of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, NY; Departments of ¶Surgery and ‖Medicine, Stanford University, Stanford, CA

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journal homepage: www.clinicaloncologyonline.net

Overview

A Review of Modern Radiation Therapy Dose Escalation in Locally Advanced Head and Neck Cancer

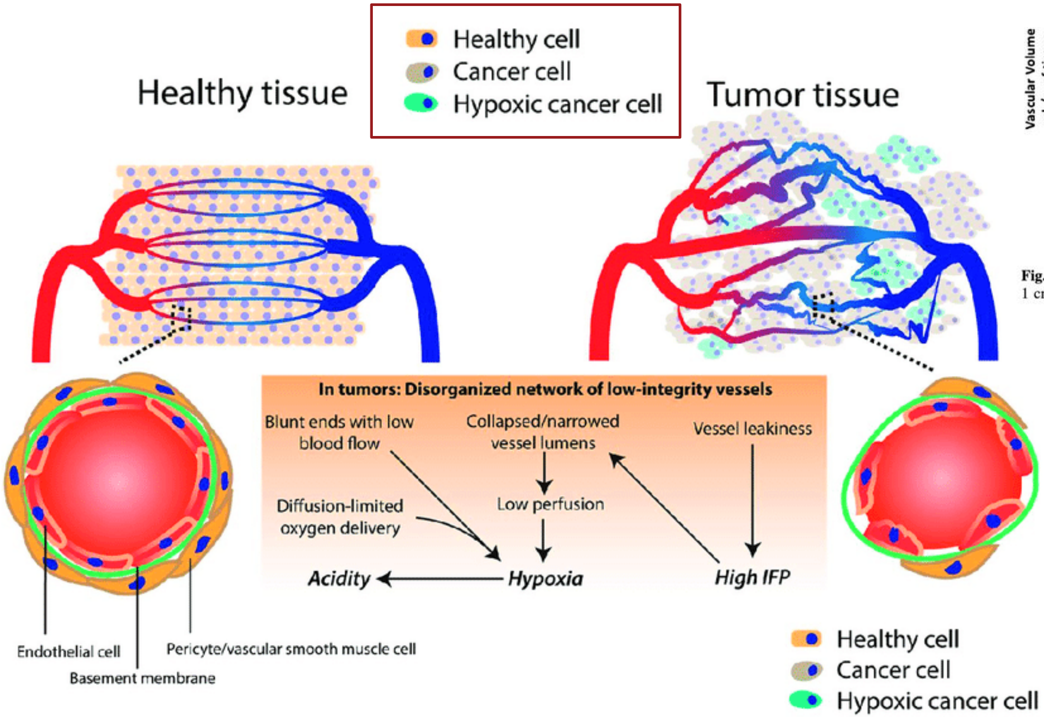
Check for updates

D. Atwell *†‡, J. Elks ‡, K. Cahill *‡, N. Hearn *†‡, D. Vignarajah *†, J. Lagopoulos ‡, M. Min *†‡

** Cancer Services, Sunshine Coast University Hospital, Birtinya, Queensland, Australia*
† Icon Cancer Centre, Maroochydore, Queensland, Australia
‡ Sunshine Coast Mind and Neuroscience – Thompson Institute, University of the Sunshine Coast, Sippy Downs, Queensland, Australia

Received 2 September 2019; received in revised form 27 October 2019; accepted 7 November 2019

Tumor and non-tumor vascularity differences & vascularity as a target



Schaaf et al. Cell Death and Disease (2018) 9:115

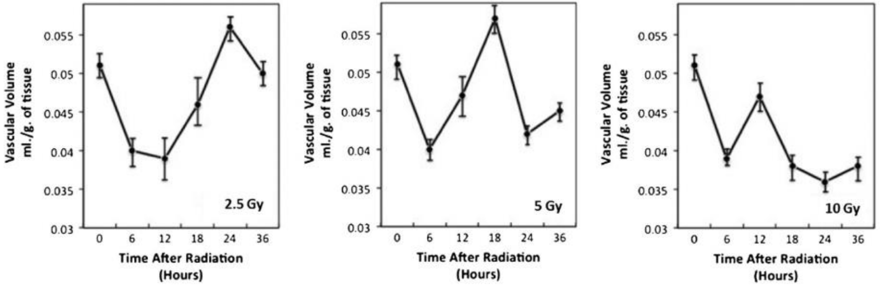
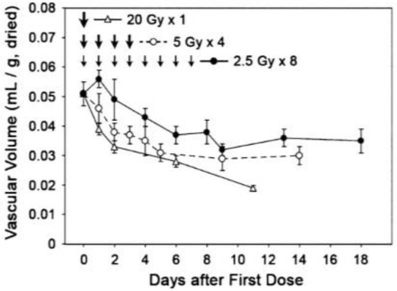


Fig. 1 Effect of various doses of X-irradiation in a single exposure on the functional intravascular volume in Walker 256 carcinomas of about 1 cm diameter grown subcutaneously in the thigh of Sprague–Dawley rats. Each data point is the average of 14–30 tumors with 1 SE



Various studies have shown that increased dose per fraction has a greater effect on vascular structures.

Radiobiological basis of SBRT and SRS
Int J Clin Oncol (2014) 19:570–578

Other factors possibly affecting post-radiation cell death

Other effects have been hypothesized that lead to increased cell death post-radiation:

- high dose irradiation could induce acid sphingomyelinase (ASMase) mediated generation of ceramide causing rapid endothelial apoptosis[1]

- swelling and degeneration of ‘low integrity’ tumor endothelium after high dose irradiation leads to vascular collapse

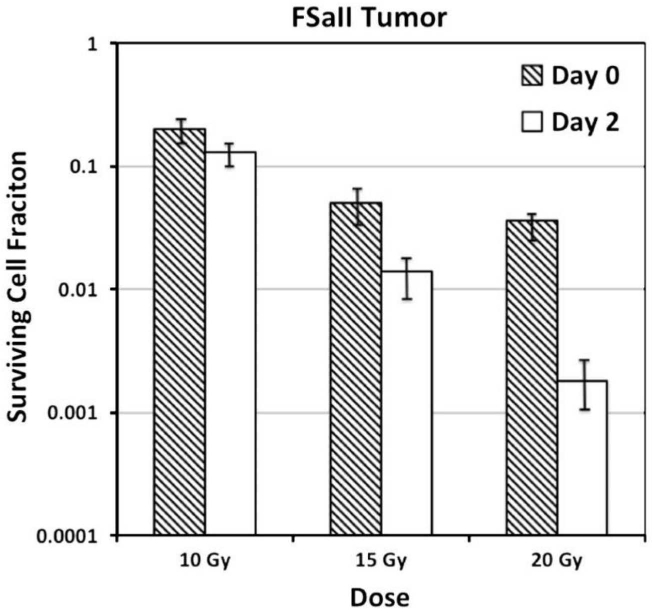


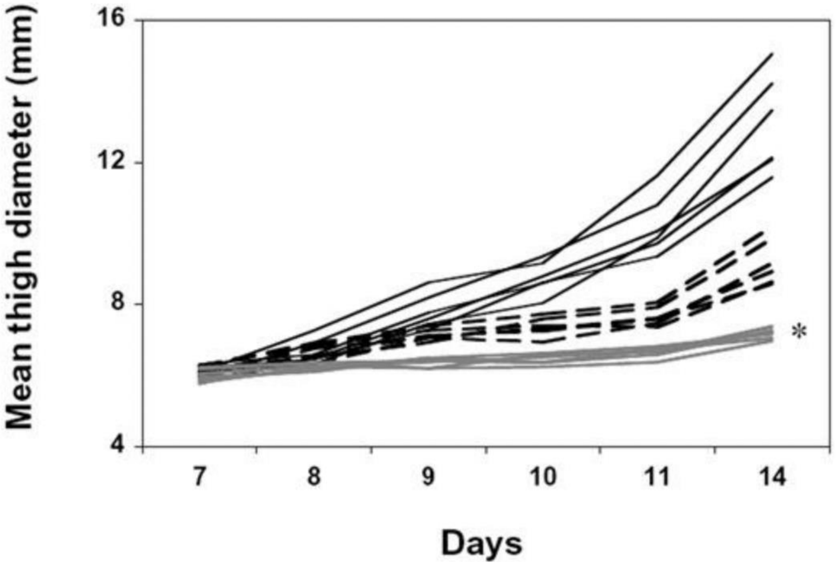
Fig. 5 Surviving cell fractions in FSaII mouse fibrosarcomas grown subcutaneously in the legs of C3H mice determined immediately after and 2 days after 10–20 Gy irradiation in a single exposure

[1]M Garcia-Barris, Tumor response to radiotherapy regulated by endothelial cell apoptosis, Science 300:1155–1159

Radiobiological basis of SBRT and SRS, Int J Clin Oncol (2014) 19:570–578

Immune system responses following high dose irradiation

Irradiation of B16 melanoma of mice with 15 Gy in a single exposure increased the generation of antitumor immune effector cells by facilitating antigen presentation and priming of anti-tumor T-cells within draining lymph nodes. Furthermore, radiation improved the trafficking of effector T cells into tumors. Compared to the 15 Gy irradiation in a single dose, treating tumors with 15 Gy in 5 daily fraction of 3 Gy was less effective, pointing to the importance of fraction size in eliciting anti-tumor immunity



Tumor growth after different doses of ionizing radiation. B16/OVA tumors were initiated in the thigh muscle of C57BL/6 mice by injecting 1 × 10^5 viable cells. Tumors were either nonirradiated (solid black lines), irradiated with five daily local doses of 3 Gy on days 7–11 (dotted black lines), or irradiated with a single local dose of 15 Gy on day 7 (solid gray lines). Mean thigh diameters were measured using calipers. Each line represents an individual mouse. *, $p < 0.001$ for 15 Gy of treatment compared with 0 Gy on day 14.

AA Lugade et.al., J Immunol (2005) 174 (12): 7516–7523.

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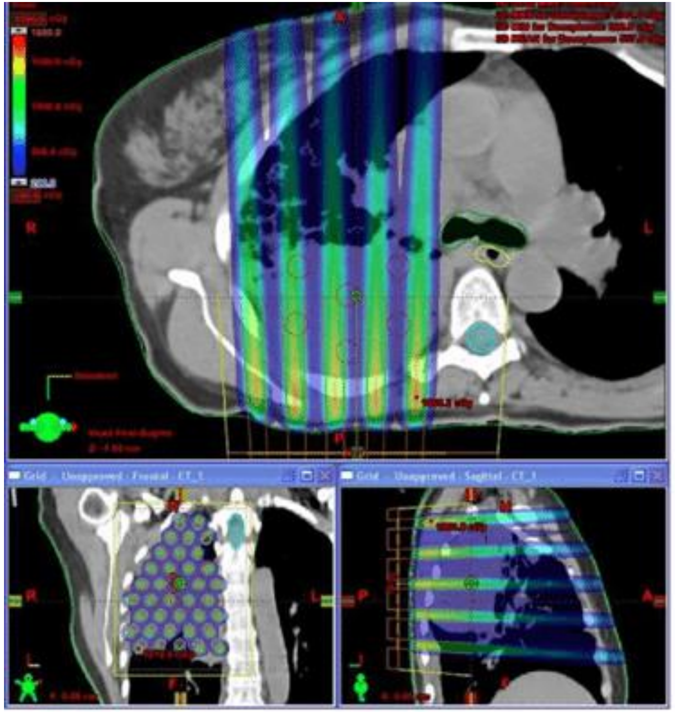
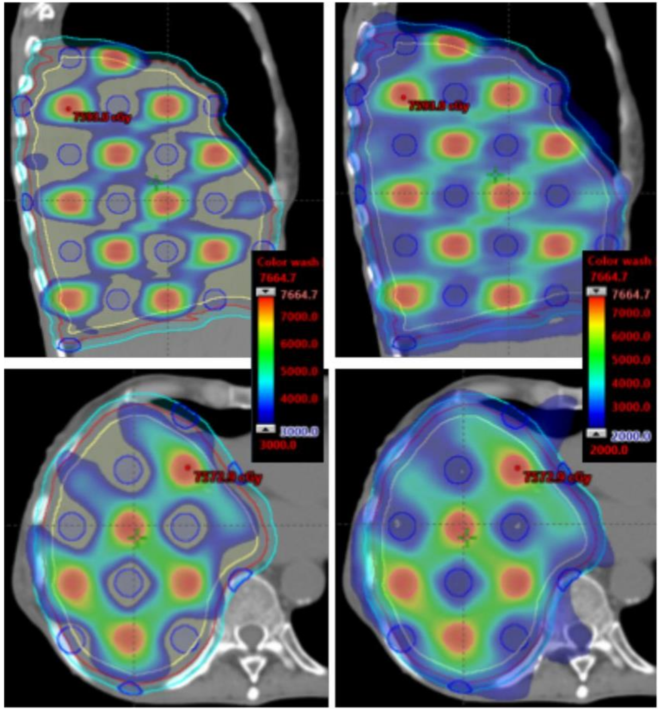


Khan, et.al. Spatially Fractionated Radiation Therapy: History, Present and the Future, CTRO DOI:10.1016/j.ctro.2019.10.004



Duriseti, et.al. Spatially fractionated stereotactic body radiotherapy (Lattice SBRT) for large tumors, Adv Radiat Oncol doi: 10.1016/j.adro.2020.1

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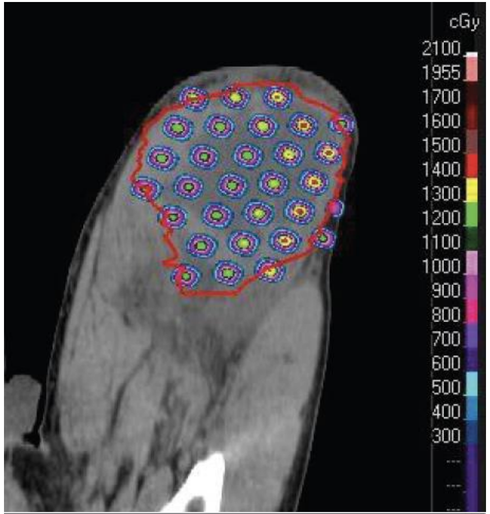
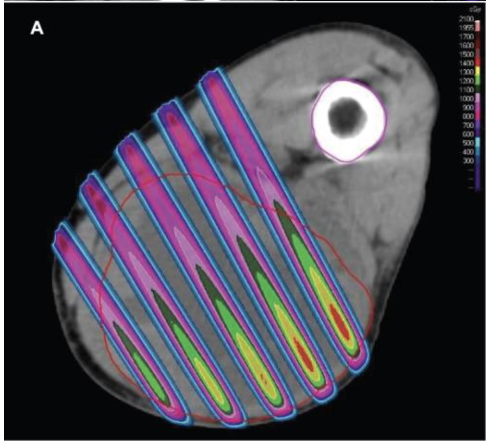
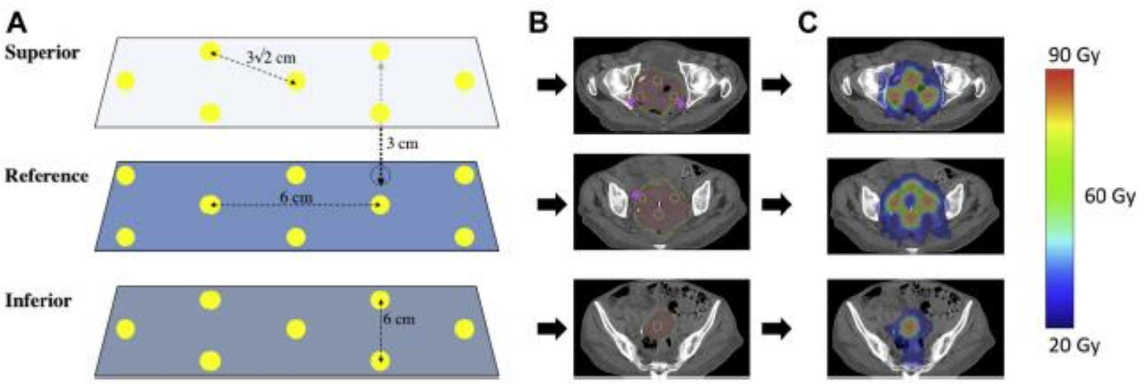




- Twenty-six patients treated with MLC GRID therapy to a D_{max} of 15 Gy followed by conventionally fractionated radiation therapy to an additional 45 to 50.4 Gy.
- The pathologic complete response rate was 35.3% in high grade tumors.
- This pCR exceeded those achieved with chemoradiotherapy (27.5%) and conventional radiation therapy alone (19.4%) in the **RTOG 9514** and **0630** studies, respectively.

The average tumor size was 15.8 cm (8.8-40 cm)

Spatially Fractionated Radiotherapy Prior to Standard Neoadjuvant Conventionally Fractionated Radiotherapy for Bulky, High-Risk Soft Tissue and Osteosarcomas: Feasibility, Safety, and Promising Pathologic Response Rates, Snider et.al. Radiat Res. 2020 194:707-14



Two Targets present:
PTV_2000
PTV_6670

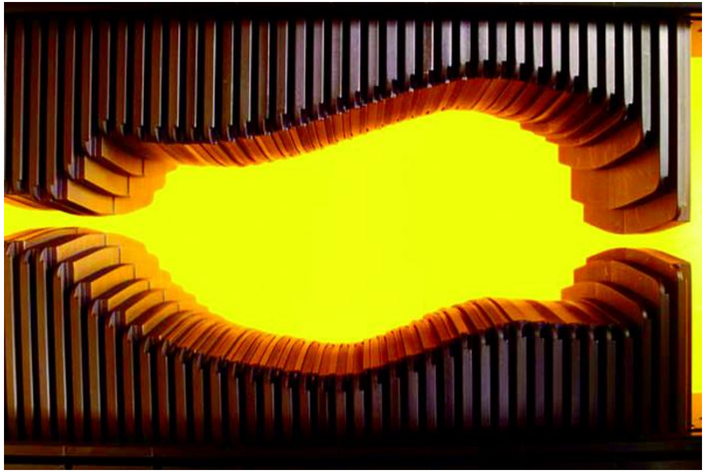
- Twenty-two patients enrolled (50% thorax, 45% abdomen, 5% extremity)
- Median GTV was 579.2 cc (range: 54.2–3713.5 cc)
- One grade 3+ toxicity (two tumors treated: 3700 & 1400cc)
- At 1.8 months, GTV shrank by a median of 24.4% [2.4–91.7%]

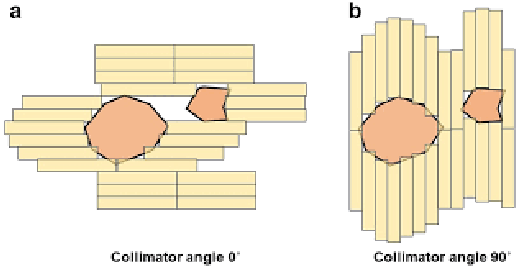
Clinical trials:
NCT04553471
NCT04133415

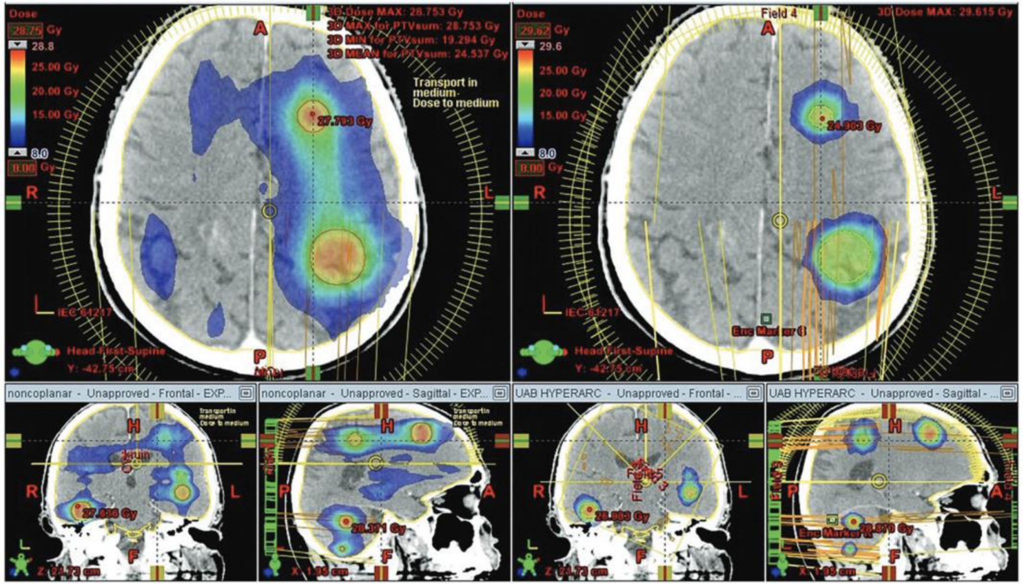
Spatially fractionated stereotactic body radiation therapy for large tumors
Sai Duriseti, James Kavanaugh, MS, et al, Adv Radiat Oncol 2021 6:100639

LITE SABR M1: A phase I trial of Lattice stereotactic body radiotherapy for large tumors
Sai Duriseti, James Kavanaugh, MS, et al, Radiother Oncol: 2022 176:317-22

A quick SRS treatment planning interlude…







Dianne Hartgerink, et.al. . LINAC based SRS for multiple brain metastases: guidance for clinical implementation. Acta Onco 2019 58:9 1275-1282 doi: 10.1080/0284186X.2019.1633016

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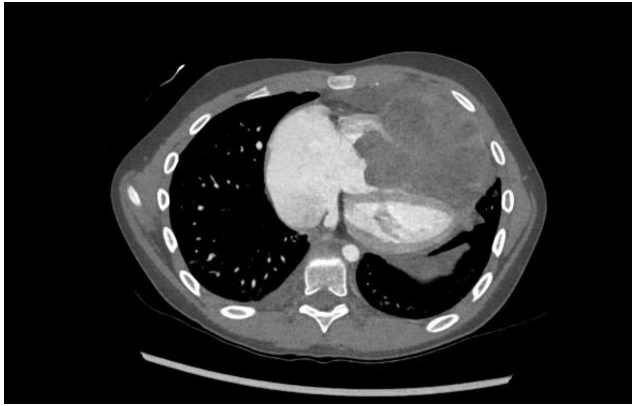
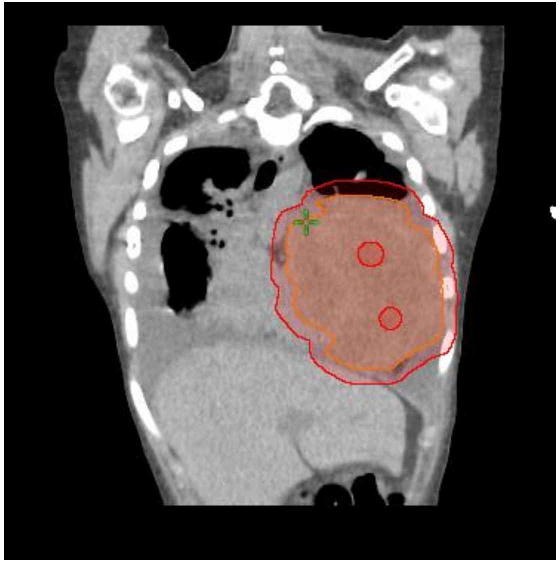
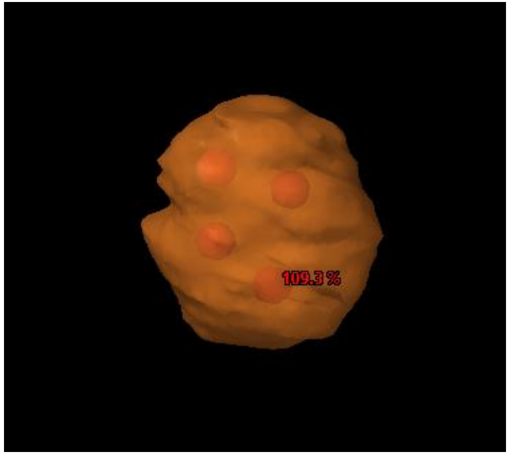
Case Study #1



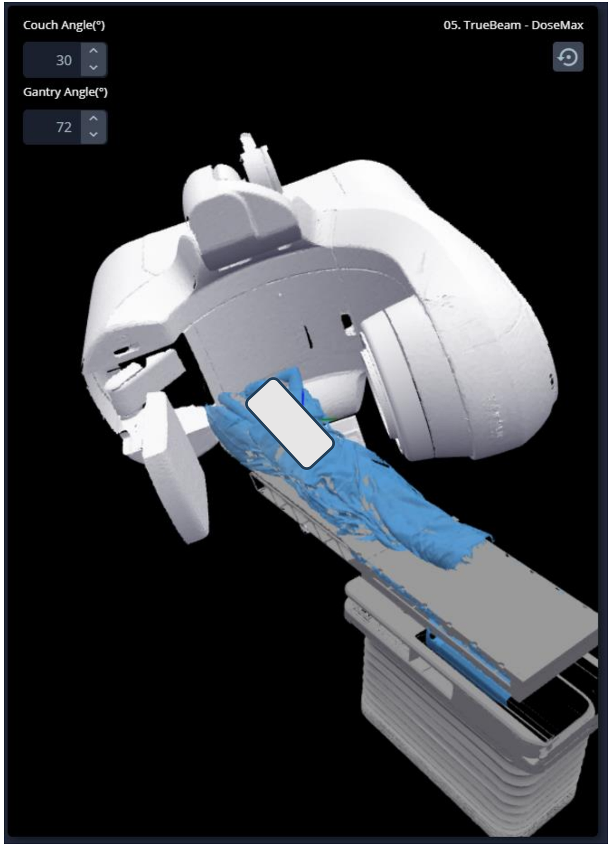




Case 1 : Sarcoma of the heart with pulmonary metastatic spread

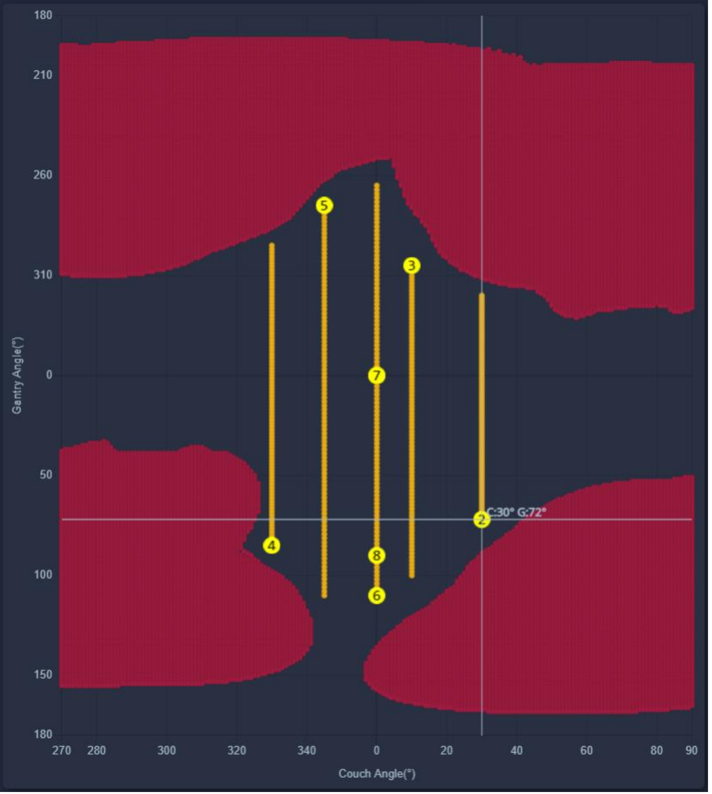
- Age 13
- GTV : 1285.86 cc
- PTV : 15.77 cc
- Heart PTV overlap: 86.3 cc

- GTV : 20 Gy in 5fx
- PTV : 50 Gy in 5fx



Heart SFRT

Status	#	ID	Type	Gantry	Couch	Direction	
	1	CBCT	Static	0°	0°	--	
	2	1A CCWc30	Arc	72° to 320°	30°	CC	
	3	1B CWc10	Arc	305° to 100°	10°	CW	
	4	1C CCWc330	Arc	85° to 295°	330°	CC	
	5	1D CWc345	Arc	275° to 110°	345°	CW	
	6	1E CCW	Arc	110° to 265°	0°	CC	
	7	AP Ortho	Static	0°	0°	--	
	8	LLat Ortho	Static	90°	0°	--	



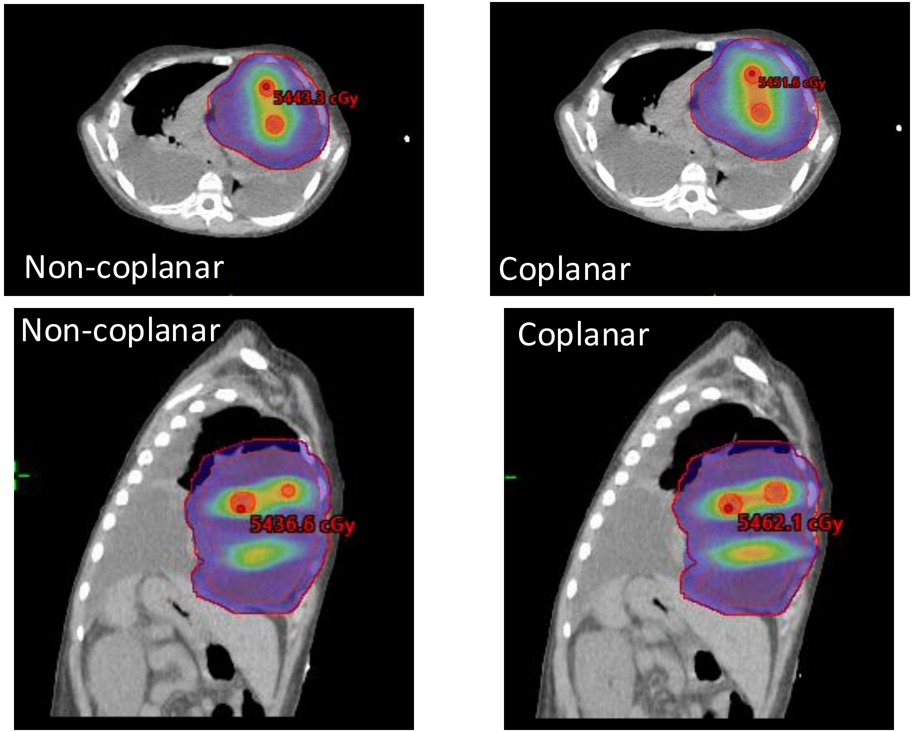
Target dosimetric coverage was similar between the two plans. Organ at risk values were superior for the five partial arc, non-coplanar plan versus the corresponding coplanar plan.

NON-COPLANAR VS COPLANAR

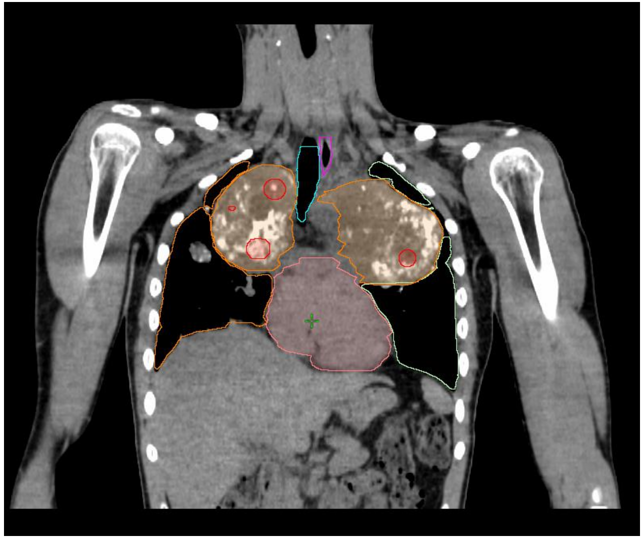
High Dose Target D95%: 50.4 vs 50.4 Gy
Low Dose Target D95%: 20.5 vs 20.5 Gy

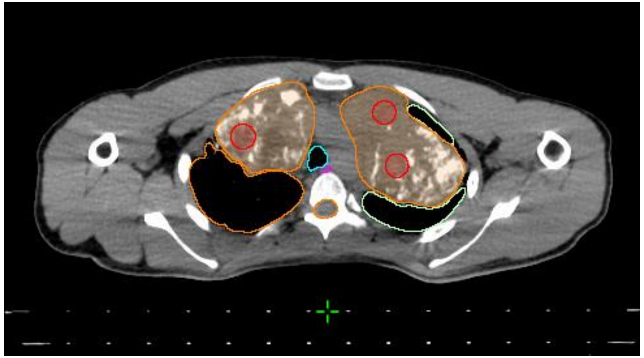
Esophagus mean: 6.9 vs. 7.8 Gy
Heart mean: 15.8 vs. 17.4 Gy
Canal max: 6.9 vs. 8.0 Gy

Lung_L mean: 10.5 vs. 9.7 Gy
Lung_R mean: 5.9 vs. 8.7 Gy
Lungs mean: 7.7 vs. 9.1 Gy



Case Study #2

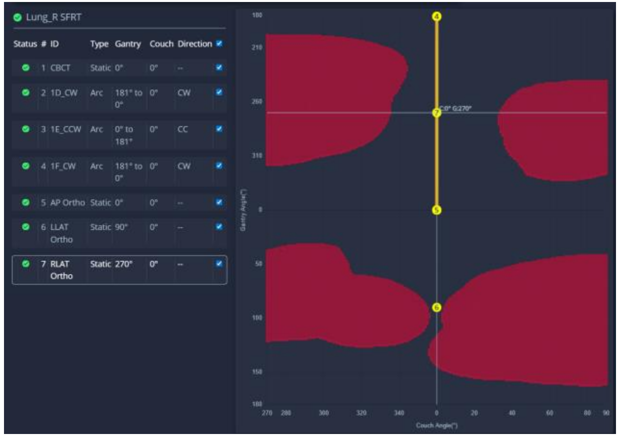


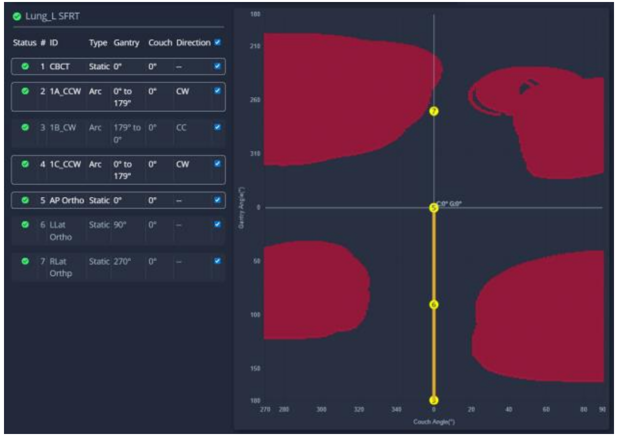


Case 2 : Metastatic Osteosarcoma

- Age: 24
- Metastatic refractory osteosarcoma to both lungs, primary site was right distal femur
- Lung_L PTV 19.7cc, GTV 419cc
- Lung_R PTV 15.8cc, GTV 295cc

  - PTV: 15 Gy in 1fx, GTV: 4 Gy in 1fx, 3 arcs for each plan





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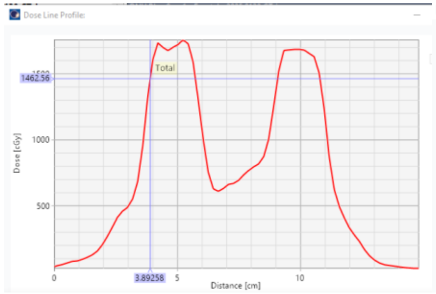
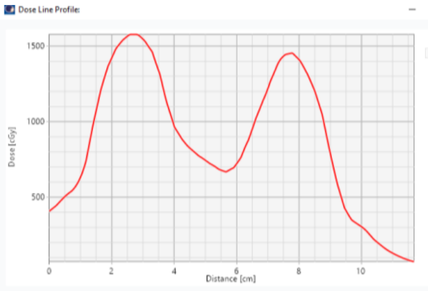
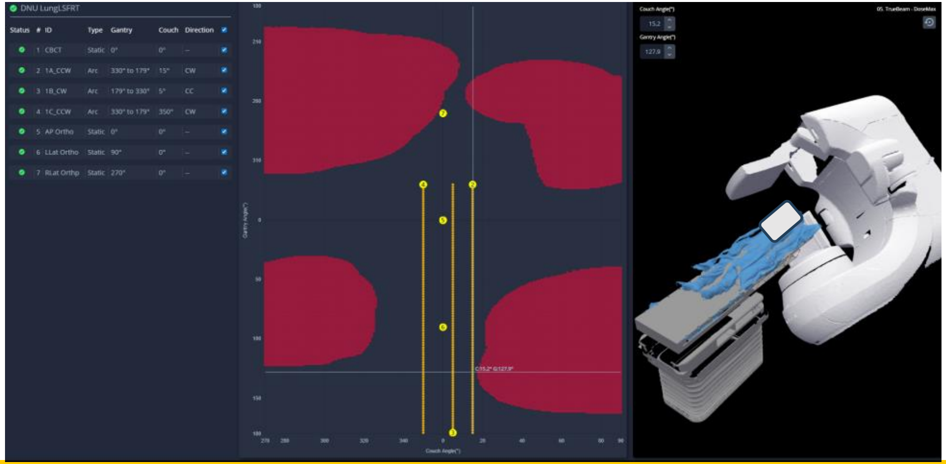
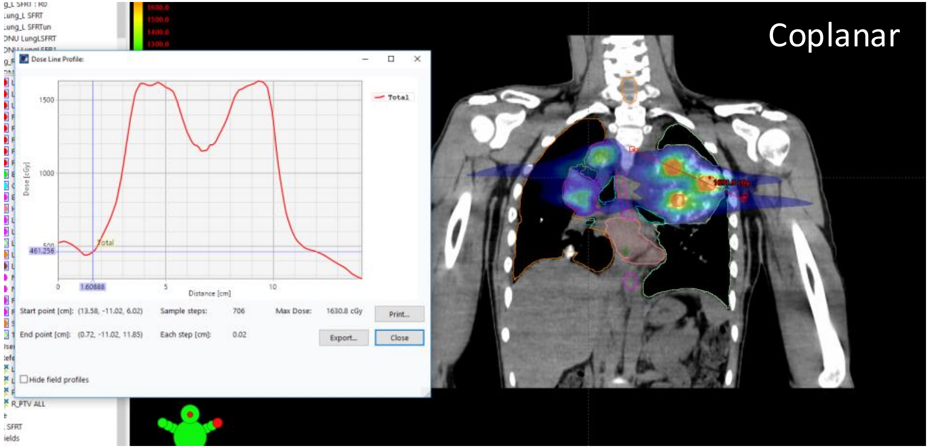
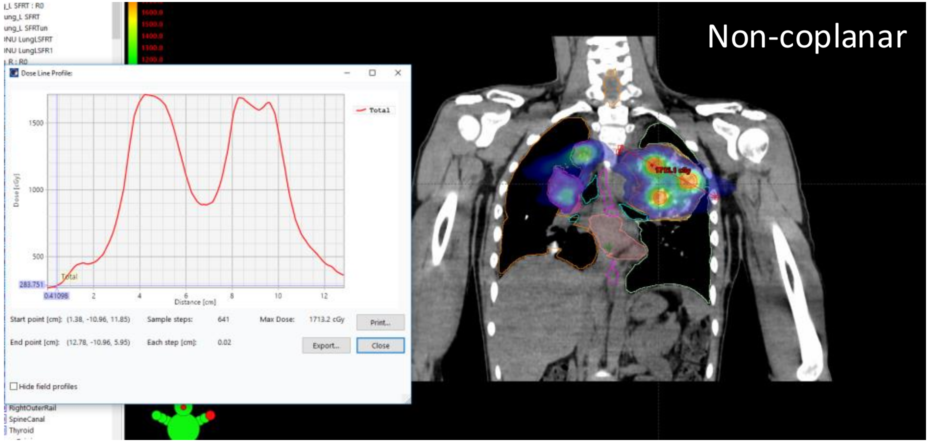




- PTV 15 Gy in 1fx, GTV 4 Gy in 1fx







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Non-coplanar treatment plan had slightly lower OAR doses than coplanar plan.

Non-coplanar treatment plan yielded superior SFRT dosimetric ratios than the coplanar treatment plan.

Non-coplanar:

R_Lung: D_5/D_{95} – 4.00, D_{10}/D_{90} – 3.03
L_Lung: D_5/D_{95} – 3.94, D_{10}/D_{90} – 2.86

Four beams:

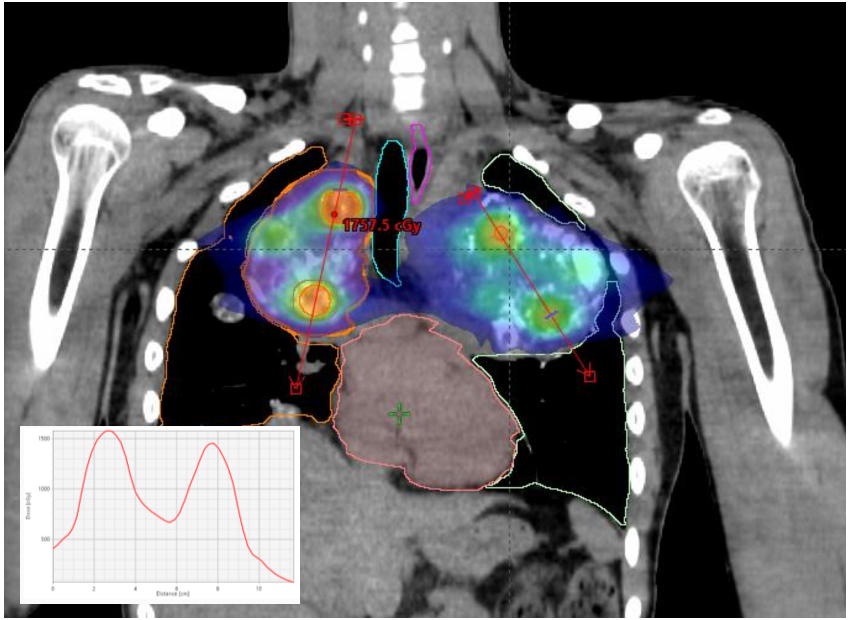
R_Lung: D_5/D_{95} – 3.99, D_{10}/D_{90} – 3.22
L_Lung: D_5/D_{95} – 3.90, D_{10}/D_{90} – 2.85

Coplanar:

R_Lung: D_5/D_{95} – 3.72, D_{10}/D_{90} – 2.93
L_Lung: D_5/D_{95} – 3.68, D_{10}/D_{90} – 2.86

Spatially fractionated radiation therapy is designed for large lesions with otherwise low control rates.

The treatment takes advantage of the extra biological damage of the high dose and the high/low dose combination to enhance efficacy.



Carefully chosen treatment delivery parameters – optimal non-coplanar beam selection – improve SFRT target and lower organ at risk dosimetric values.


Questions?