Spatially Fractionated Radiation Therapy for Durable Palliation

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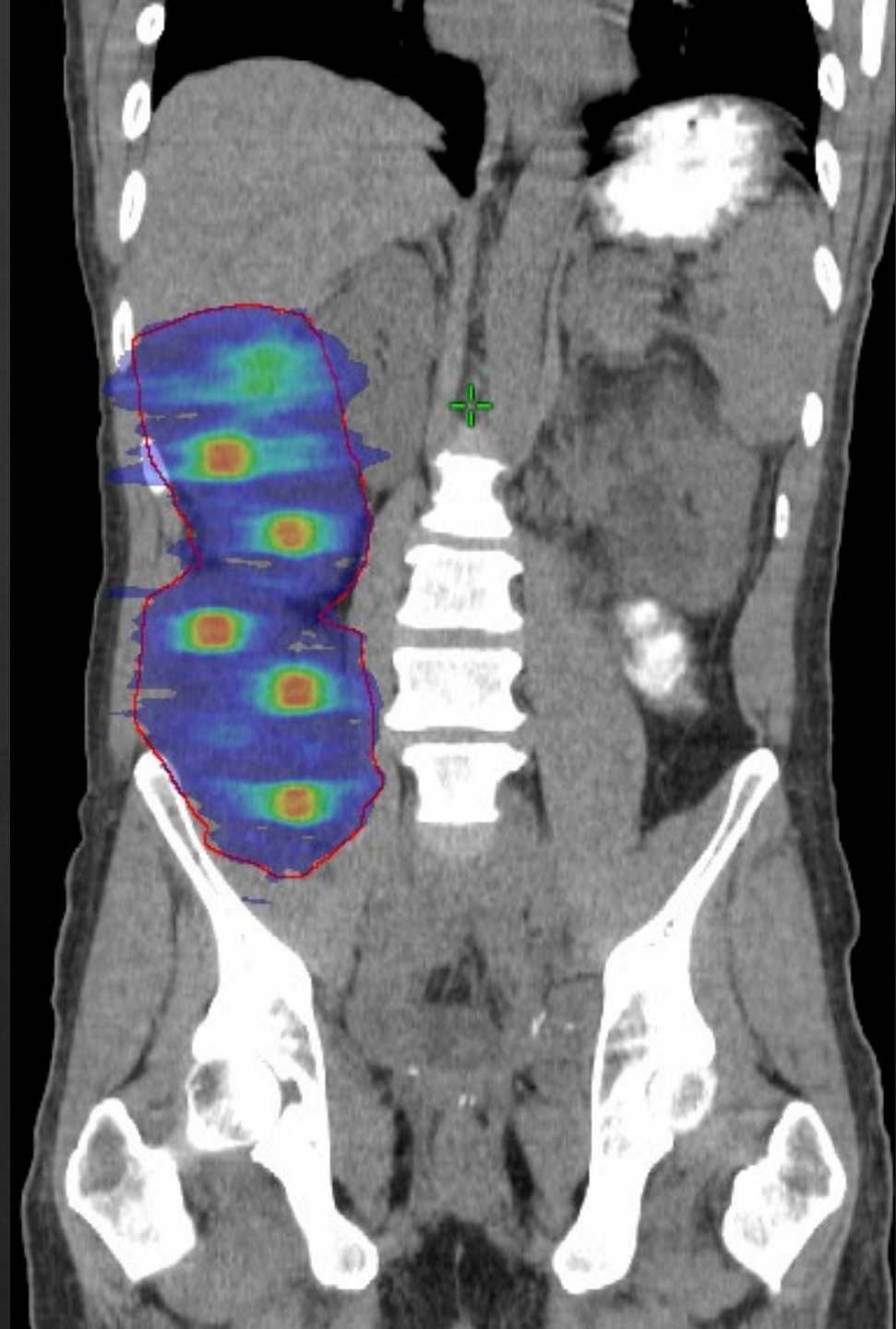


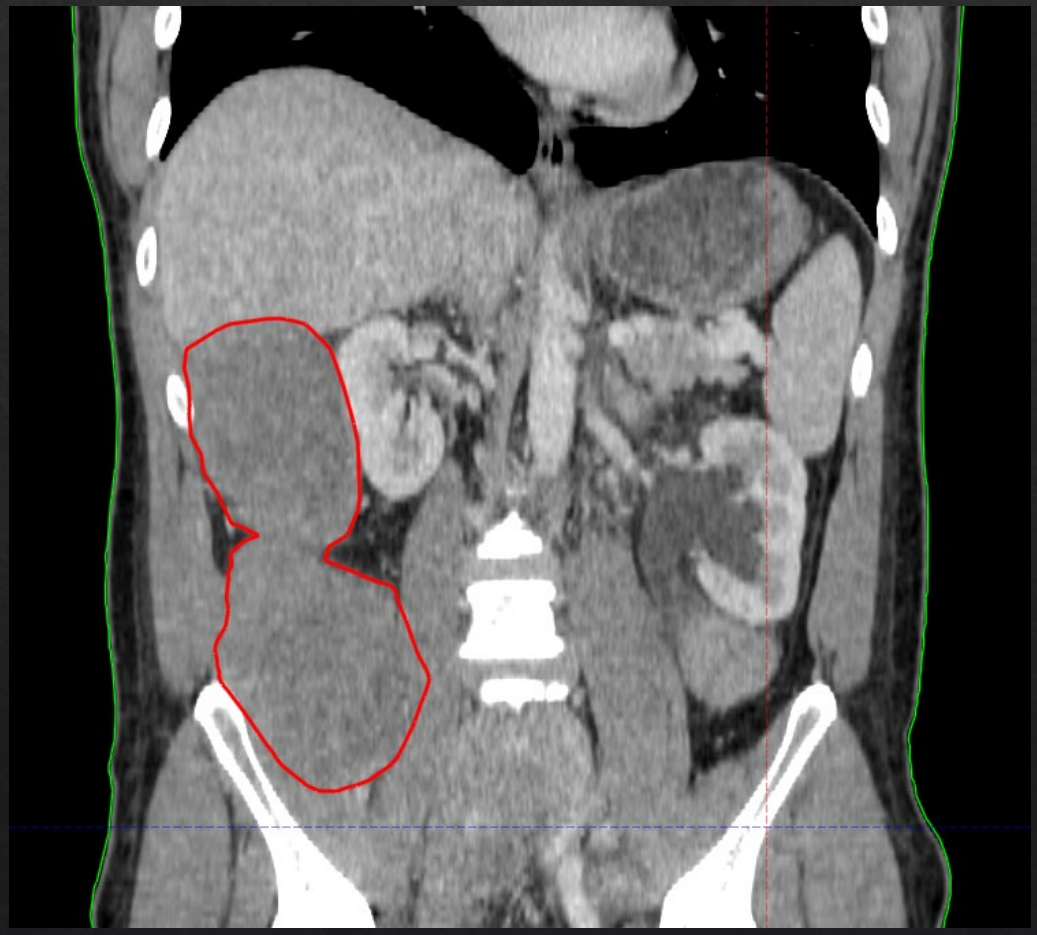
Objectives

- Define SFRT
- Discuss the challenges of treating bulky tumors
- Review the history of SFRT
- Case discussions
- Overview of the USC experience

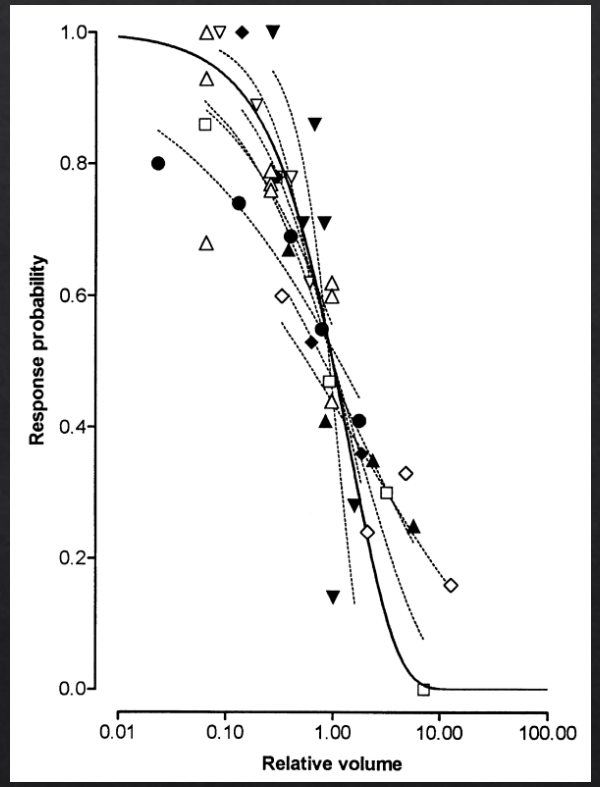
What is Spatially Fractionated Radiation Therapy?

- SFRT is a mode of external beam radiation therapy characterized by a highly non-uniform dose distribution
- It's "spatially fractionated" because the dose varies across space
- Often described as having "peak" and "valley" doses

The challenge of bulky tumors



The challenge of bulky tumors: volume

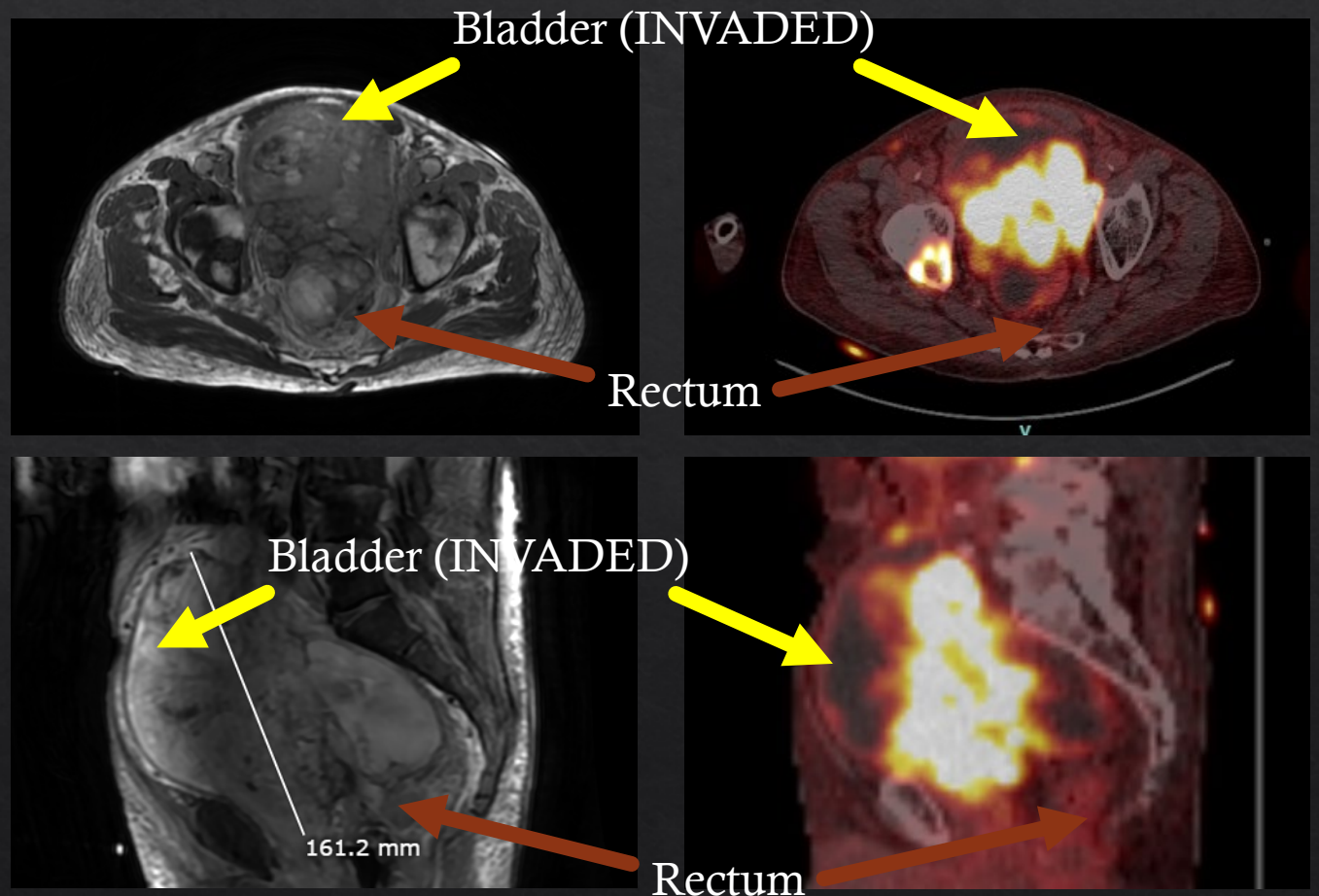


Expected response probability
Head and neck [Hjelm-Hansen et al. 1979]
Head and neck [Van den Bogaert et al. 1995]
Head and neck [Johnson et al. 1995a]
T3 glottic larynx [Pameijer et al. 1997]

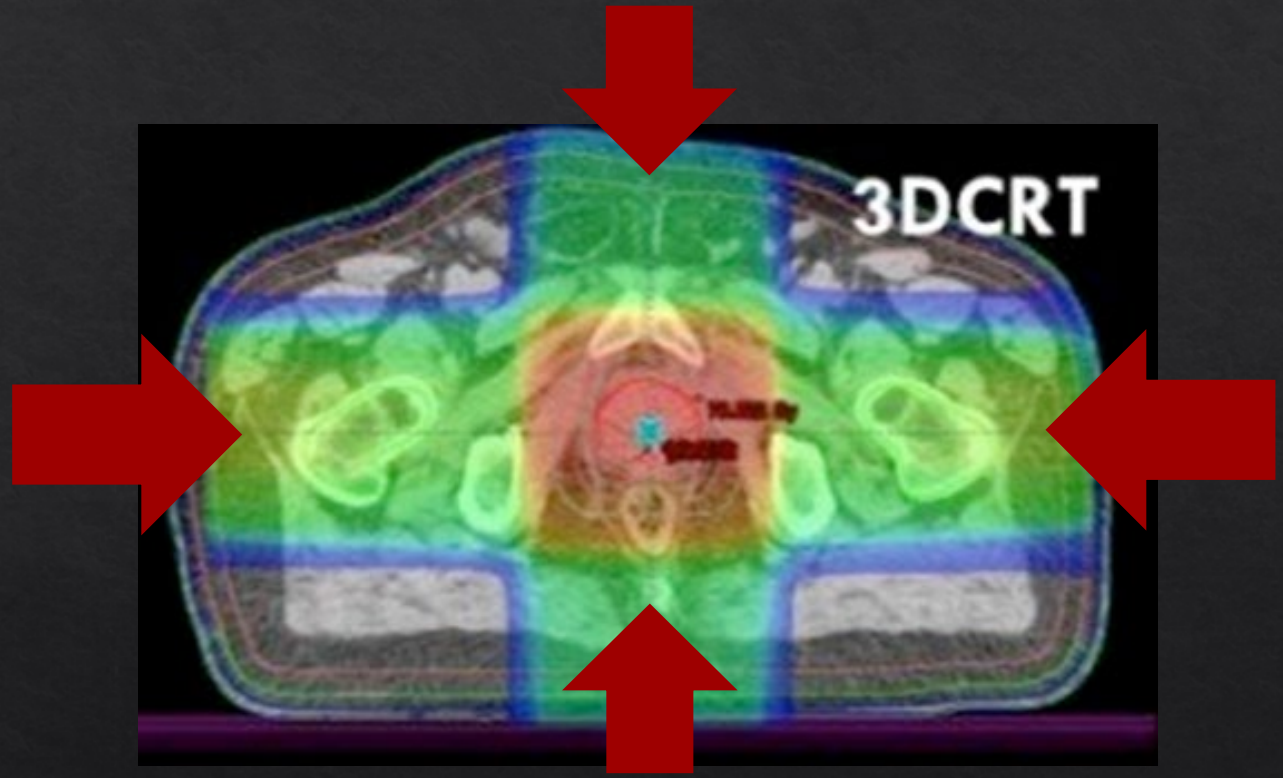
Melanoma [Overgaard et al. 1986]
Breast cancer [Arriagada et al. 1985]
Cervix cancer [Mendenhall et al. 1994]
Cervix cancer [Magee et al. 1991]

Dubben, Hans-Hermann, Howard D. Thames, and Hans-Peter Beck-Bornholdt. "Tumor volume: a basic and specific response predictor in radiotherapy." Radiotherapy and oncology 47.2 (1998): 167-174.

The challenge of bulky tumors: OAR overlap



The challenge of bulky tumors: OAR overlap



Sveistrup et al. *Radiation Oncology* 9.1 (2014): 44.

History of Spatially Fractionated Radiation Therapy

- 1909: Kohler publishes the first description of SFRT
  - **Kilovoltage x-rays**
  - Wire-mesh placed over x-ray tube to intentionally shield the skin in an intentional pattern to allow healing
  - Administered massive doses, 10-20 times the total dose usually given at that time through a conventional open field.

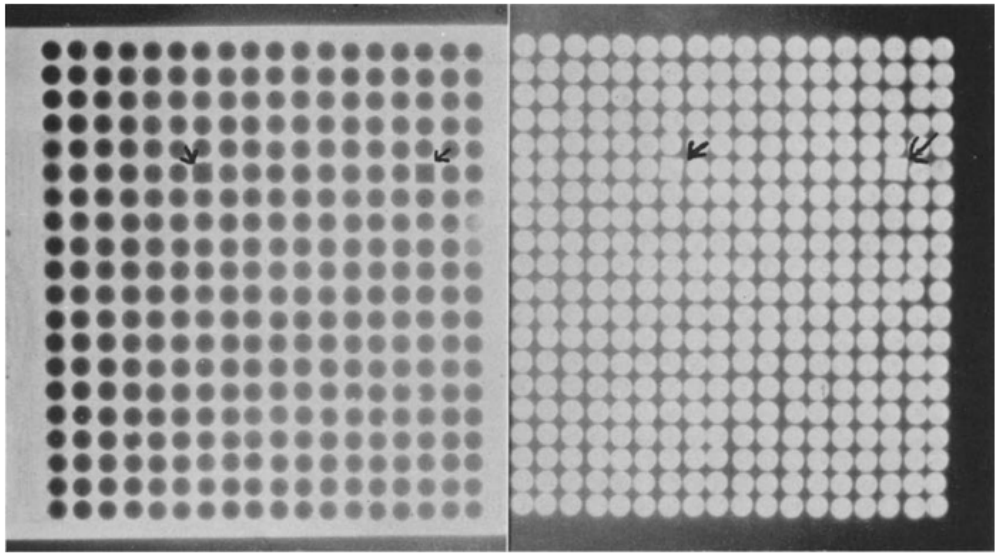
Dr. Alban Köhler

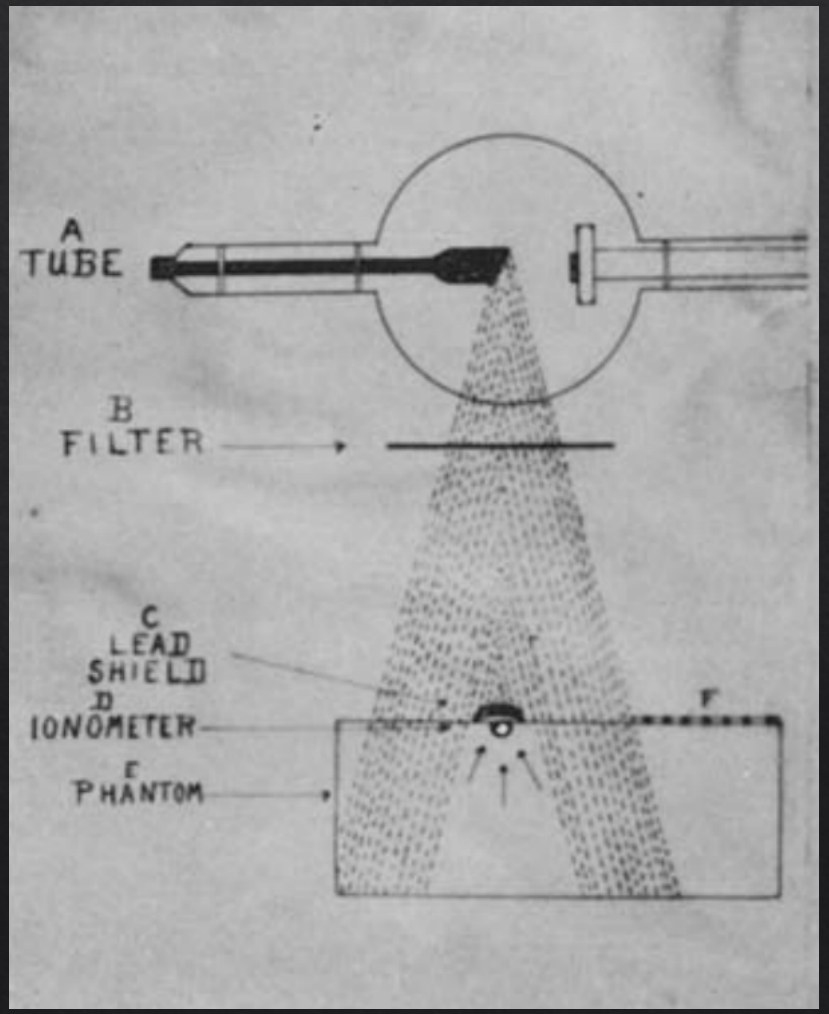
Spatially Fractionated Radiation Therapy in 1932

THE VALUE OF A MULTI-PERFORATED SCREEN IN DEEP X-RAY THERAPY[1]

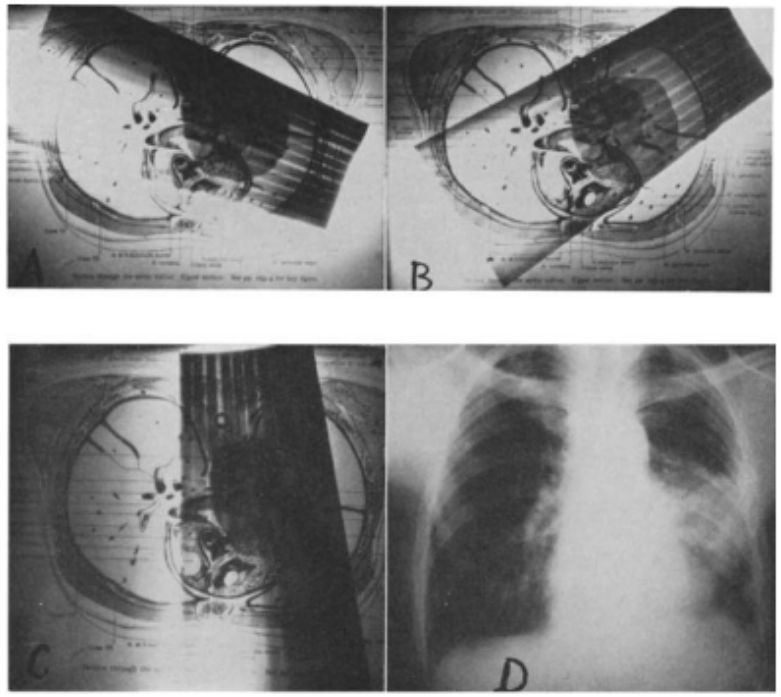
A PRELIMINARY REPORT ON A NEW METHOD OF DELIVERING MULTIPLE ERYTHEMA DOSES WITHOUT PERMANENT INJURY TO THE SKIN

By F. LIBERSON, M.D., Roentgenologist, U. S. Marine Hospitals, Stapleton, Ellis Island, and New York City





Spatially Fractionated Radiation Therapy in 1932



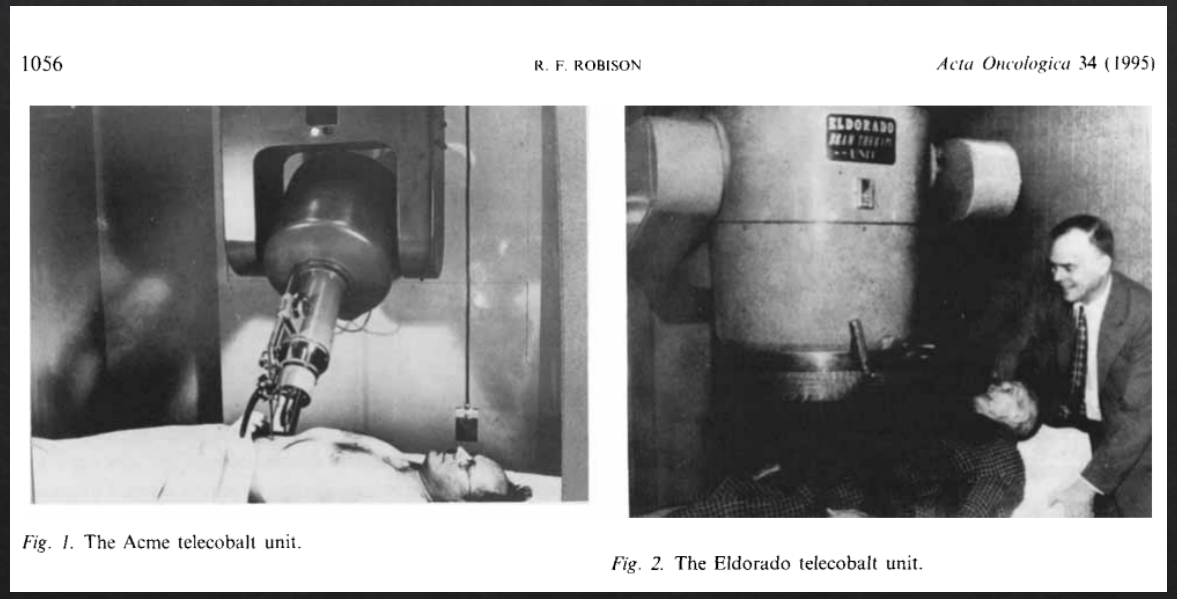
Figs. 5-*A* to 5-*F*. These show the arrangements of the portals of treatment in a case of neoplasm of the left side of the chest *D*, with metastasis in the cervical spine. The tumor is plotted on a topographical cross-section of the chest. *A* shows the plotting of one of the suitable streamers of size sufficient to cover the tumor by a small margin, the streamer directed from the left axilla anterior to the right axilla posterior. *B*, directing the streamer from the left axilla posterior to the right axilla anterior. *C*, from the left back to the left front. Note that in *E* all streamers cross in the region of the tumor, but neither the entrance nor the exit rays cross at any skin surface. *F* shows the appearance of the skin two weeks after treatment with three erythema doses through the perforator.

Spatially Fractionated Radiation Therapy in 1932

The fact that the same recommendations which I made in 1909 have also been made in December, 1932, indicates that the method has a future.

ALBAN KÖHLER

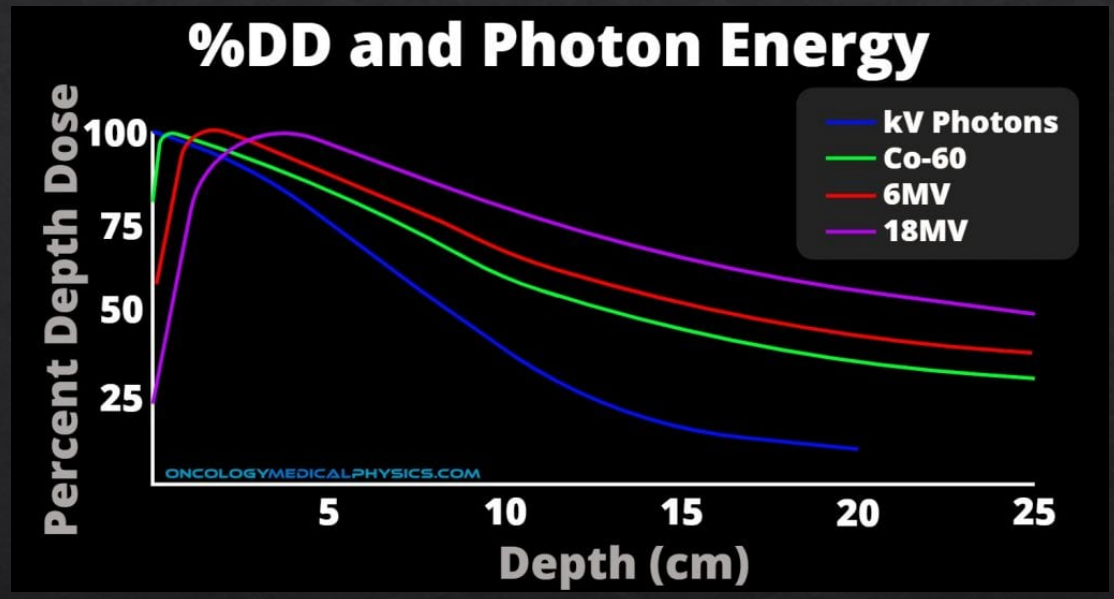
Then in the 1950s: MVs



1056 R. F. ROBISON *Acta Oncologica* 34 (1995)

Fig. 1. The Acme telecobalt unit.

Fig. 2. The Eldorado telecobalt unit.

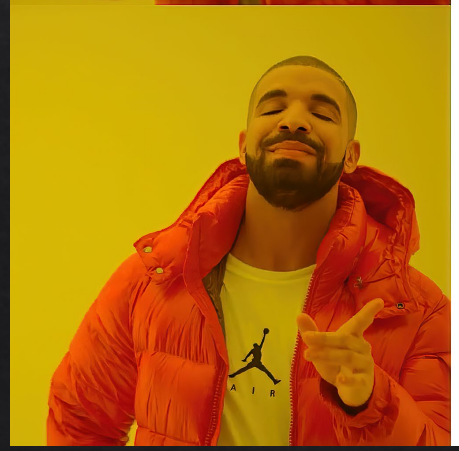


Robison, Roger F. "The race for megavoltage x-rays versus telegamma." Acta Oncologica 34.8 (1995): 1055-1074.

Then in the 1950s: MVs

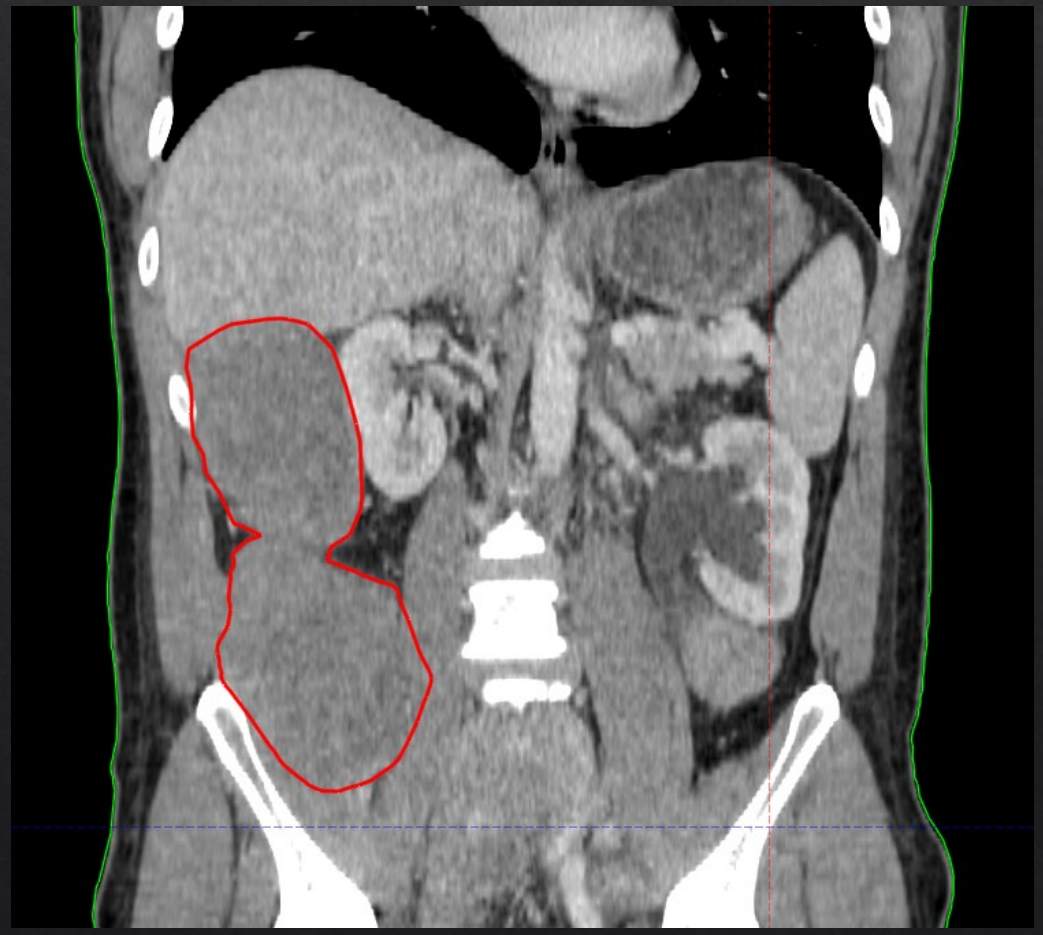
- As a result of this technology shift, grid therapy became less utilized

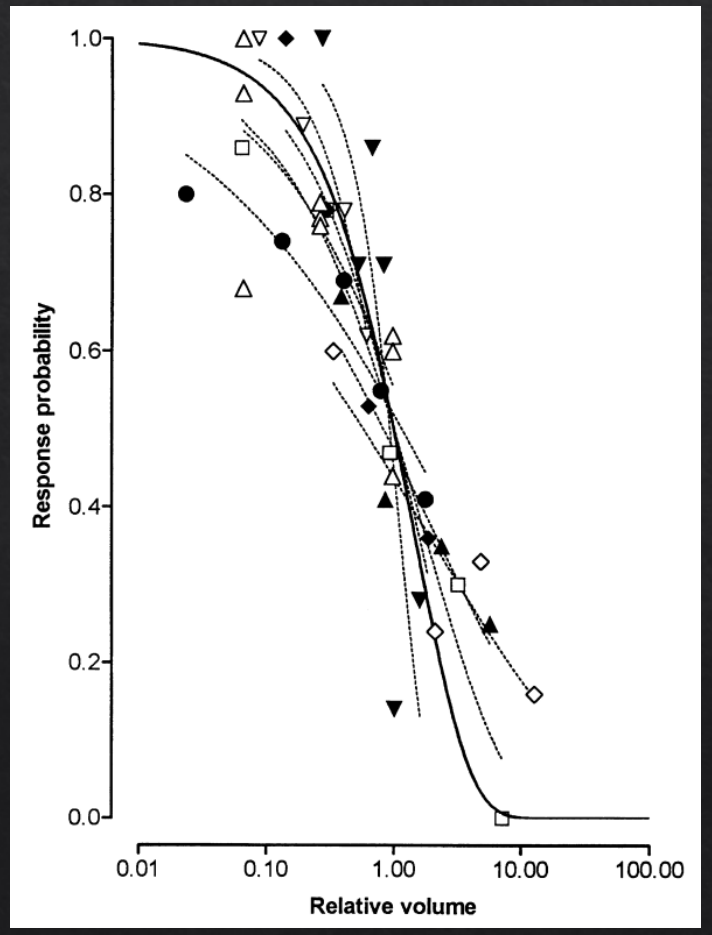
Grid for skin recovery



Inherent skin-sparing at MV energies

But the problem remains…

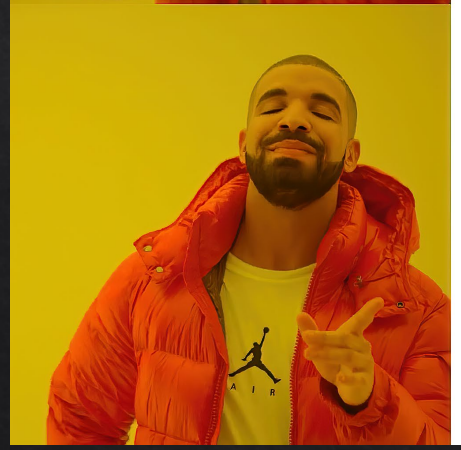




1990s:

1990s:

Grid for skin recovery



Grid for deeper normal tissue recovery

History of Spatially Fractionated Radiation Therapy

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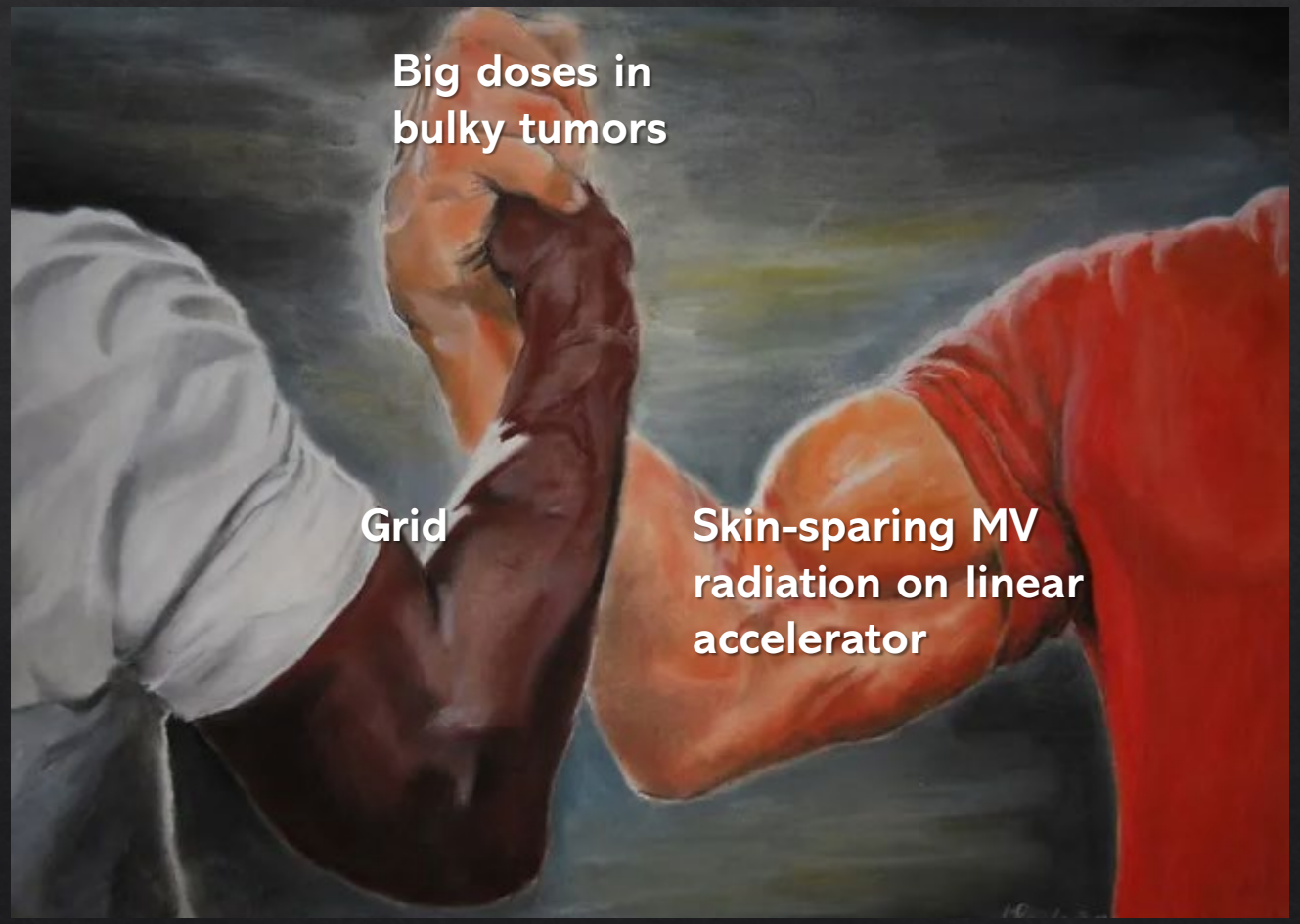
  - Wire-mesh placed over x-ray tube to intentionally shield the skin in an intentional pattern to allow healing
  - Administered massive doses, 10-20 times the total dose usually given at that time through a conventional open field.

Dr. Alban Köhler

1990s:



1990: Grid therapy on MV linac

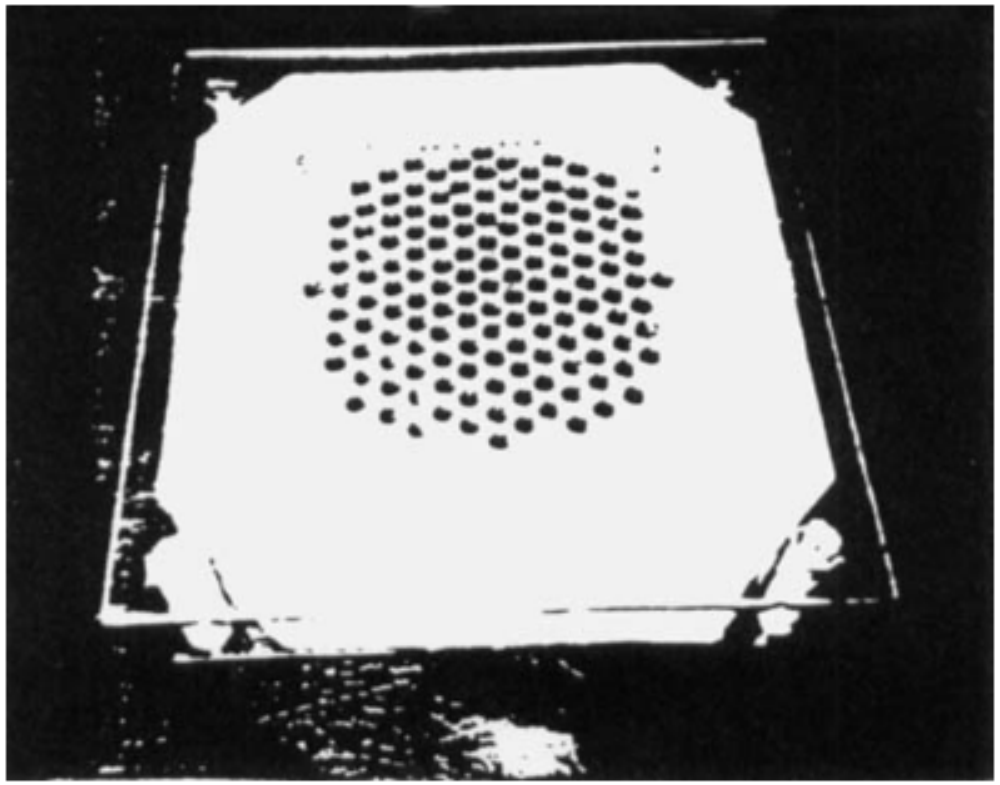


FIG. 1. The Jefferson "Hexaboard Array" GRID that fits into the alloy tray of the linear accelerator.

TABLE 1. Distribution of Patients

	No. of patients	Prior XRT	Concurrent XRT
Osteosarcoma	6	—	5
Liposarcoma	2	—	2
Leiomyosarcoma	1	—	—
Colorectal CA	6	4	2
Liver	3	—	2
Squamous (vagina)	1	1	1
Renal cell CA	1	—	1
Melanoma	1	—	1
Adeno CA (prostate)	1	1	—
Total	22	6	14

CA: carcinoma; XRT: radiation therapy; Adeno CA: adenocarcinoma.

TABLE 3. Response Rate as a Function of the Four Most Common Symptoms

Symptoms	Total no.	CR (%)	PR (%)	Total response CR + PR	NR (%)
Pain	19	5 (26)	12 (67)	89%	2 (7)
Edema	3	—	3 (100)	100%	—
Bleeding	4	4 (100)	—	100%	—
Mass effect	5	—	4 (80)	80%	—

CR: complete response; PR: partial response; NR: no response.

Mohiuddin, Mohammed, et al. "Palliative treatment of advanced cancer using multiple nonconfluent pencil beam radiation: a pilot study." Cancer 66.1 (1990): 114-118.

1990: Grid therapy on MV linac

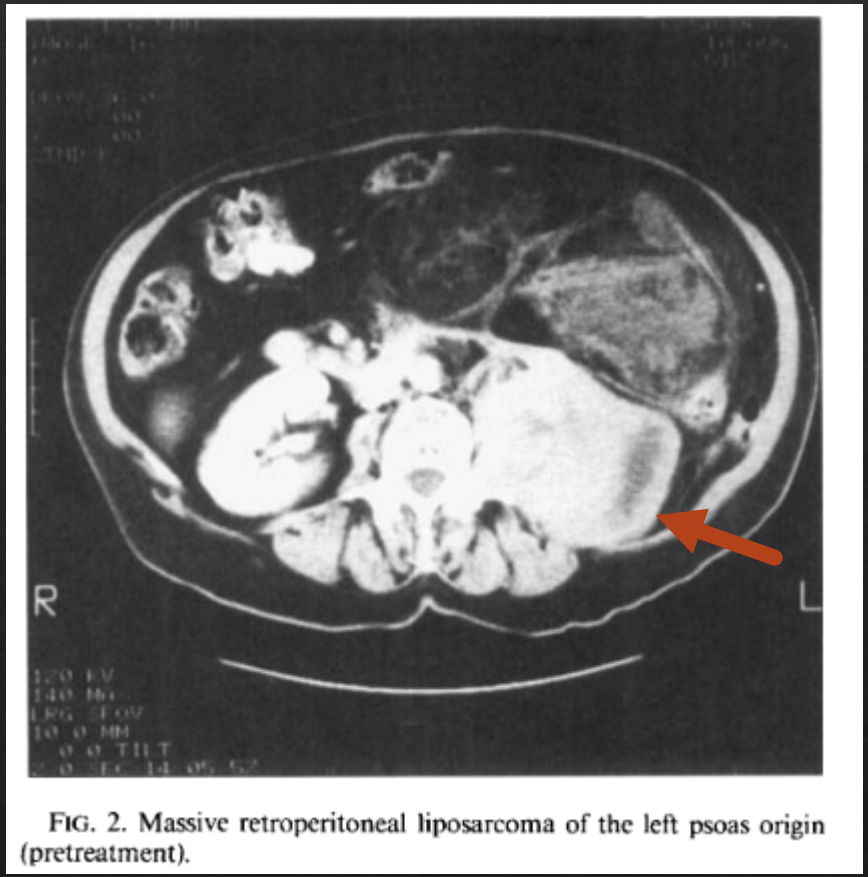


FIG. 2. Massive retroperitoneal liposarcoma of the left psoas origin (pretreatment).

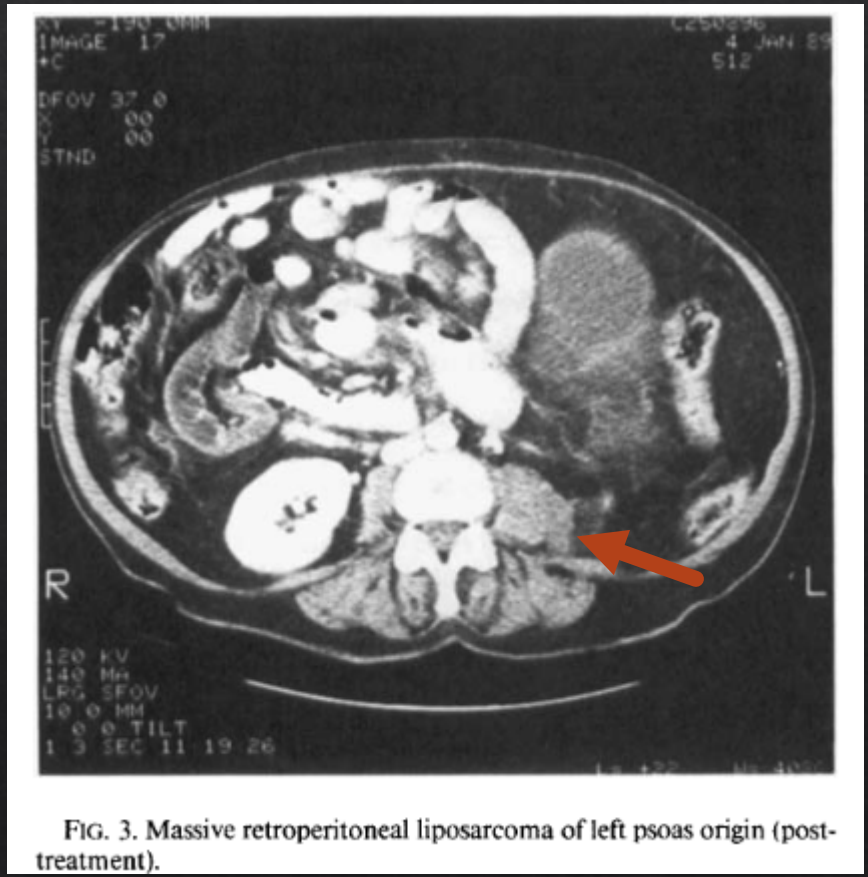


FIG. 3. Massive retroperitoneal liposarcoma of left psoas origin (post-treatment).

Mohiuddin, Mohammed, et al. "Palliative treatment of advanced cancer using multiple nonconfluent pencil beam radiation: a pilot study." Cancer 66.1 (1990): 114-118.

2000s: Grid using MLCs

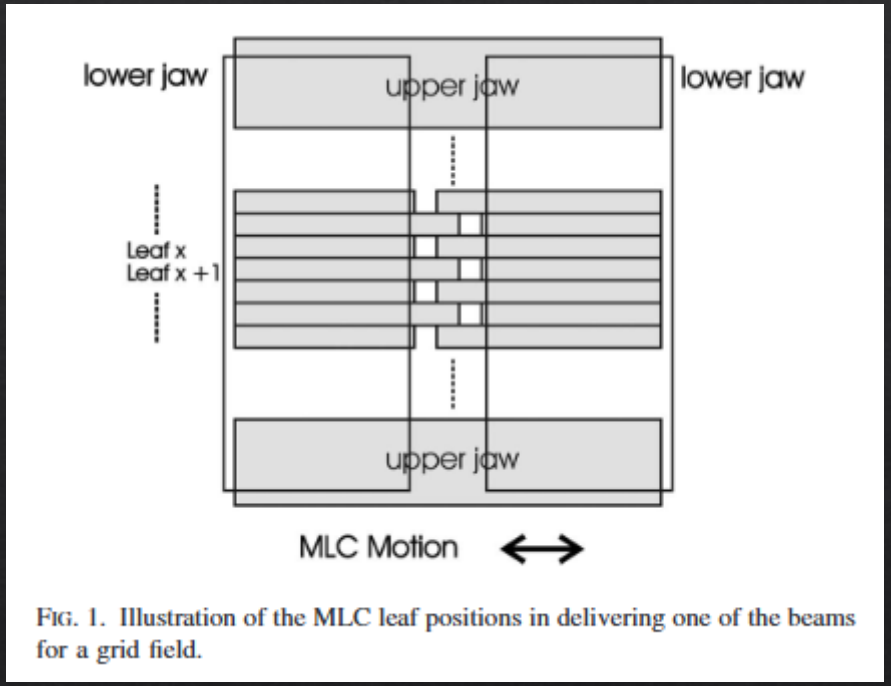


FIG. 1. Illustration of the MLC leaf positions in delivering one of the beams for a grid field.

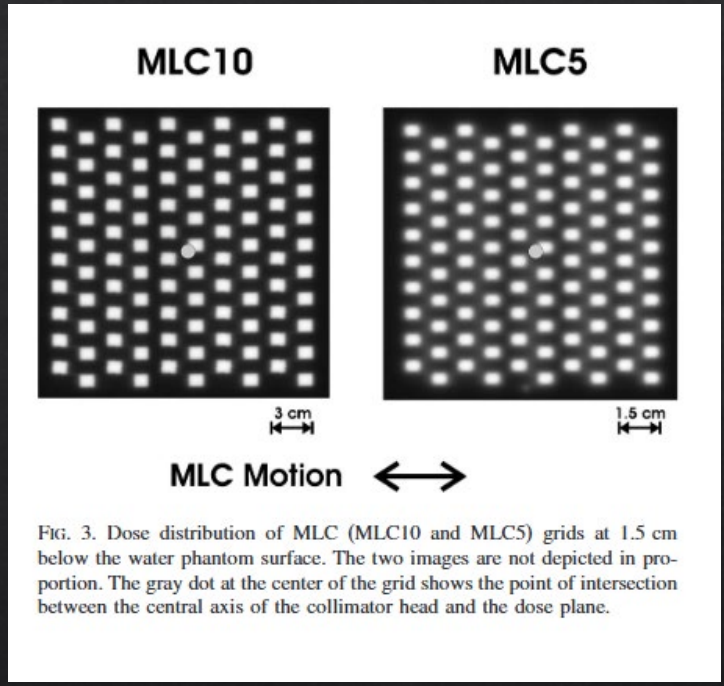
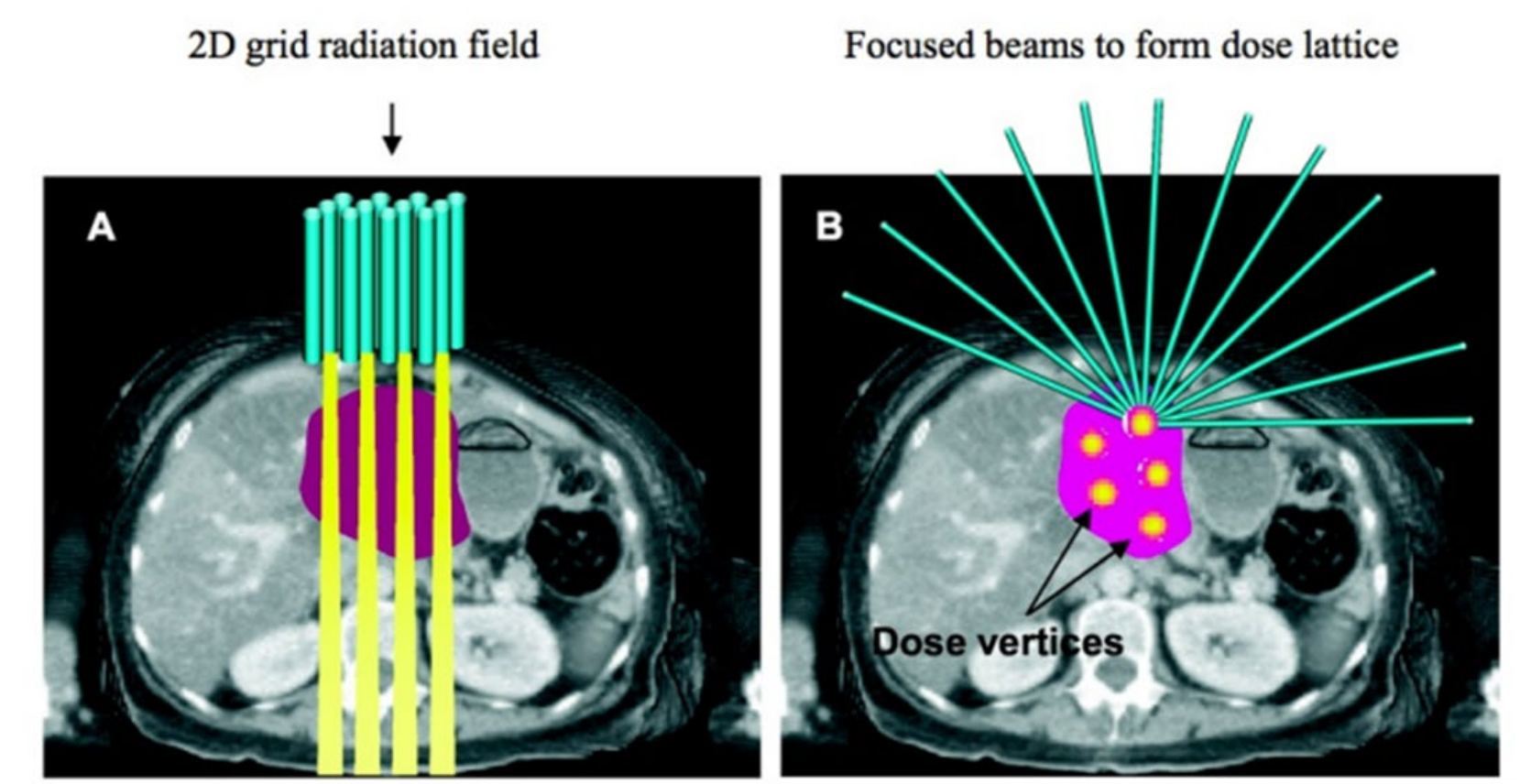


FIG. 3. Dose distribution of MLC (MLC10 and MLC5) grids at 1.5 cm below the water phantom surface. The two images are not depicted in proportion. The gray dot at the center of the grid shows the point of intersection between the central axis of the collimator head and the dose plane.

Ha, Jonathan K., et al. "Feasibility of delivering grid therapy using a multileaf collimator." Medical physics 33.1 (2006): 76-82.

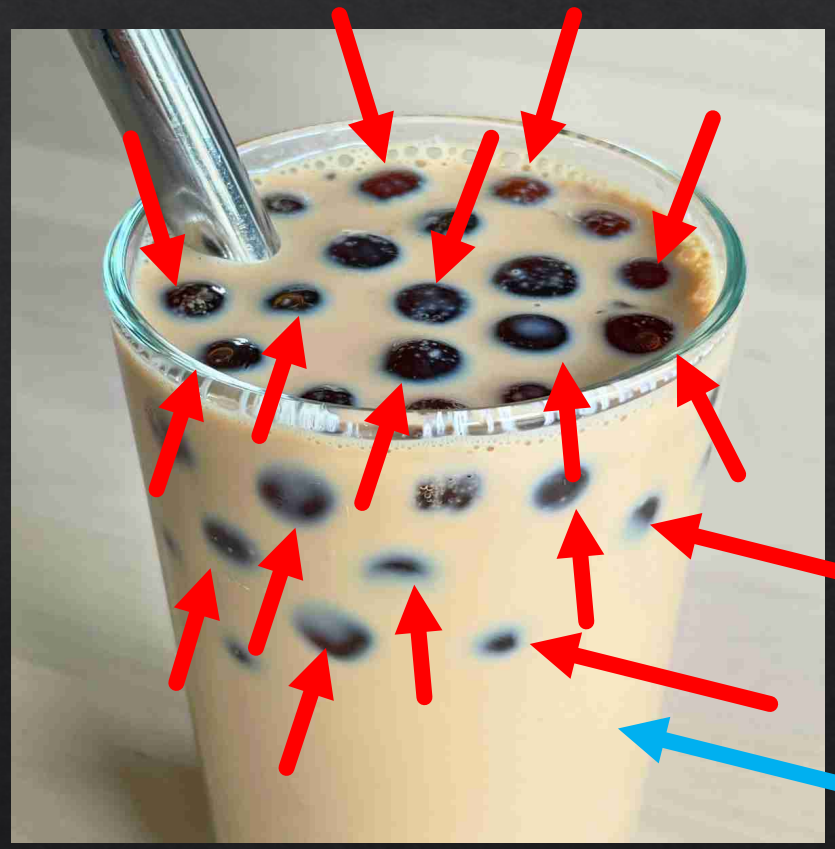
2010: Grid → Lattice



Wu et al, Cureus 2010

Wu, Xiaodong, et al. "On modern technical approaches of three-dimensional high-dose lattice radiotherapy (LRT)." Cureus 2.3 (2010).

Spatially Fractionated Radiation Therapy (SFRT)

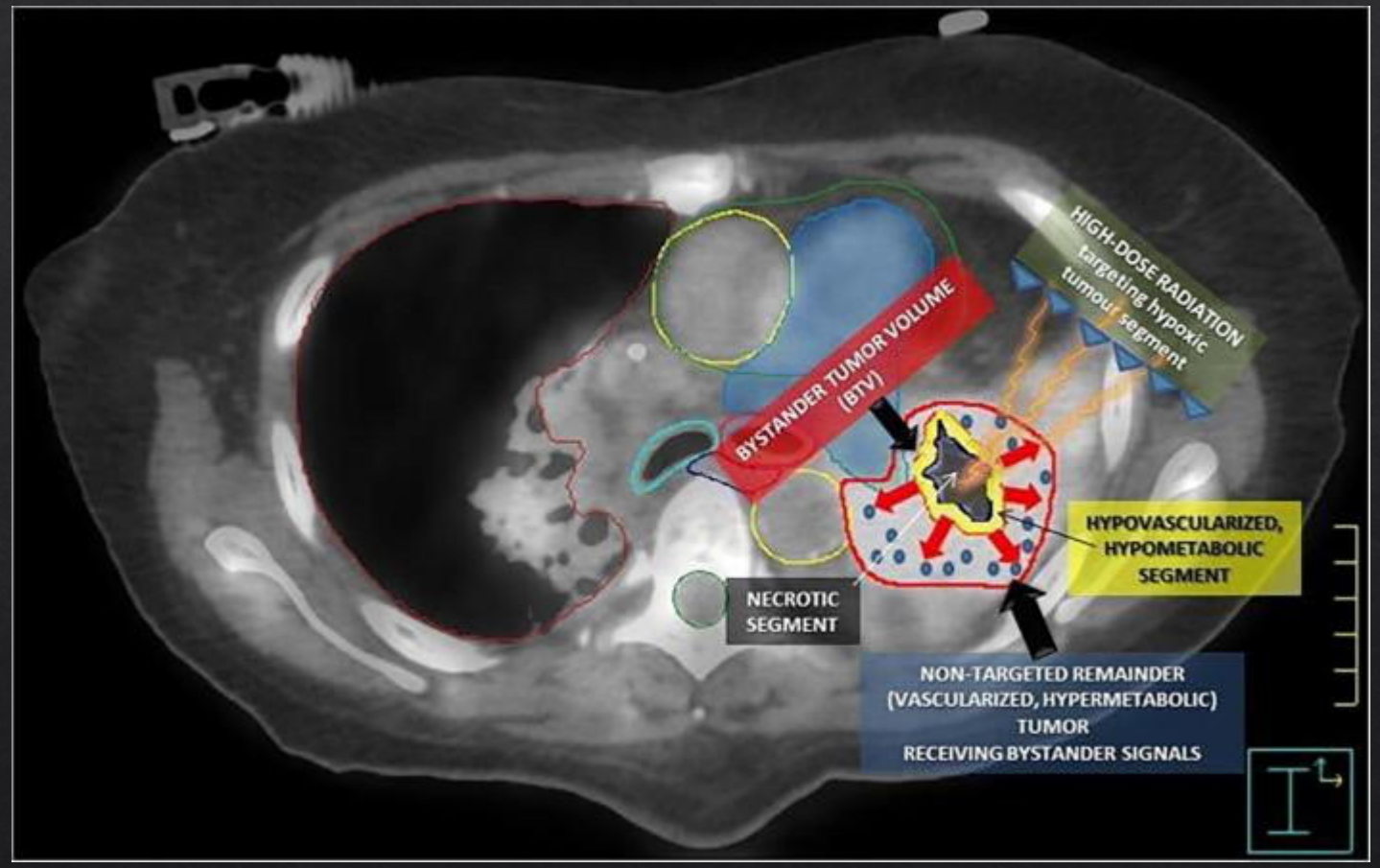


High, Tumor-Unfriendly dose

Low, ORGAN-FRIENDLY dose

How does it work?

- Bystander effect
- Vascular effects
- Immunomodulation



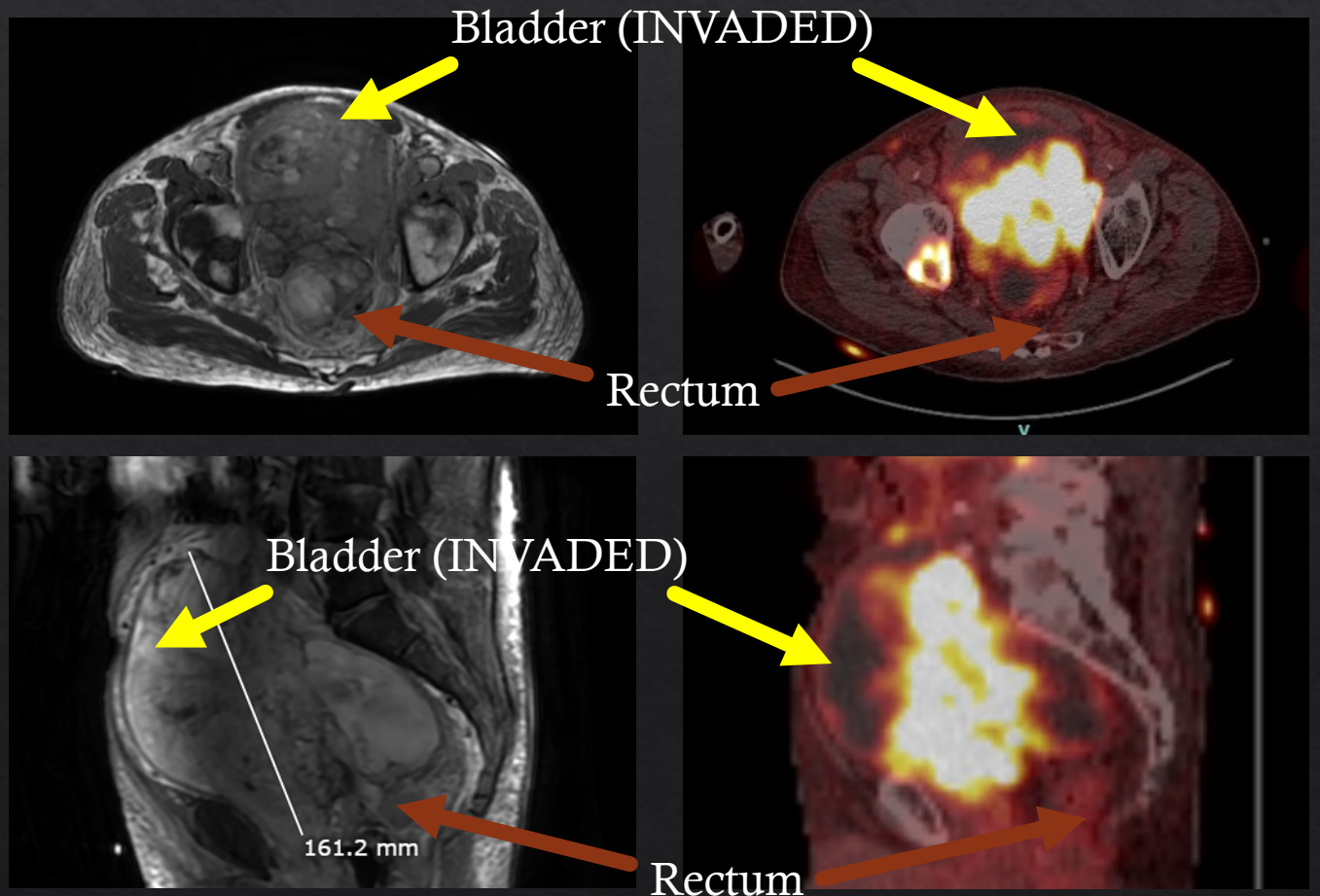
Tubin et al., Radiation Oncology 14.1 (2019): 21.

How we plan SFRT at USC

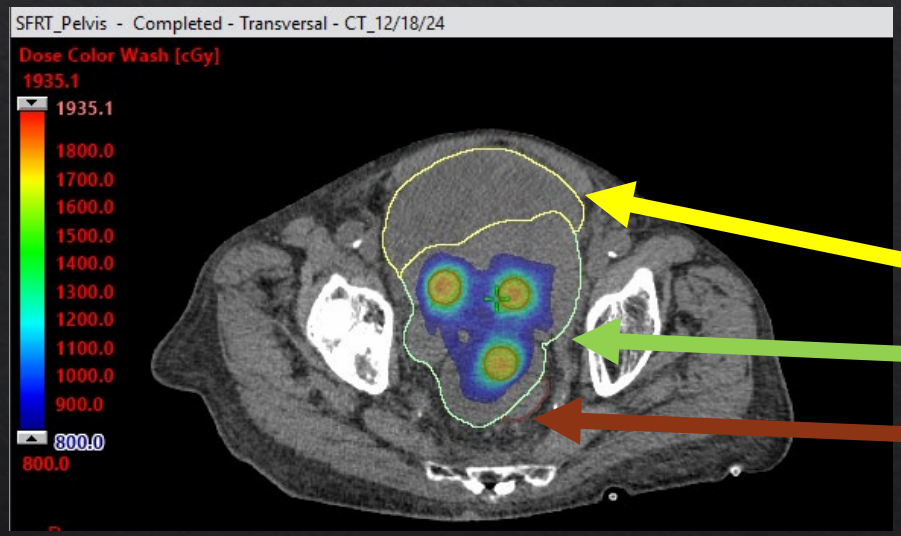
- 4 cm sphere-to-sphere distance
- 1 cm sphere-to-GTV surface distance
- Homegrown software to maximum number of spheres in GTV while still meeting the above criteria

Case 1:

- 86 yo man with metastatic castrate-resistant prostate cancer and very locally aggressive bulky primary tumor



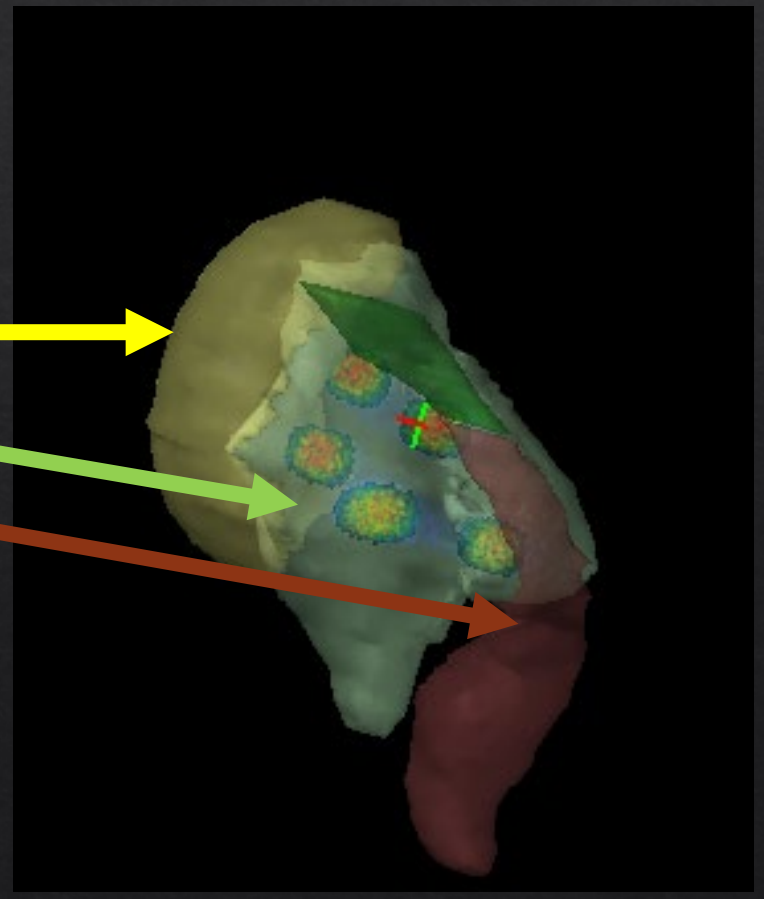
- SFRT with 15 Gy in 1 fraction to internal spheres
- VMAT with specific intent to create high-dose hot spots distributed throughout a **bulky** tumor, while keeping the remainder of the tumor volume and tumor surface dose low



Bladder (INVADED)

Tumor

Rectum



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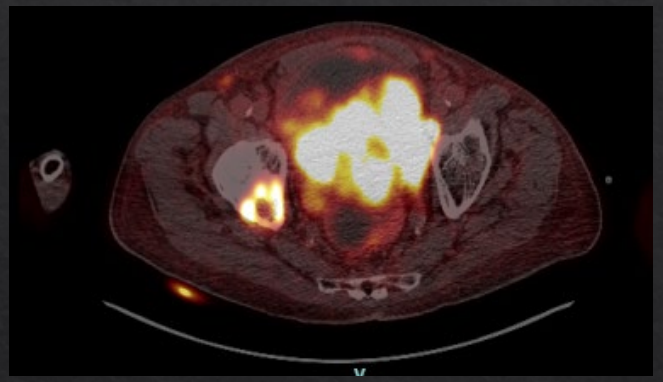
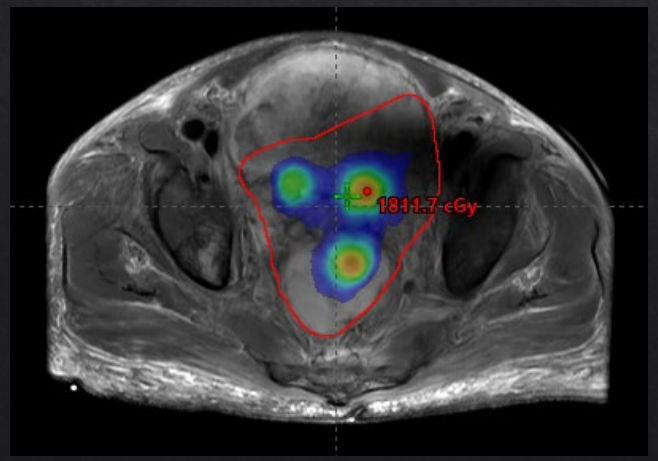
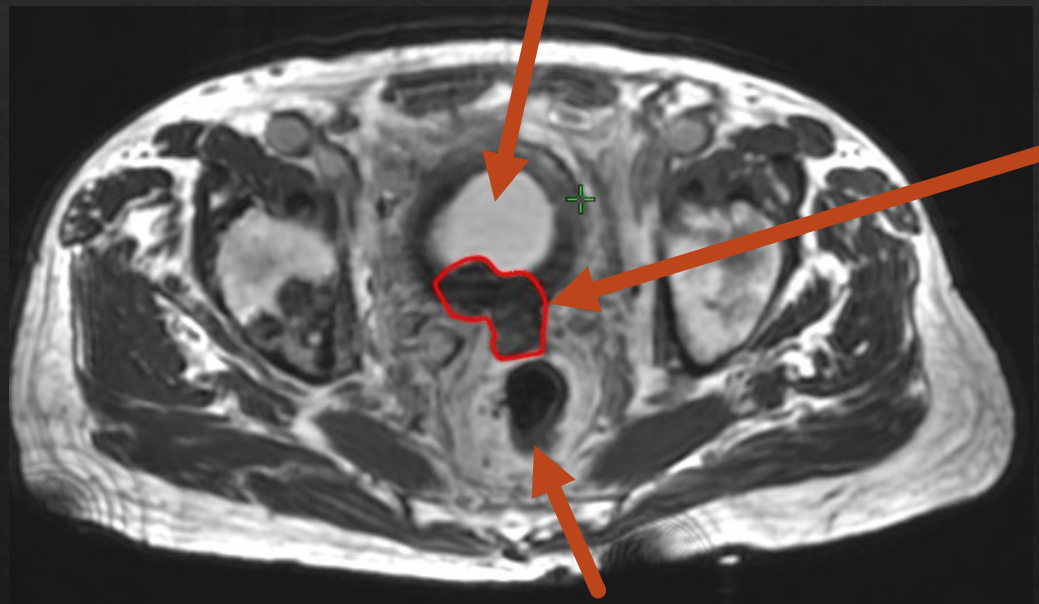
9 months later…





Bladder now identifiable



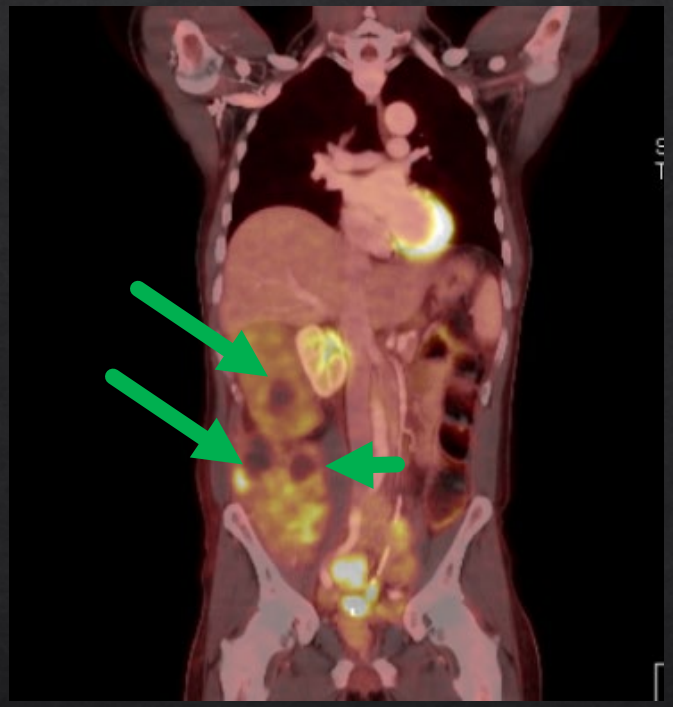
Tumor decreased from 915 cc to 47 cc (-95%)

Rectum decompressed (patient reported resolution of constipation)

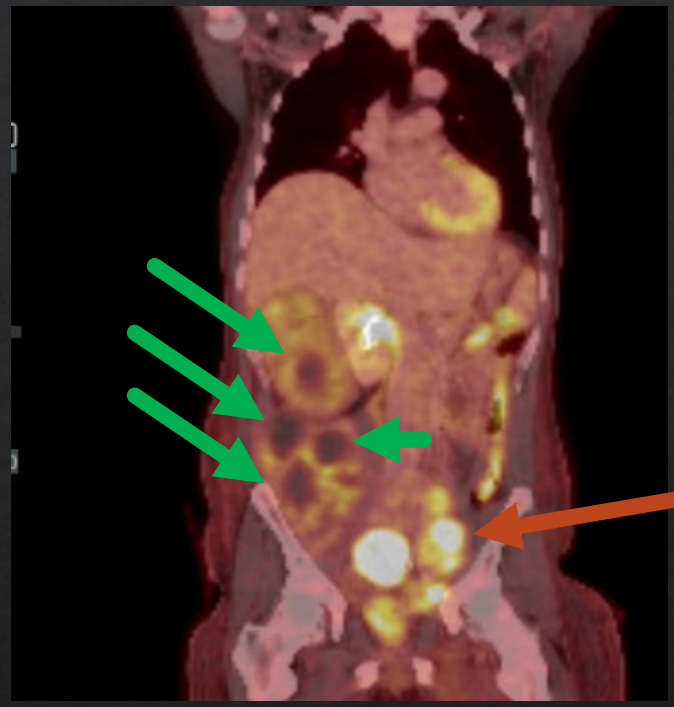
Case 2:

- 50 yo man with metastatic gastrointestinal stromal tumor (GIST) and symptomatic right retroperitoneal tumor conglomerate invading the psoas, causing pain
- SFRT with 66.7 Gy in 5 fractions SIB to internal spheres, 20 Gy in 5 fractions to entire tumor

3 months post-RT



6 months post-RT



Our institutional experience

- 29 adult patients treated with SFRT since 2024
  - 17 patients (59%) received single-fraction SFRT with 3 Gy to gross tumor volume (GTV) and 15 Gy to the vertices
  - 12 patients (41%) received 5-fraction SFRT with 20 Gy to GTV and 66.7 Gy to the high-dose vertices
- 6X-FFF VMAT technique

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Patient Characteristics

- Median age 71
- Median ECOG 1
- Median of 3 prior lines of systemic therapy
- 12 patients (41%) received prior radiation to the local site
- Median GTV size **368.3 cc** (IQR 205.8 cc – 903.4 cc)
- Most patients (21, 72.4%) presented with pain

Outcomes

- 24 of 29 patients (83%) had follow up, median 7 months.
  - Only 3 patients (12%) did not experience improvement of symptoms.
  - Of the 22 patients who had post-SFRT diagnostic imaging, objective response rate was 72.7%, with median GTV volume decrease of 54.4% at last imaging evaluation.

Toxicities

- The most common acute toxicity was fatigue (24%).
- 13 patients (52%) had no acute toxicities.
- One grade 3+ toxicity observed as fistula between neobladder and pre-existing anorectal fistula, possibly due to either tumor progression or radiation treatment.

Conclusion:
SFRT is a modern solution for a modern problem

- Oncologic advances have enabled patients with metastatic disease to live longer, often after multiple lines of systemic therapy and prior radiation
- SFRT is a novel option which was well-tolerated and provided a favorable objective response rate of 72.7% in our patients with limited alternatives for palliation.
- Larger prospective studies are needed to refine patient selection and guide clinical guidelines for SFRT.

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Acknowledgements

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    - Arjun Karnwal
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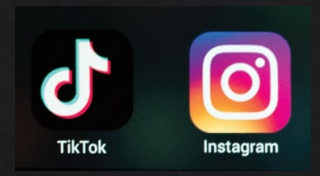
    - Jason Ye, MD
    - May Tao, MD
    - Hirsch Matani, MD
    - Andrew Lim, MD
    - Lauren Lukas, MD
    - Joshua Schiff, MD
    - Diane Ling, MD
  - Medical Physics
    - Arthur Olch, PhD
    - Hualin Zhang, PhD
    - Salim Balik, PhD
    - Zhengzheng Xu, PhD
    - Benjamin Ziemer, PhD
    - Zhilei Shen, PhD



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