Proton Therapy:

What is it?

How does it work?

Who should be getting it?

Singapore Advanced Medicine

www.advancedmedicine.sg

www.ro-se.org

Dr Looi Wen Shen

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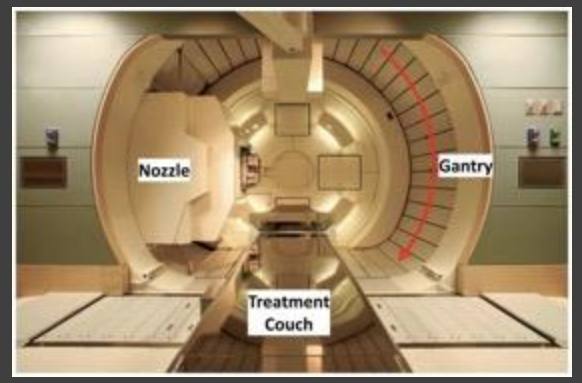
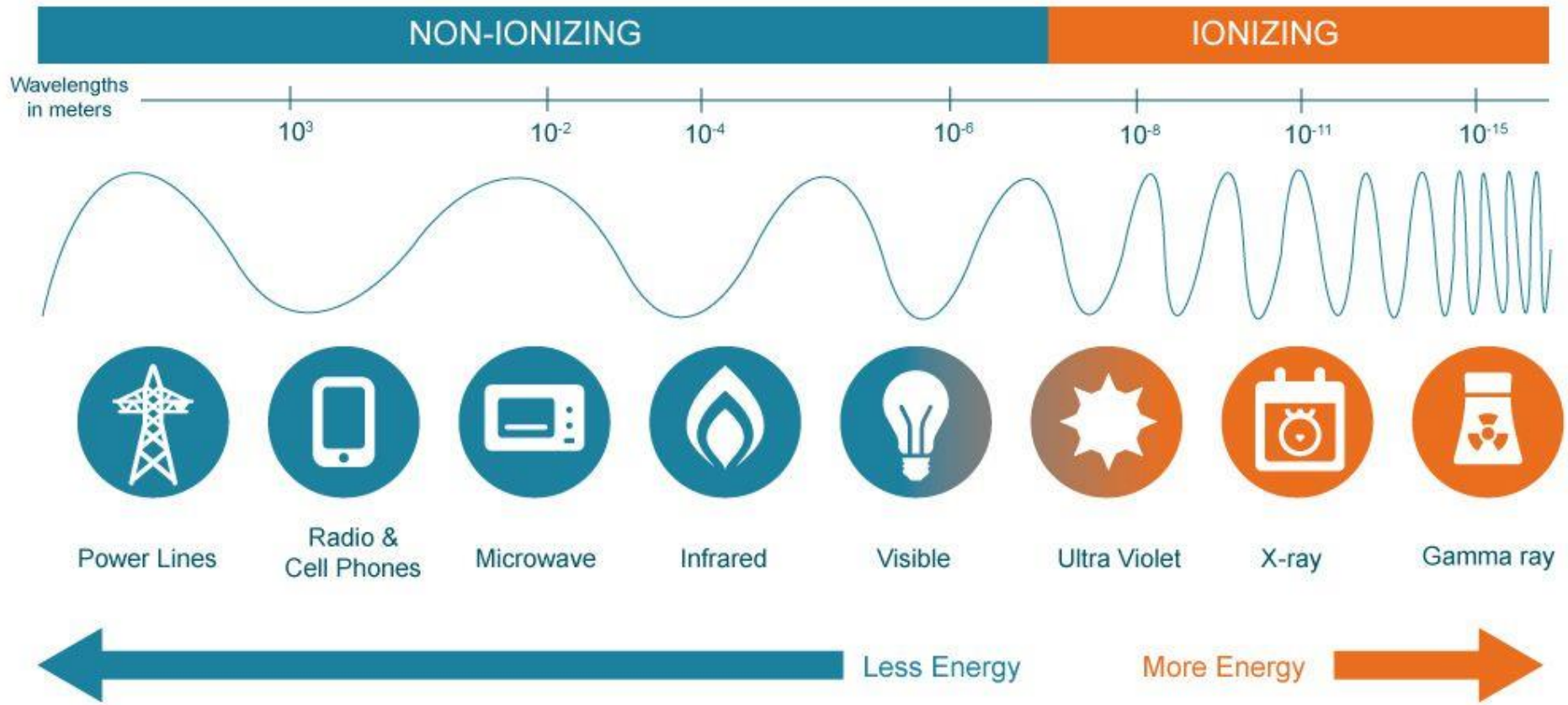
2024



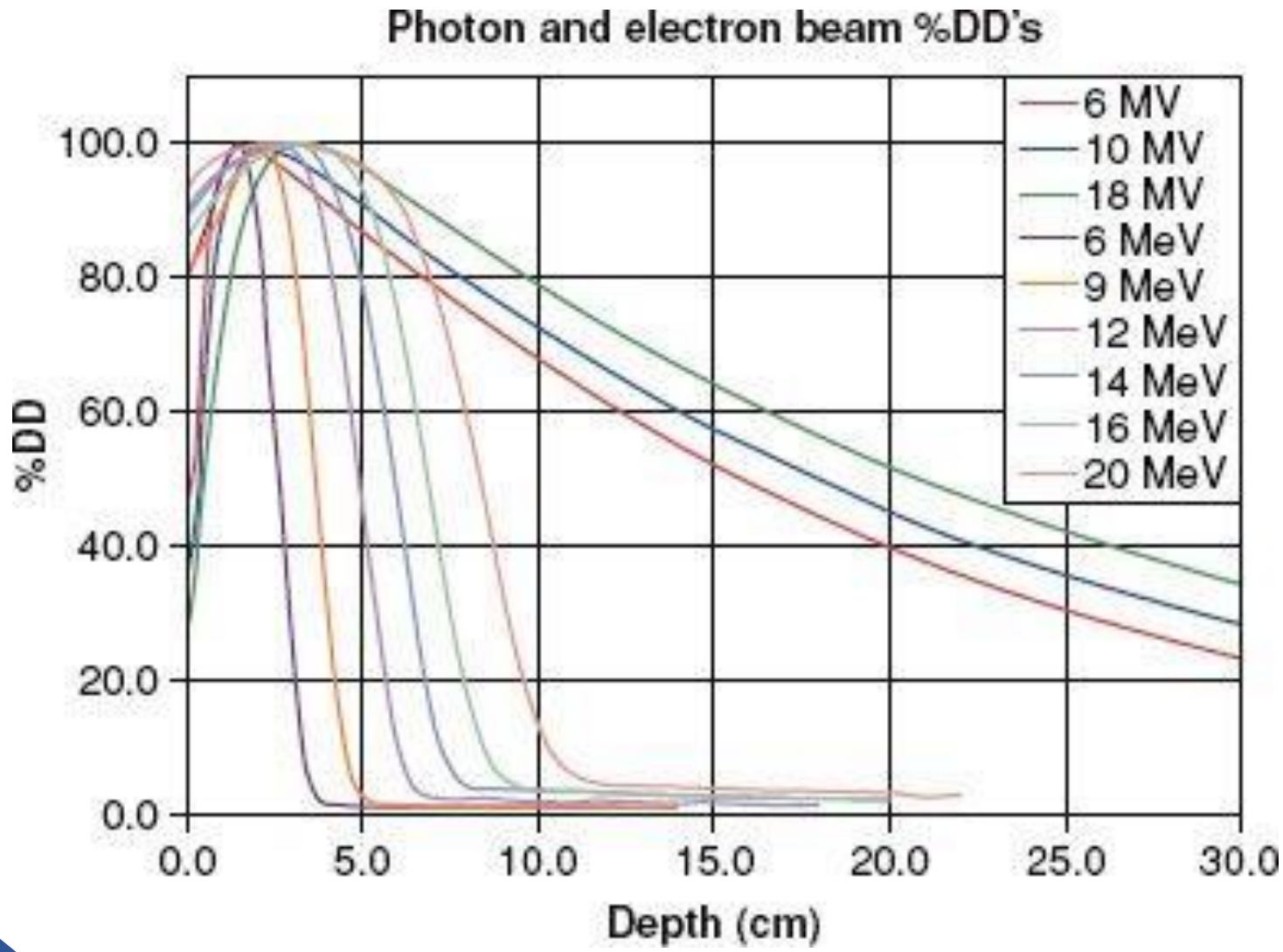
Outline

- Photon (x-ray therapy)
- Proton therapy
- Dosimetric benefits of proton therapy
- MOH indications (restrictions)
- Case examples
- Access
- Future developments

What is radiotherapy?



Dose distribution- x-rays and electrons



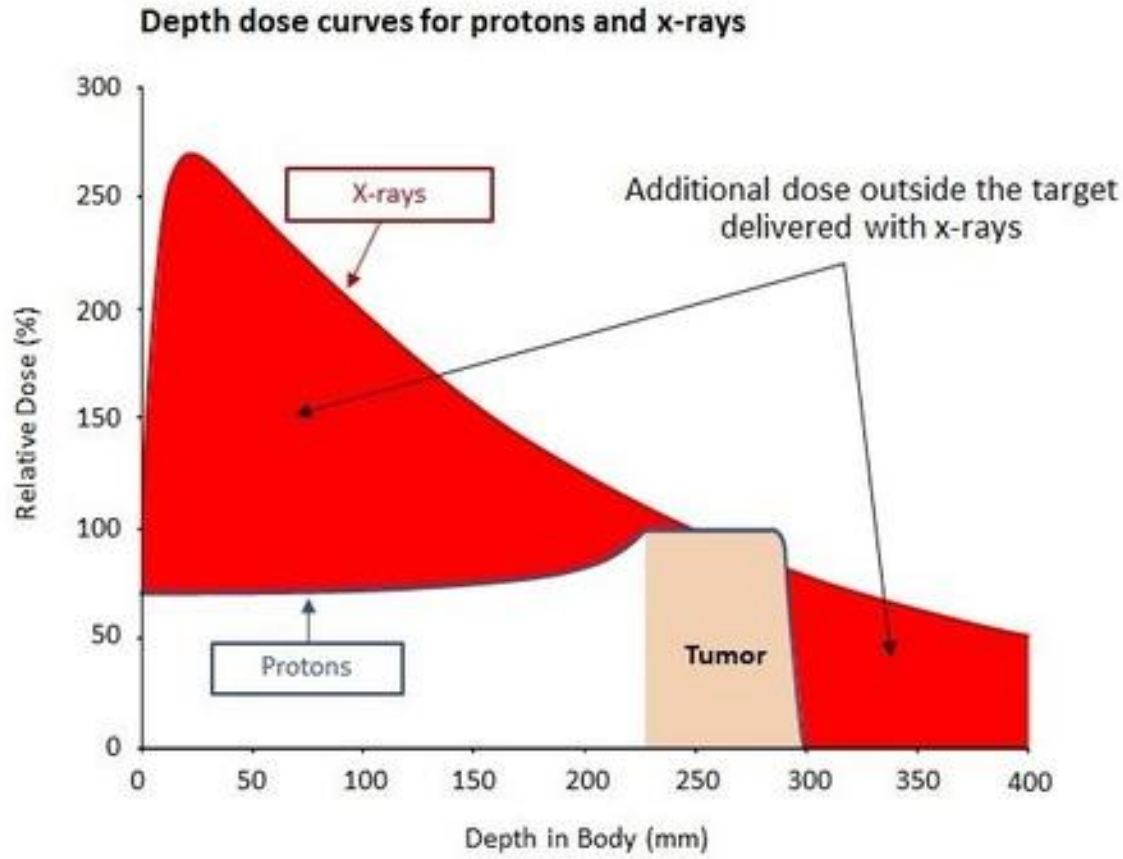
Proton therapy is another step in the direction of improved dose distribution

Combines the long range of x-rays with the quick stop of electrons

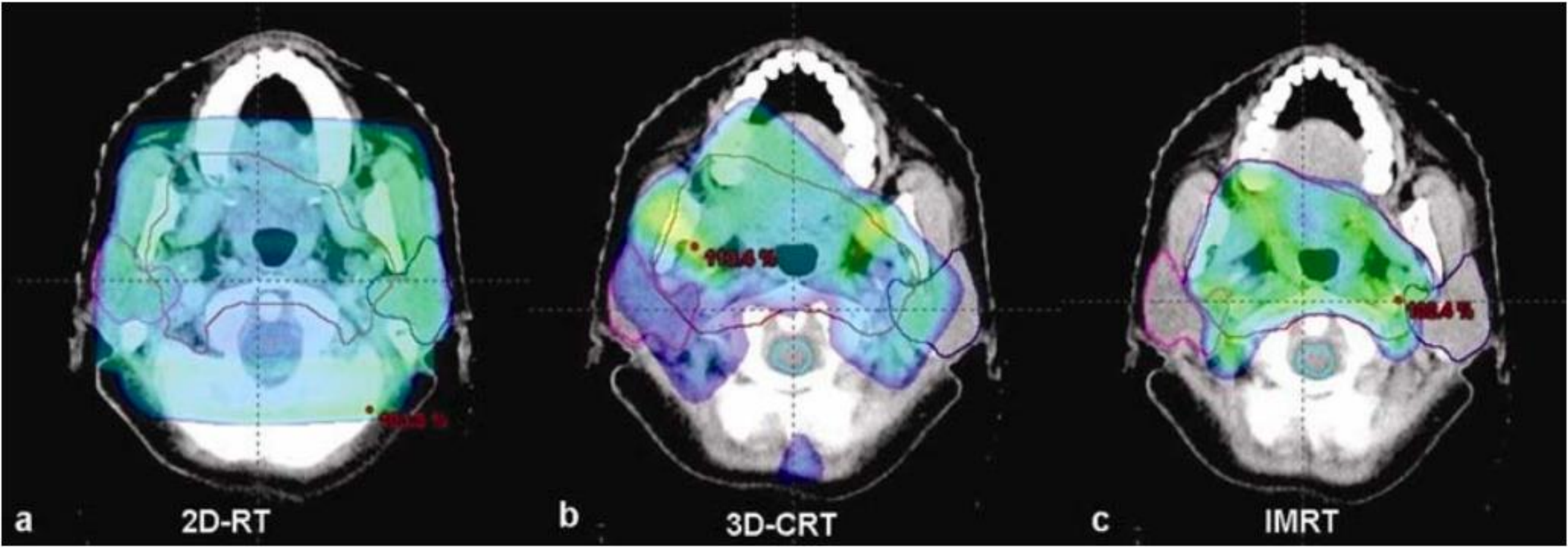
Dose distribution- Protons

The Physics of Protons

*In order to deliver the same dose to the tumor, x-rays **must** deliver a greater dose outside the target than protons do*



Radiotherapy techniques have been improving with X-rays



More conformality of **high-dose** region

Tejpal et al. 2010 PMID: 22930632

Why Proton Therapy?

Two main applications of proton therapy

Dose Escalation

- Keep the toxicity in adjacent organs constant but increase the radiation dose to the tumour
- Curing more spine chordomas without causing paralysis

Reduce Collateral Injury

- Keep radiation to the tumour constant but reduce toxicity to adjacent normal organs
- Curing the same rate of medulloblastomas in children but reducing the damage to heart and lungs and secondary malignancies

Naima et al. PMID 17439713

Mittal et al. PMID 28073921

Late Toxicity

- Children have a greater number of at-risk years for side effects
- Normal tissues are still developing and are more radiosensitive
- The proportion of irradiated volume vs. normal tissue is higher due to small size
- However, even older adults benefit as well

Children and Young Adults are the most at risk

- Children have a greater number of at-risk years for side effects
- Normal tissues are still developing and are more radiosensitive
- The proportion of irradiated volume vs. normal tissue is higher due to small size
- However, even older adults benefit as well

MOH Indications for Medisave/national insurance claims <25 years-old

Cancer subtypes for patients younger than 25 years				
Central and peripheral nervous system				
17	Retinoblastoma	2	$500 per treatment	$360 per treatment
18	Chordoma/ chondrosarcoma base of skull or spine	3	$1,800 per treatment	$2,800 per treatment
19	Ependymoma			
20	Craniopharyngioma			
21	Pineal parenchymal tumours (not pineoblastoma)			
22	Medulloblastoma	1	$300 per treatment	$80 per treatment
23	Intracranial germ cell tumour			
24	Primitive neuroectodermal tumours			
25	Esthesioneuroblastoma			
26	Neuroblastoma			
27	Glioma			
Musculoskeletal				
28	Ewing sarcoma	1	$300 per treatment	$80 per treatment
29	Spinal/ paraspinal bone and soft tissue sarcoma			
30	Rhabdomyosarcoma: orbit, parameningeal, head and neck, pelvis			
31	Pelvic Sarcoma			
32	Osteosarcoma			
Others				
33	Salivary gland cancer	1	$300 per treatment	$80 per treatment

MOH Indications >25 years-old **MSK**

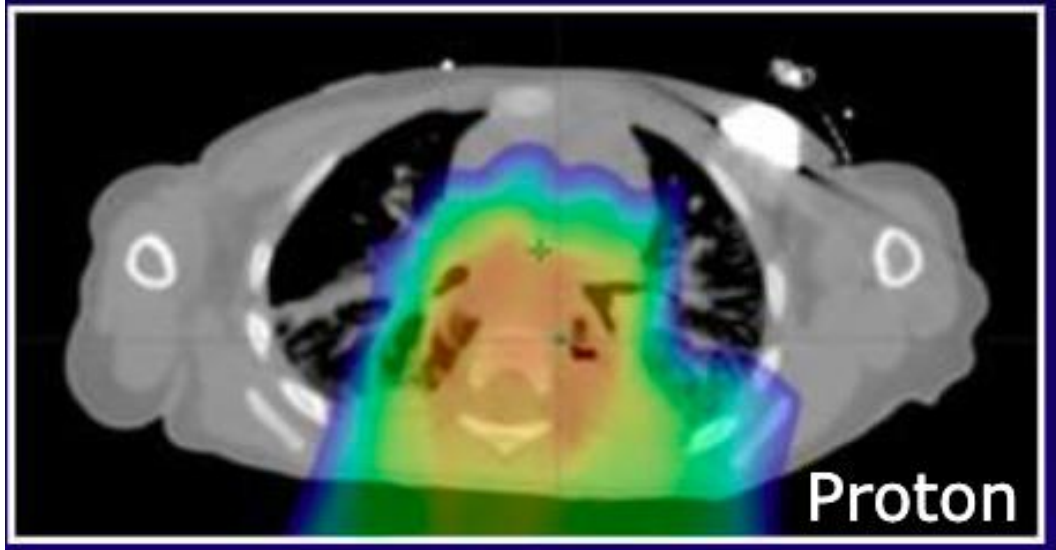
Musculoskeletal	
28	Ewing sarcoma
29	Spinal/ paraspinal bone and soft tissue sarcoma
30	Rhabdomyosarcoma: orbit, parameningeal, head and neck, pelvis
31	Pelvic Sarcoma
32	Osteosarcoma

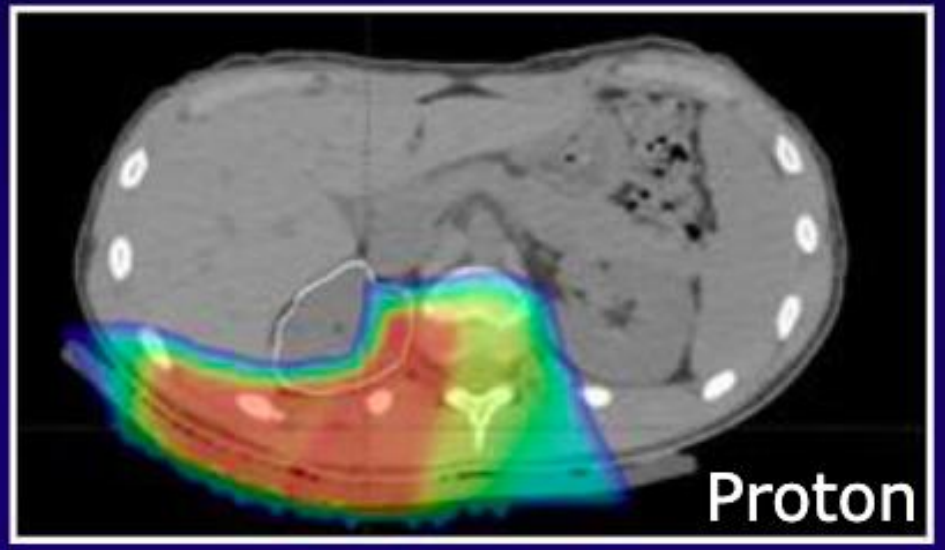
N.B.- Concurrent chemotherapy is an indication for proton therapy for all sites

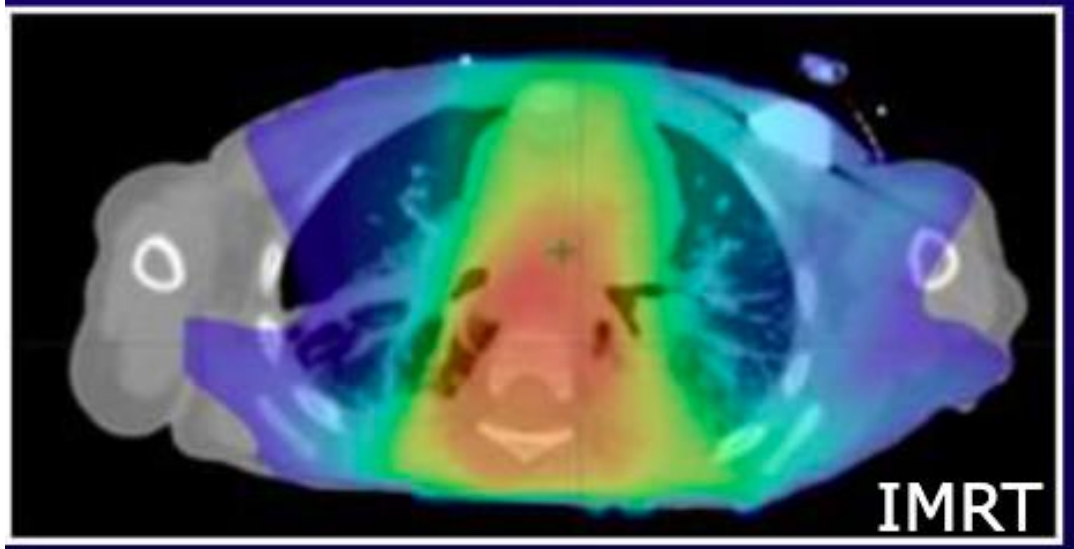
Full list available at

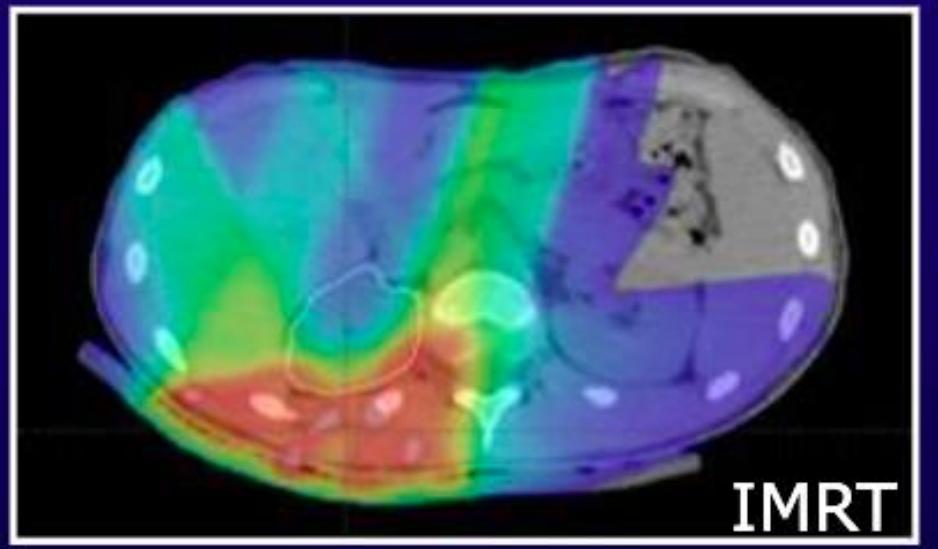
https://www.moh.gov.sg/home/our-healthcare-system/medishield-life/what-is-medishield-life/what-medishield-life-benefits/approved-indications-for-use-of-pbt-in-treatment

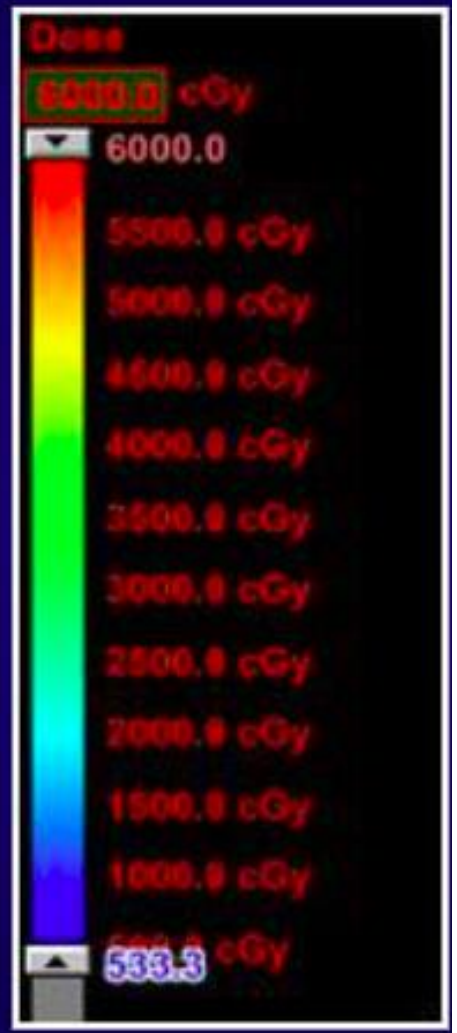
Dose distribution comparisons











Depending on the chest wall sub-region, proton therapy has the potential to minimize cardiac, pulmonary, and renal toxicity. In long term survivors, there may be lower risks of radiation-induced second malignancies, particularly breast cancer.

Second cancer risk after primary cancer treatment with three-dimensional conformal, intensity-modulated, or proton beam radiation therapy

Michael Xiang MD, PhD, Daniel T. Chang MD, Erqi L. Pollom MD, MS

First published: 19 May 2020 | https://doi.org/10.1002/cncr.32938 | Citations: 80

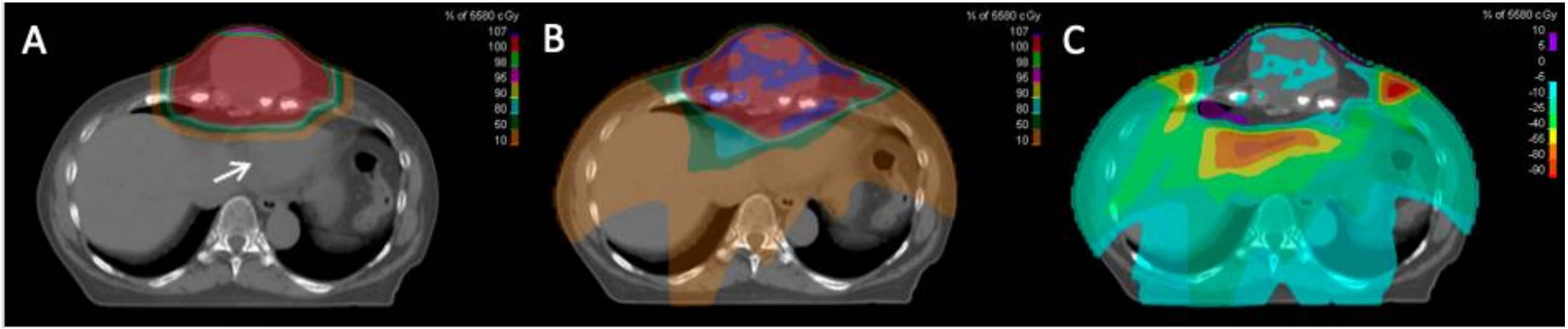
- 450,373 paediatric and adult patients in the National Cancer Database analysed for second cancer
  - 33.5% 3DCRT; 65.2% IMRT; 1.3% Proton therapy
  - Median f/u 5.1 years
- Modeled using multivariable logistic regression adjusting for age, follow-up, cancer type, RT dose, chemotherapy and other factors
- Propensity score matching was used to balance baseline characteristics

Results

- IMRT vs 3DCRT no difference in risk of subsequent cancer diagnosis (adjusted OR 1.00)
- Proton therapy significantly lower risk relative to IMRT (adjusted OR 0.31; 95% CI, 0.26-0.36; P < .0001)
- Benefit persisted in sensitivity analyses that excluded patients with prostate cancer, chemotherapy, and/or follow-up time less than 5 years

Xiang et al. PMID 32426866

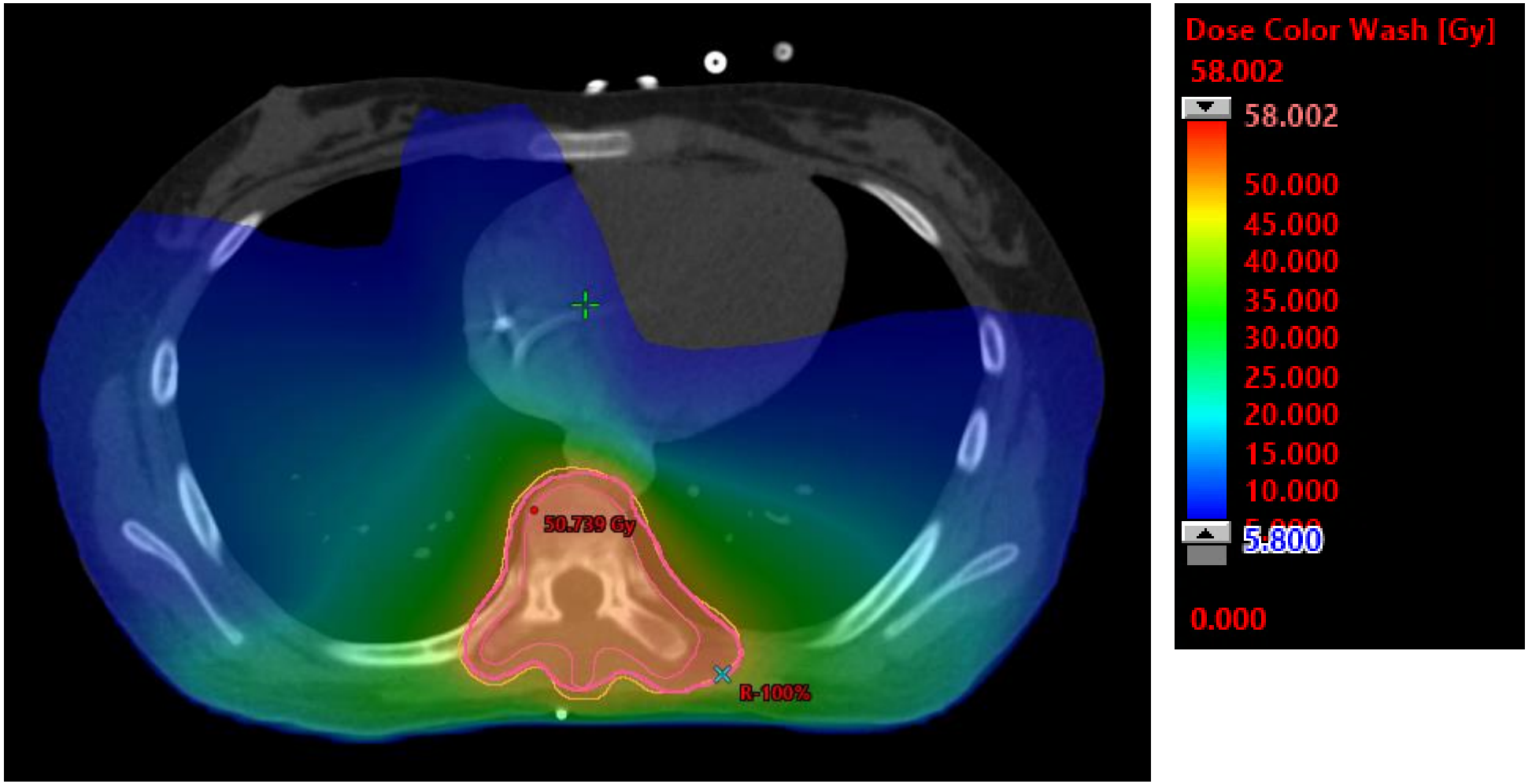
Desmoid tumor of chest wall



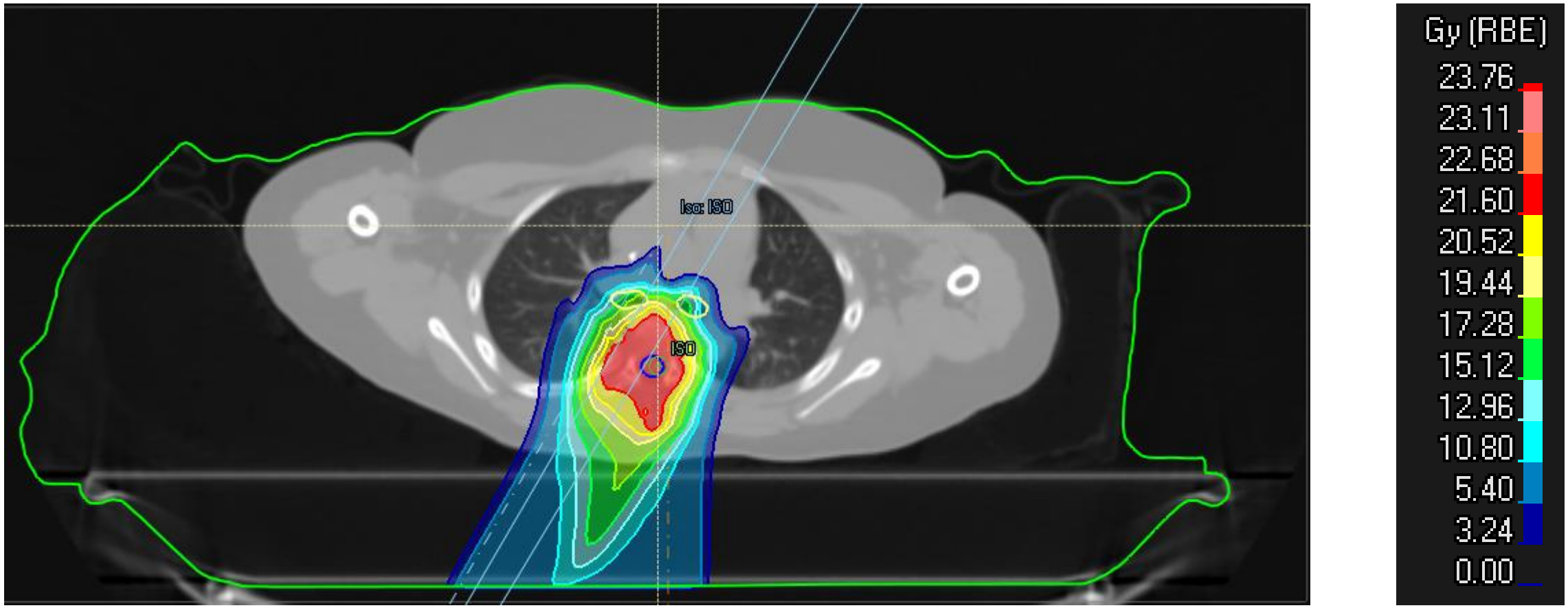
Looi et al. 2021. PMID 33649873

- Reduction in both high and low-dose splash in this case with the use of proton therapy
- Large eduction in cardiac dose

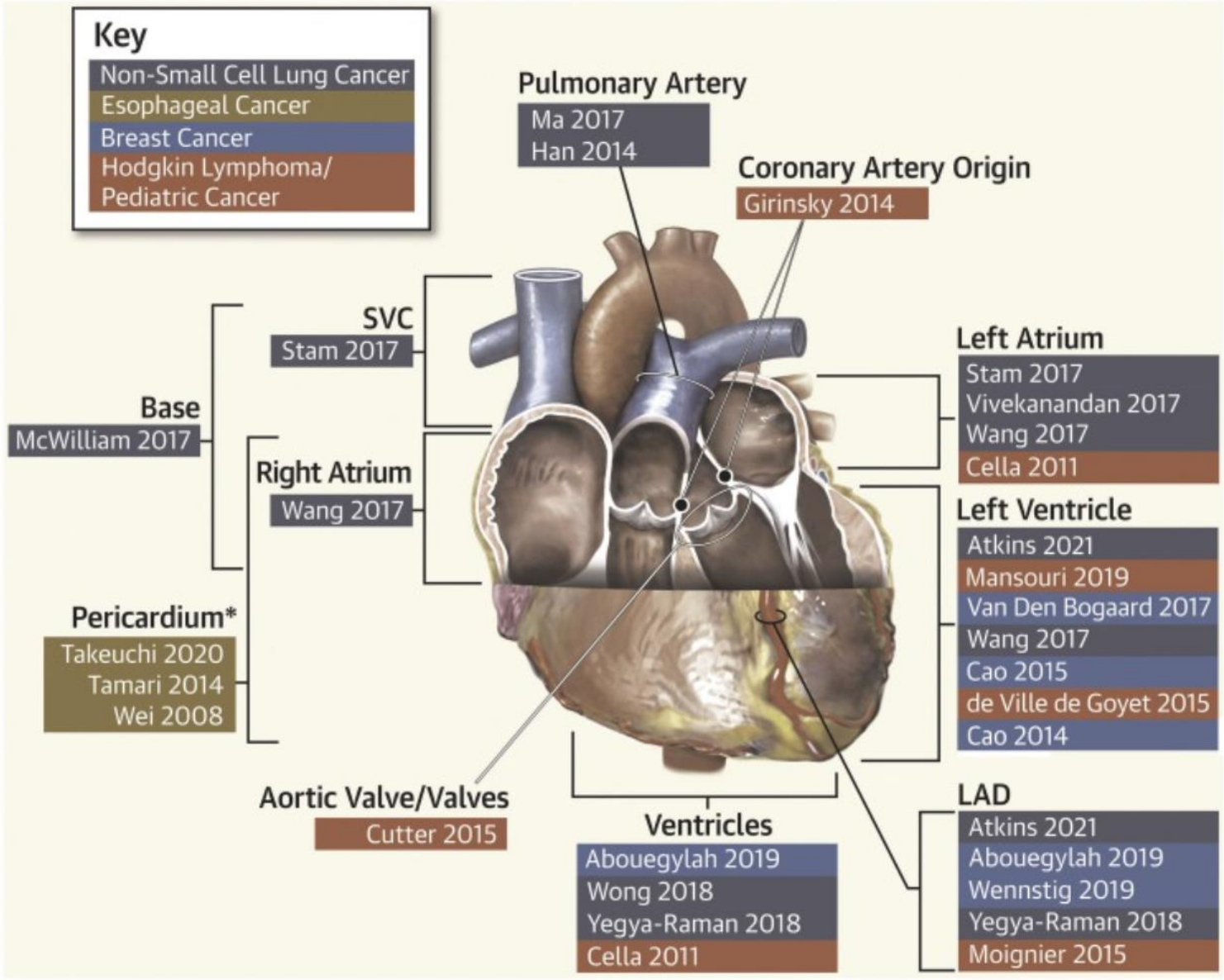
Ewing sarcoma- x-rays with dose splash



Relapsed neuroblastoma



CENTRAL ILLUSTRATION: Heart Regions Associated With Radiation-Induced Cardiovascular Disease and/or Survival



Bergom, C. et al. J Am Coll Cardiol CardioOnc. 2021;3(3):343-359.

Therapy-Related Cardiac Risk in Childhood Cancer Survivors: An Analysis of the Childhood Cancer Survivor Study

James E. Bates, MD[1]; Rebecca M. Howell, PhD[2]; Qi Liu, MSc[3]; Yutaka Yasui, PhD[4]; Daniel A. Mulrooney, MD[4]; Sughosh Dhakal, MD[5]; Susan A. Smith, MPH[2]; Wendy M. Leisenring, ScD[6]; Daniel J. Indelicato, MD[1]; Todd M. Gibson, PhD[4]; Gregory T. Armstrong, MD[4]; Kevin C. Oeffinger, MD[7]; and Louis S. Constine, MD[5]

PMID 30860946

- 24,214 long-term survivors of childhood cancer
- Diagnosed between 1970 and 1999 at a median age of 7.0 years (range, 0 to 20.9 years)
- Median attained age of 27.5 years (range, 5.6 to 58.9 years)
- **Low to moderate doses 5 Gy to 19 Gy** (≥ 50% of heart) were associated with an increased rate of cardiac disease (relative rate, 1.6; 95% CI, 1.1 to 2.3)
- **High doses (≥ 20 Gy) to small cardiac volumes** (0.1% to 29.9%) were associated with an elevated rate (relative rate, 2.4; 95% CI, 1.4 to 4.2).

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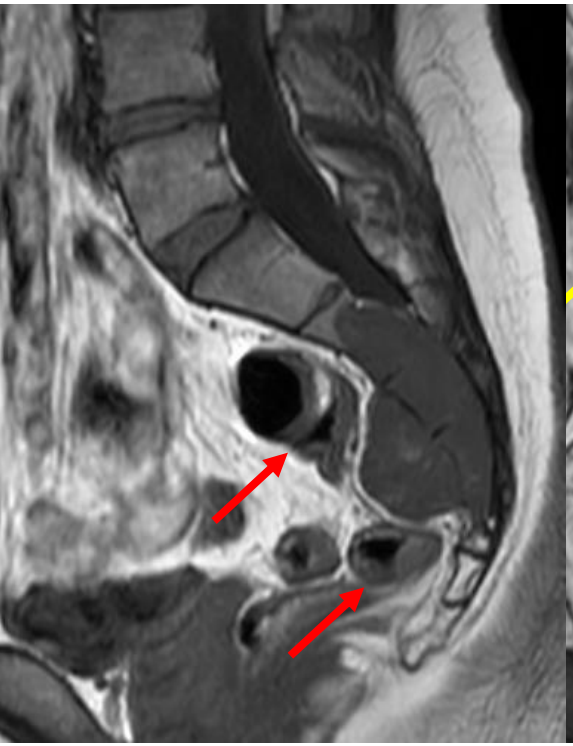
Childhood soft tissue sarcomas

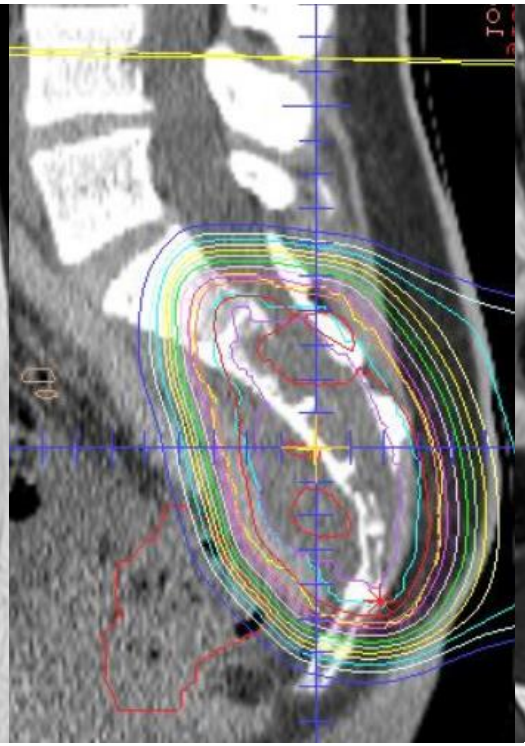
- Some sarcomas are unresectable, or located near critical structures
- E.g. chordomas, ewing’s, rhabdomyosarcoma

Case: 20s male, sacral chordoma

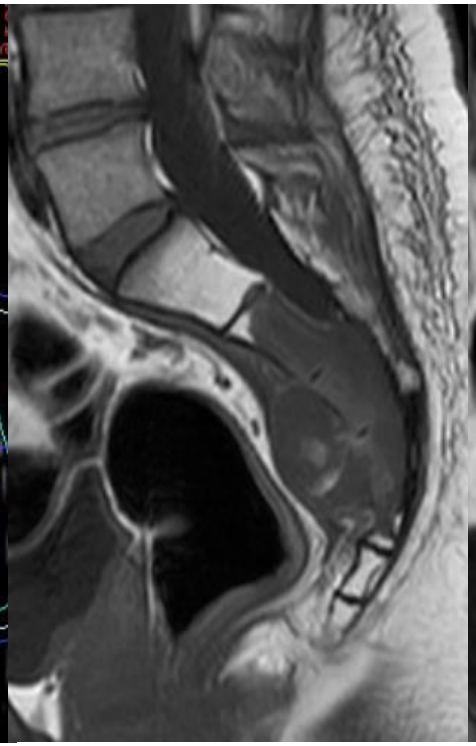


Before surgical spacer placement (SSP)

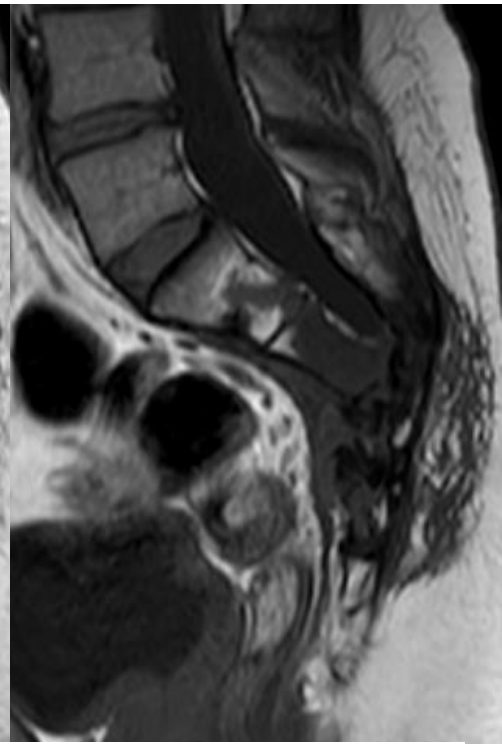
After SSP



PBT
70.4 Gy (RBE)
/16 fr



7M later
Tumor shrank
Spacer disappeared



6Y 8M later
No relapse
No severe toxicity

Credits Dr Demizu

PEDIATRIC BONE SOFT TISSUE SARCOMA

Indication for particle therapy

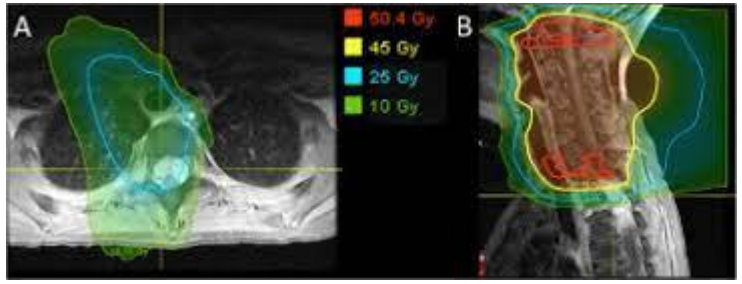
- Ewing sarcoma family of tumors, rhabdomyosarcoma, etc.
- Definitive RT if surgery is too morbid,
- adjuvant RT is almost always needed unless small and good response to chemo
- One of the best indications for PBT

SPINAL EWING MODERN SERIES

Indelicato et al 2022

32 patients, 14 definitive, 18 after biopsy/STR decompression

5 year LC 92%



PELVIC RHABDOMYOSARCOMA

Outcomes Following Proton Therapy for Group III Pelvic Rhabdomyosarcoma

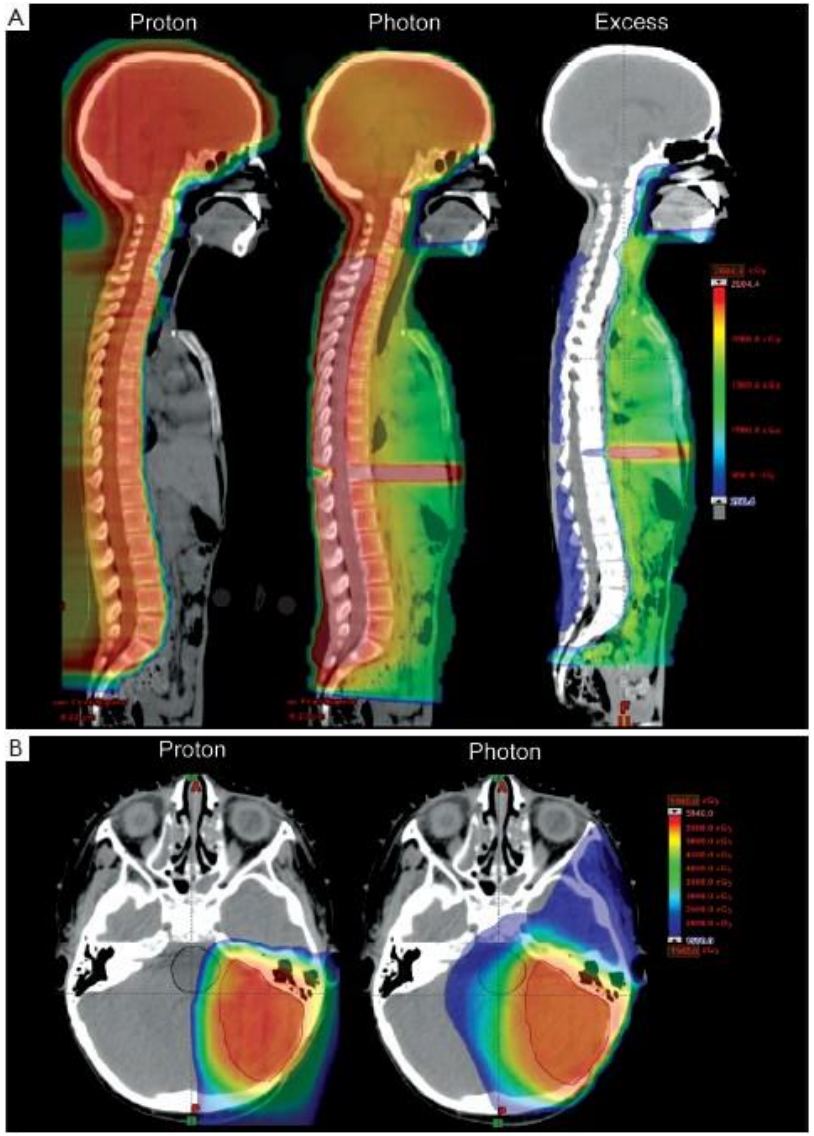
Indelicato et al, red journal 2020

- n=31 (14 had resection)

- 5 year LC 83%

- no diff btw sx/definitive proton

Proton Beam Therapy



Proton Therapy Access in Singapore

- 3 proton centres
  - Restructured x1
  - 2 private centres
- NCCS >> Referral for ‘subsidised’ patients (slightly cheaper than private)
- Private >> covered by national savings (Medisave), medishield (national insurance) or private insurance (integrated plans)

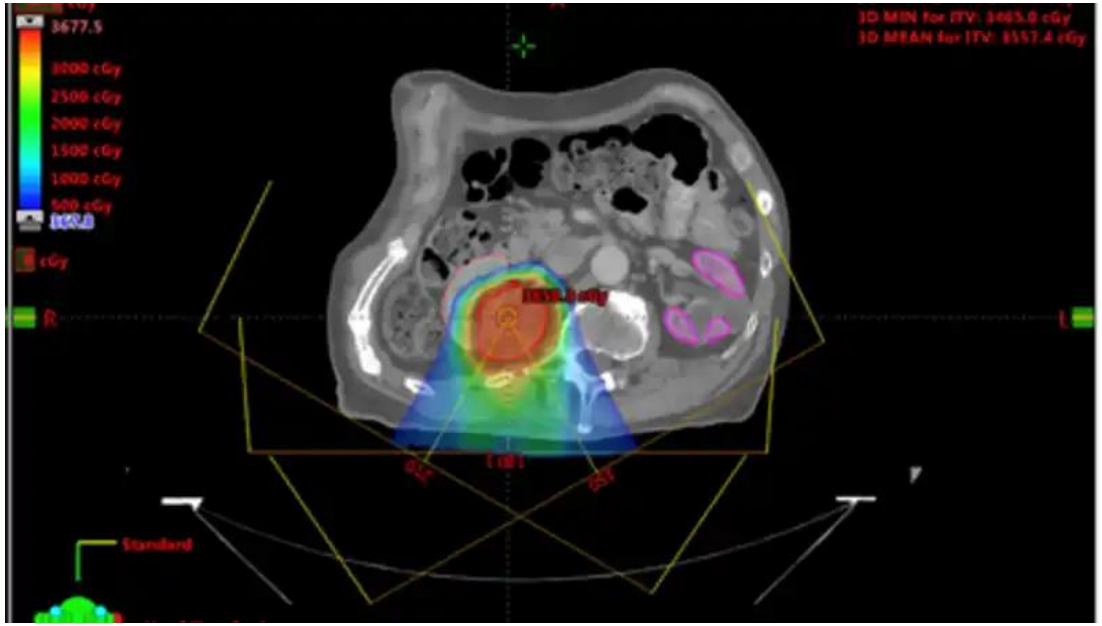
SAM machine

Varian Probeam

NCCS: Hitachi probeat
Parkway: IBA Proteus One

Future of proton therapy

- STEREOTACTIC BODY RADIOTHERAPY (SBRT)
- Highly targeted conformal therapy delivered in 5 or fewer fractions
- Very high dose to overcome radioresistance or cell cycle stage
- Delivering SBRT with proton therapy is a new area of interest



Future of proton therapy- FLASH?

- Delivery of proton therapy with very high dose rates >40 Gy per sec versus 5 Gy per minute
- Sparing of normal tissue whilst still suppressing tumour growth
- 1 clinical study published, FAST-02 (lung) ongoing
- Available in 5-10 years time in SG (Varian probeam at biopolis centre)

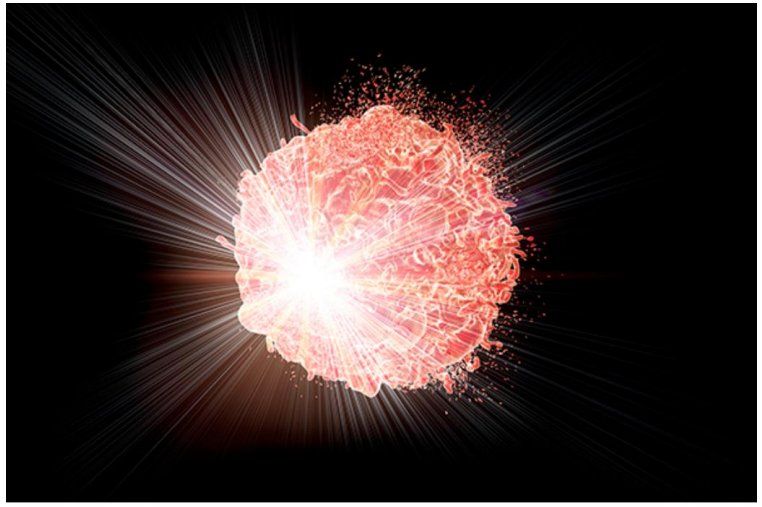
6 | VOLUME 114, ISSUE 3, SUPPLEMENT , S4, NOVEMBER 01, 2022

FAST-01: Results of the First-in-Human Study of Proton FLASH Radiotherapy

E.C. Daugherty • A.E. Mascia • M.G.B. Sertorio • ... D. Khuntia • J.P. Perentesis • J.C. Breneman •

Show all authors

DOI: https://doi.org/10.1016/j.ijrobp.2022.07.2325



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Thank you!

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