THE UNIVERSITY OF KANSAS
CANCER CENTER

Grid / Lattice / Spatially Fractionated Radiotherapy

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NCI Designated Comprehensive Cancer Center

Who Benefits Most from Grid?

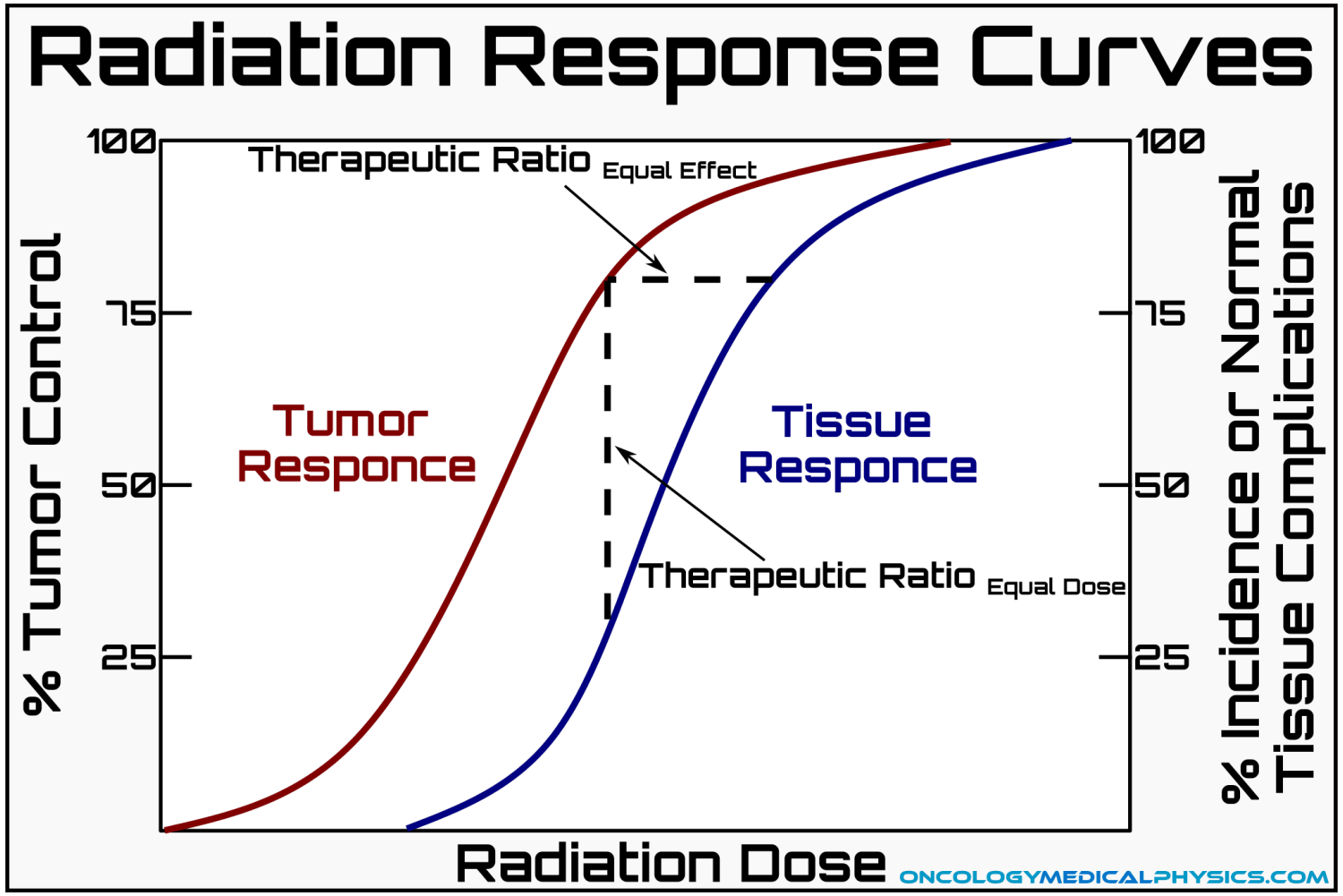
- Most important
  - Large, bulky tumors not amenable to surgical resection
- Other factors
  - Radioresistant tumors
  - Patients with previous overlapping radiotherapy
  - Large tumors adjacent to critical structures limiting radiation dose
  - Systemic therapy resistant tumor or patients ineligible for systemic therapy

History of Grid Radiotherapy

- 1909 – Dr. Kohler described filtering radiotherapy through a "perforated screen" to create multiple small beams
- 1933 – Liberson described utilizing a grid technique for deep tumors

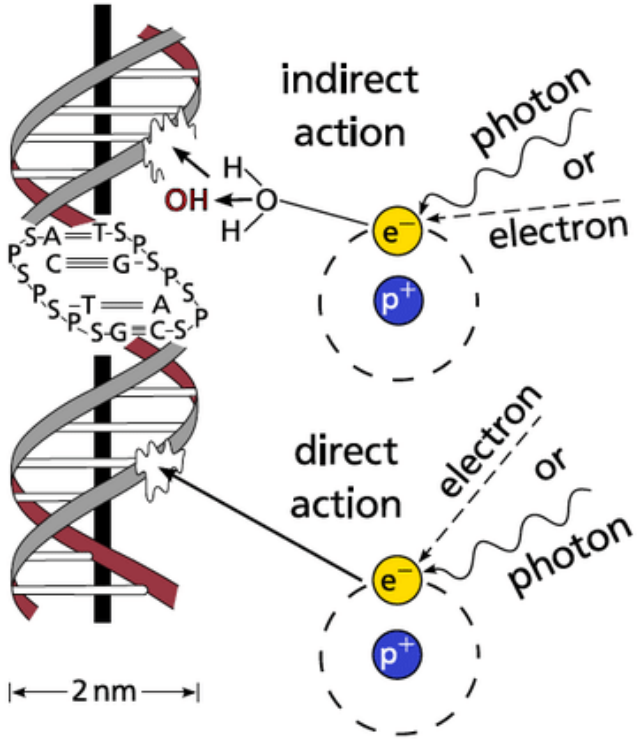
Why Does Grid Work?

- Harnesses the therapeutic ratio

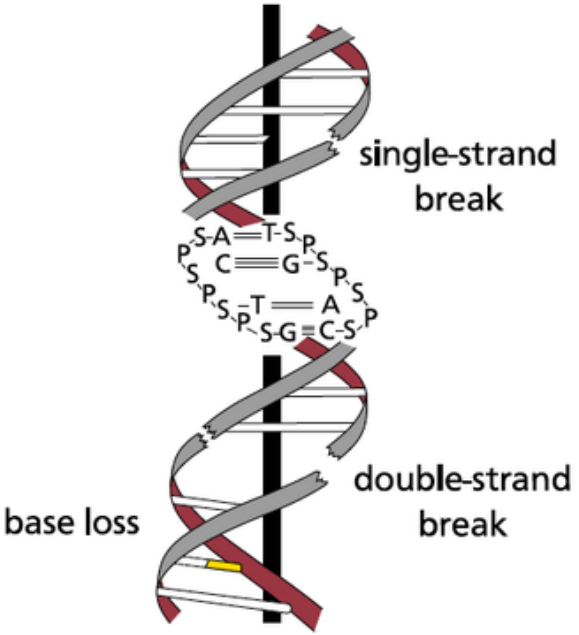


How Does Grid Work?

- Pure cytoreduction
  - 20Gy/1Fx is an ablative, tumor cell killing dose
- Overcoming hypoxia
  - Large tumors are generally hypoxic at their core (resistant to radiation and chemo)
  - Direct and enhanced indirect effect of radiotherapy



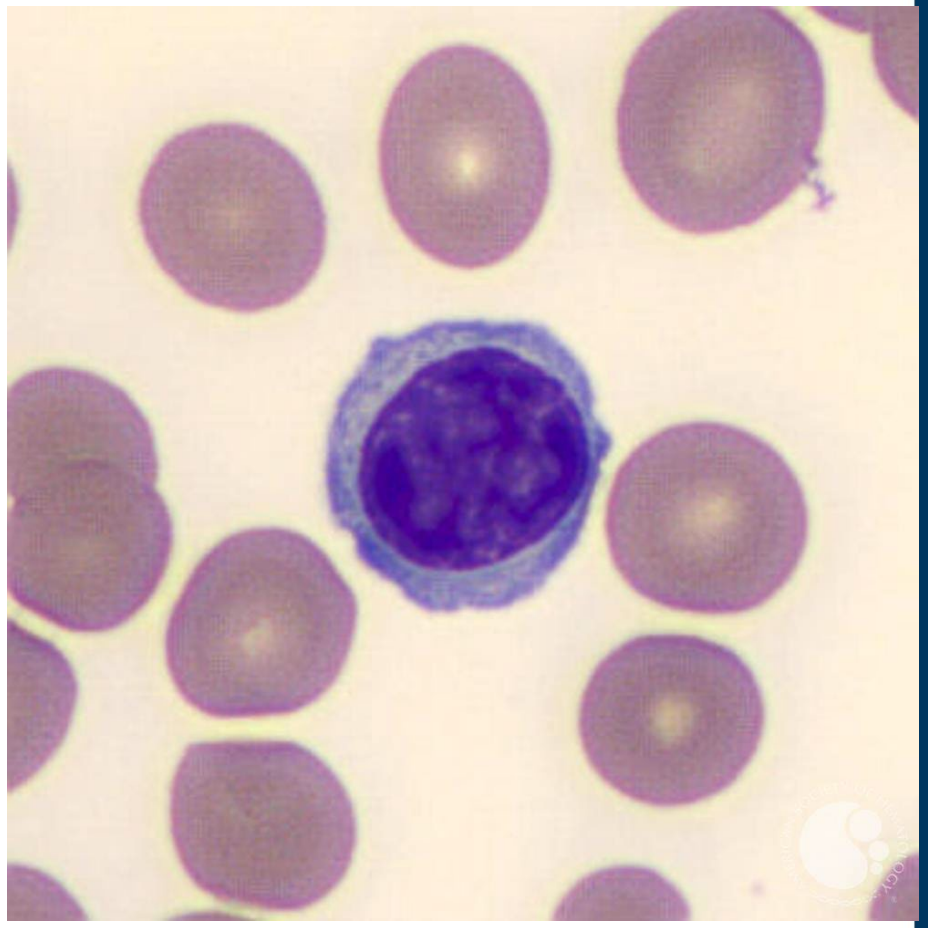
(a)



(b)

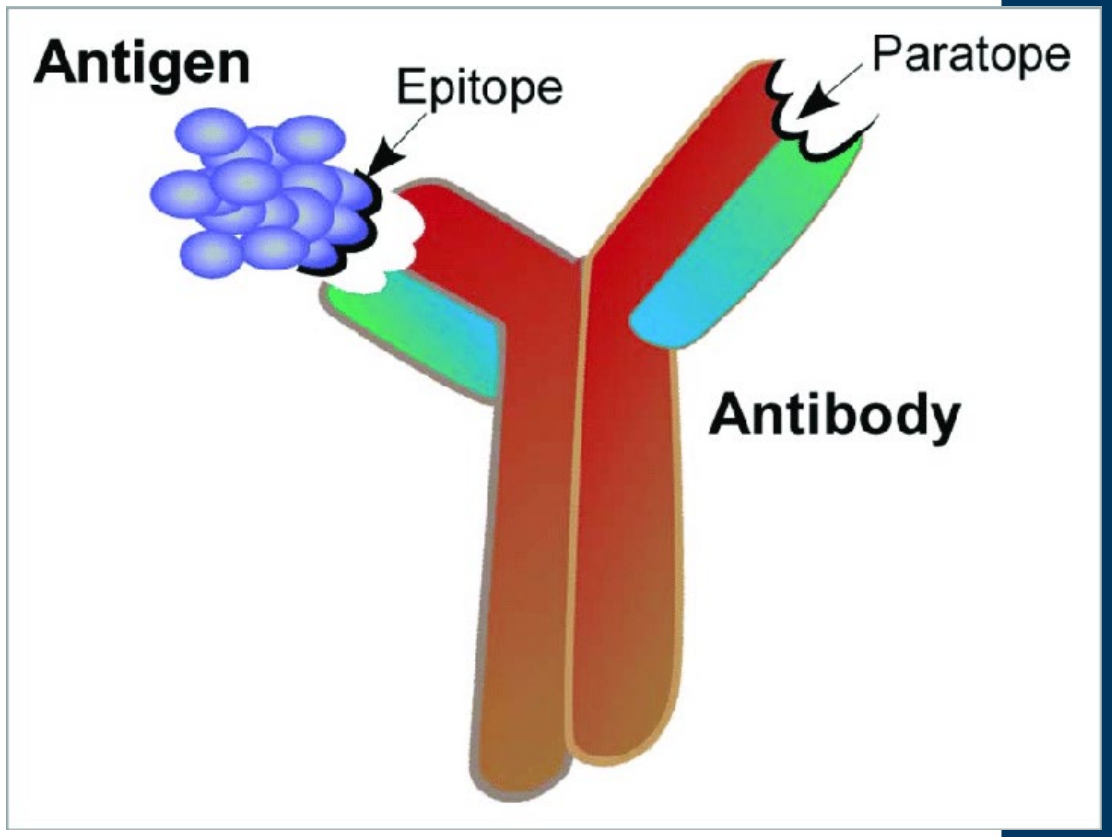
How Does Grid Work?

- The peaks (>=20Gy/1Fx) are as important as the valleys (<2Gy)
  - It only takes 2 Gy to kill a lymphocyte
  - We need tumor infiltrating lymphocytes for an immune responses



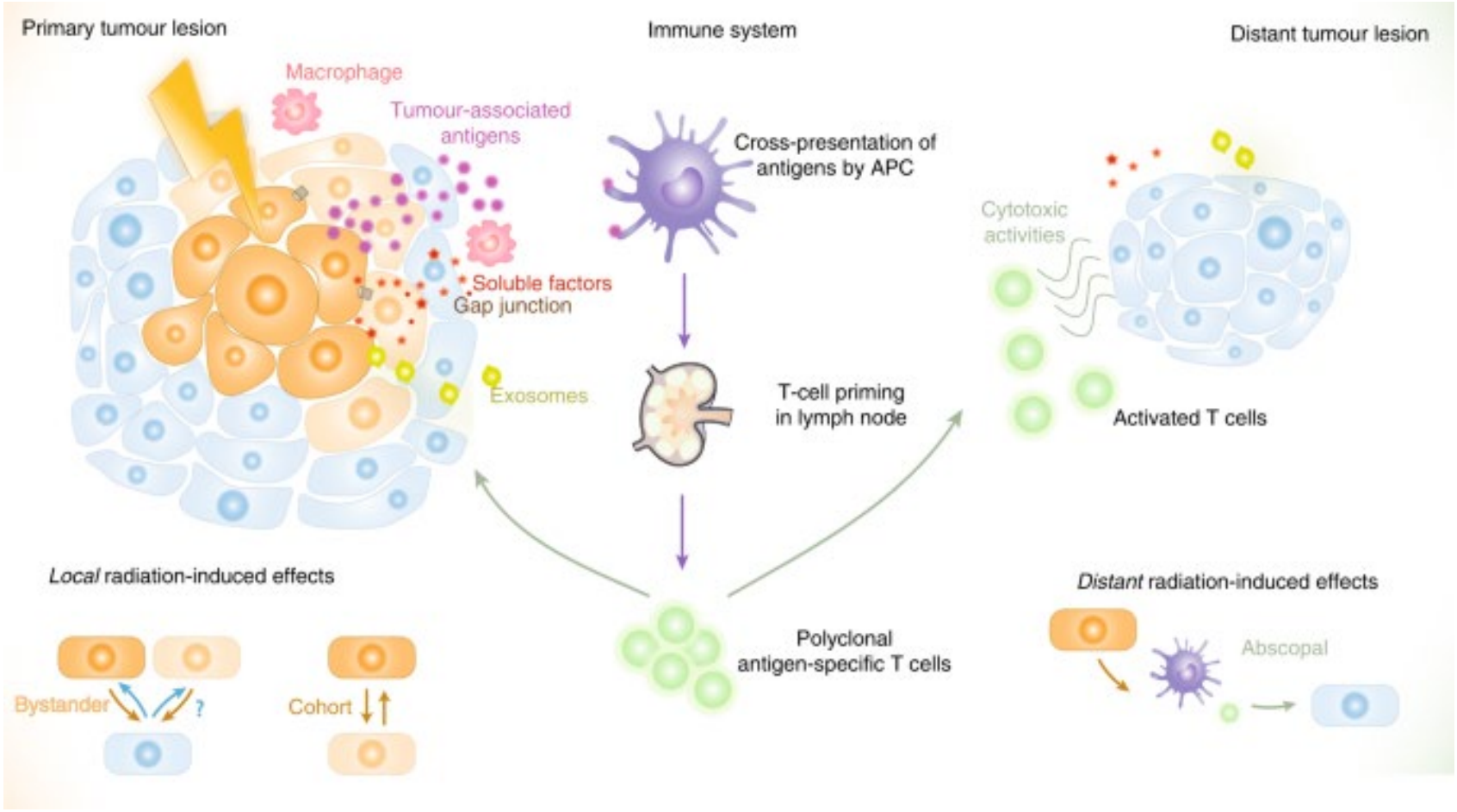
How Does Grid Work?

- Allows for immune system interplay, an ‘in situ vaccine’
  - High dose 20Gy/1Fx Grid spots create unique epitopes
  - Increased chance of immune system recognition



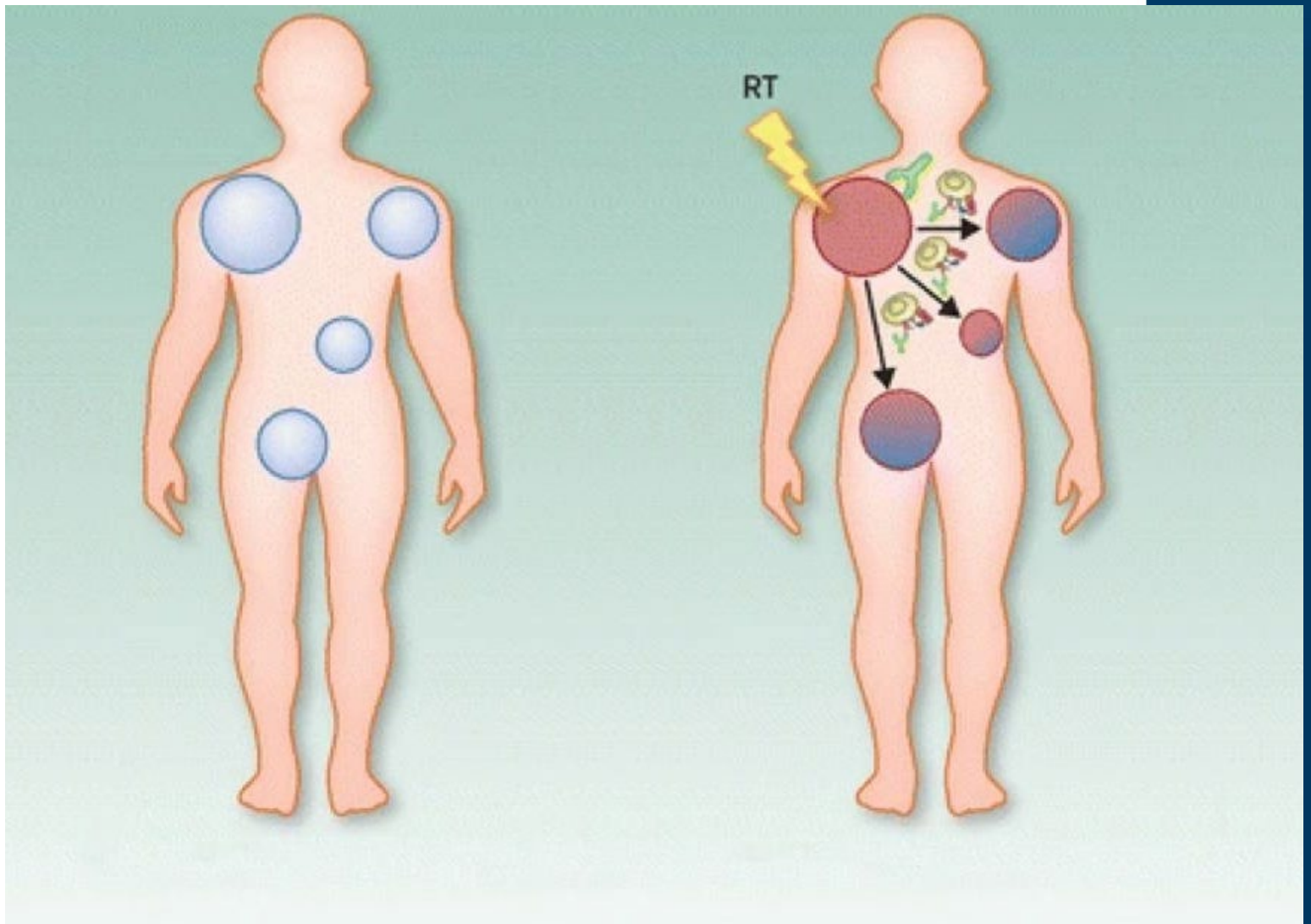
How Does Grid Work? Theories:

- Bystander effect via cytokine signaling



Ideal Outcome of Grid Therapy

- Abscopal effect



Interplay of Grid therapy and Systemic Therapy

- Best
  - Immunotherapy
    - Ex: Pembrolizumab, Nivolumab, Atezolizumab, etc
  - Targeted therapy
    - Ex: Cabozantinib, alectinib,
- Least preferred: True Chemotherapies
  - Ex: Doxorubicin, Carboplatin, Paclitaxel, etc
  - Why: Interferes with immune response

Timing of Grid therapy and Systemic Therapy

- Prefer immunotherapy or targeted therapy to be started ahead of grid treatment for maximal effect
- No concurrent bevacizumab for abdominal grid therapy
  - High risk for intraluminal rupture

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Practical Aspects of Grid Therapy

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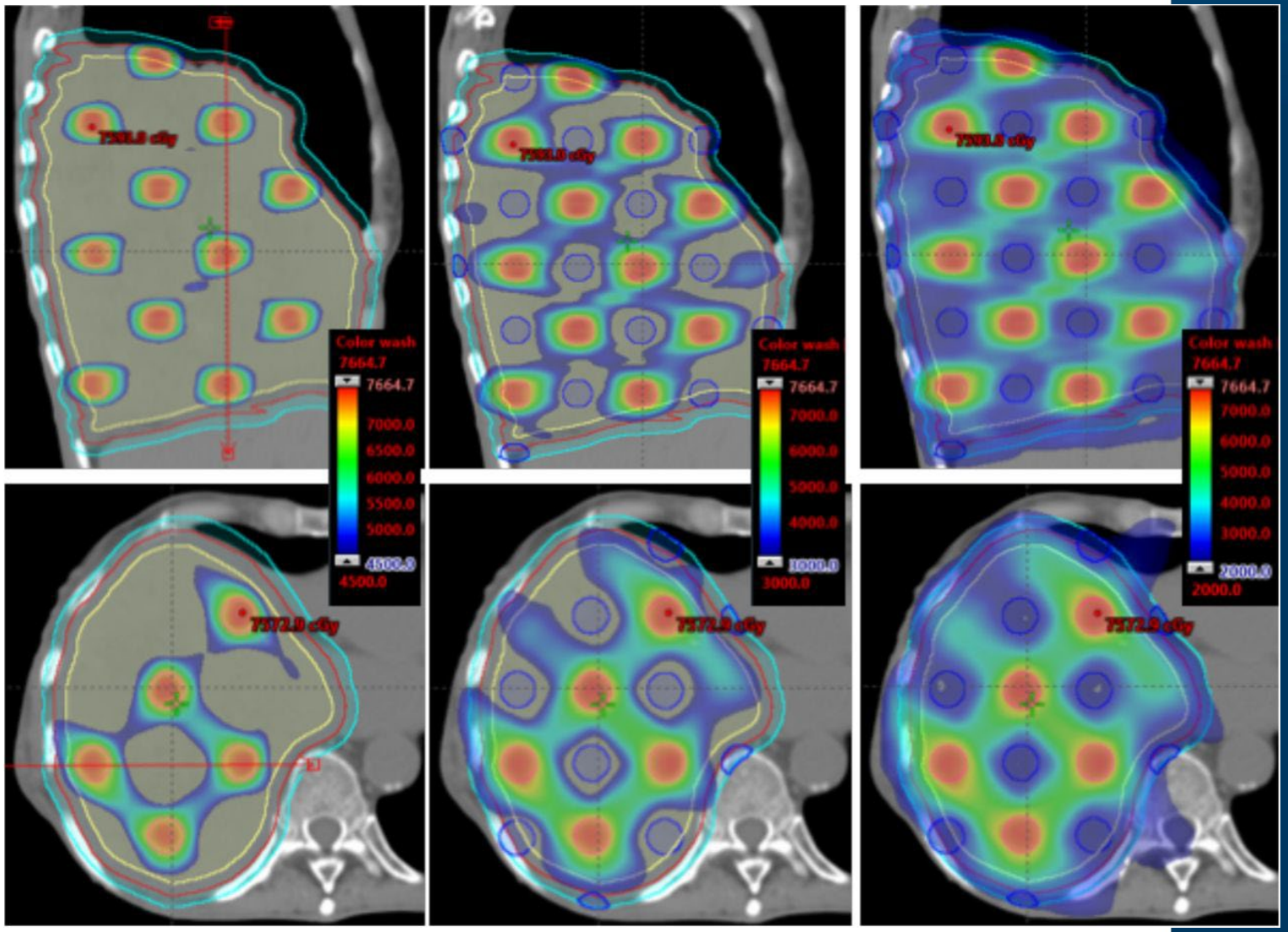
Practical: How I Contour

- Motion management for thoracic and abdominal tumors
  - 4DCT -> ITV
  - Grid is often too long to be feasible for breath hold
- Fuse all helpful imaging: PET, MRI, etc
- Contour true tumor GTV
  - When in doubt, go small

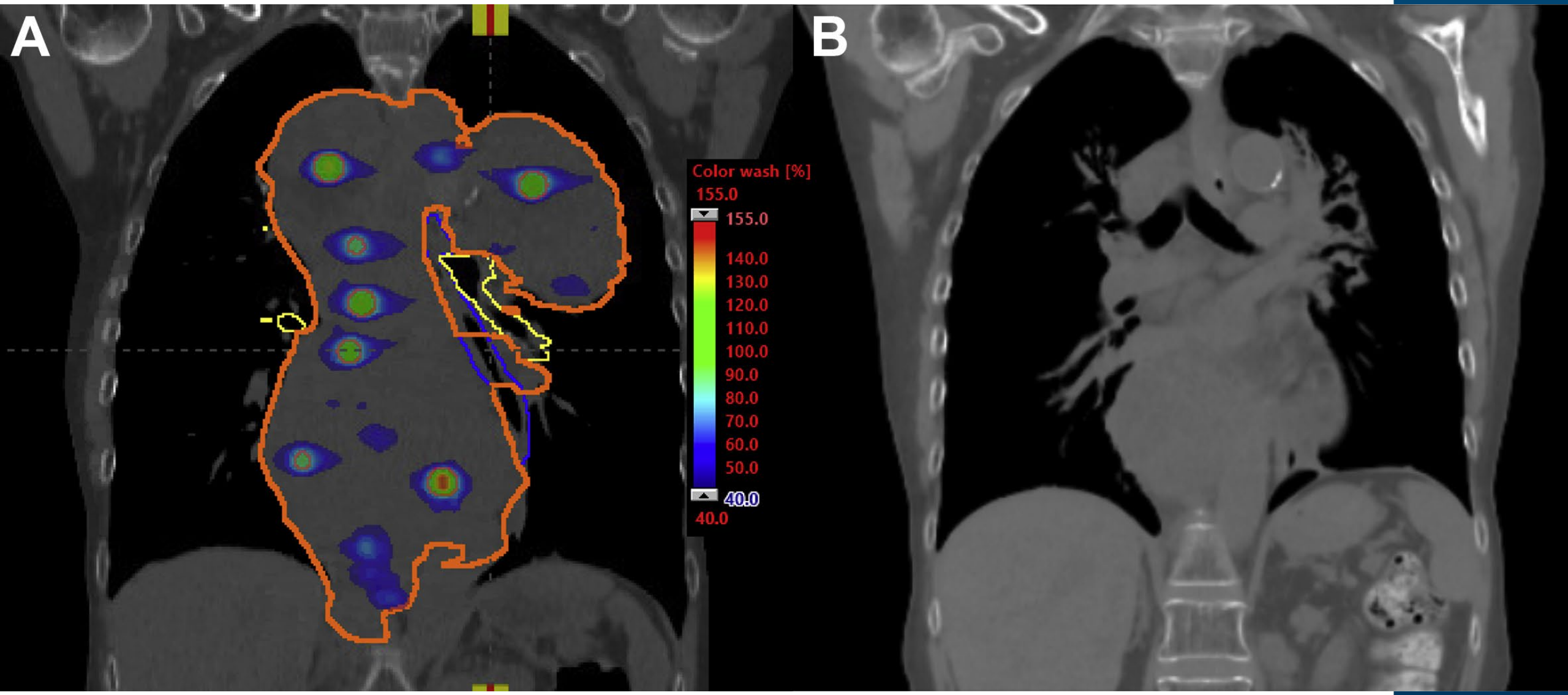
How we plan: VMAT Lattice

- Place 1.5 cm diameter spheres 3 cm apart in axial dimension and 8 cm apart sup/inf
  - Never place a sphere touching in a critical organ
    - Spinal cord, esophagus, etc



How we plan: VMAT Lattice

- Dose should break up 30-40% between spheres
- Center sphere max dose 120-140%
- Total GTV mean dose <4-7Gy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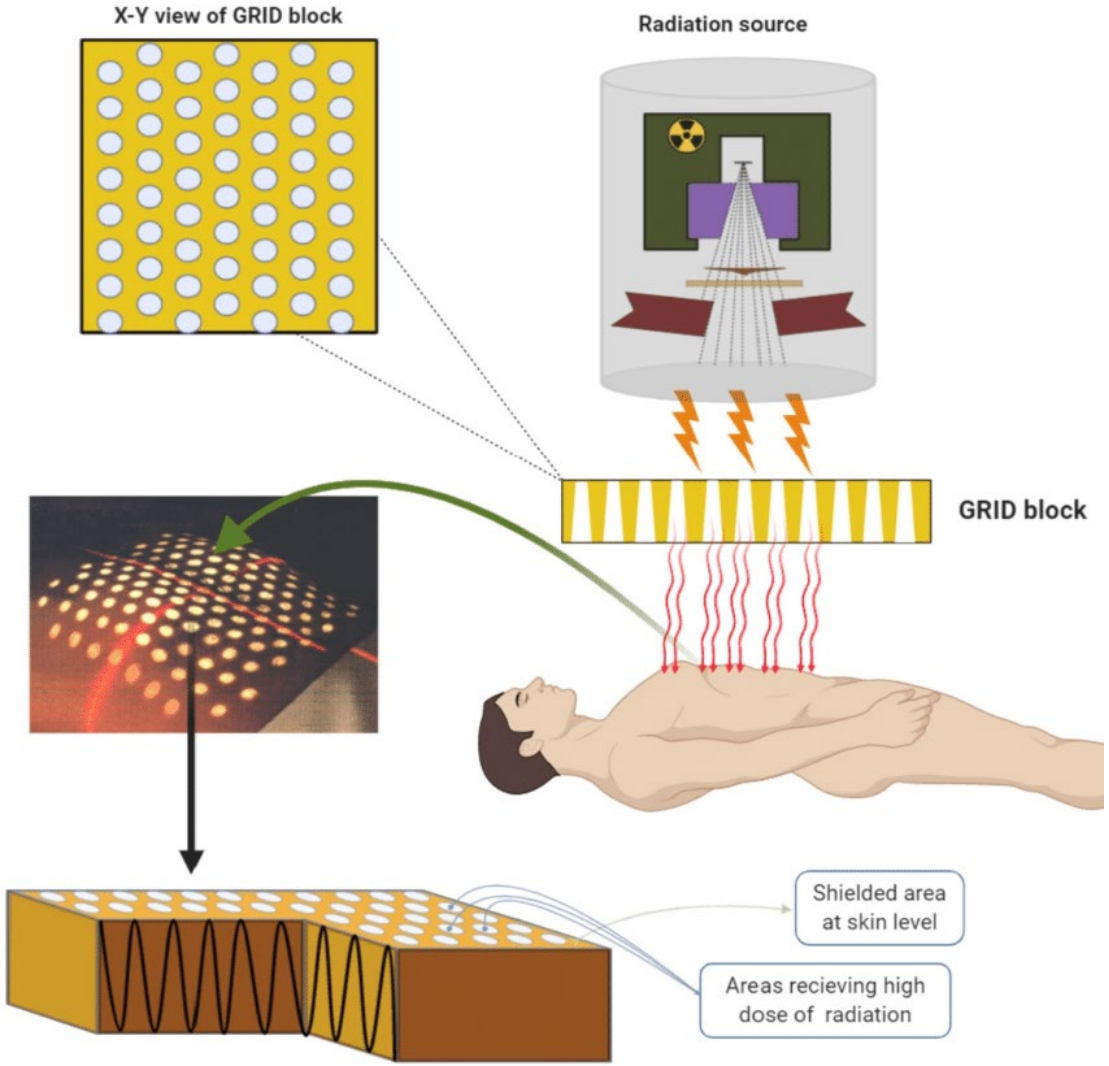
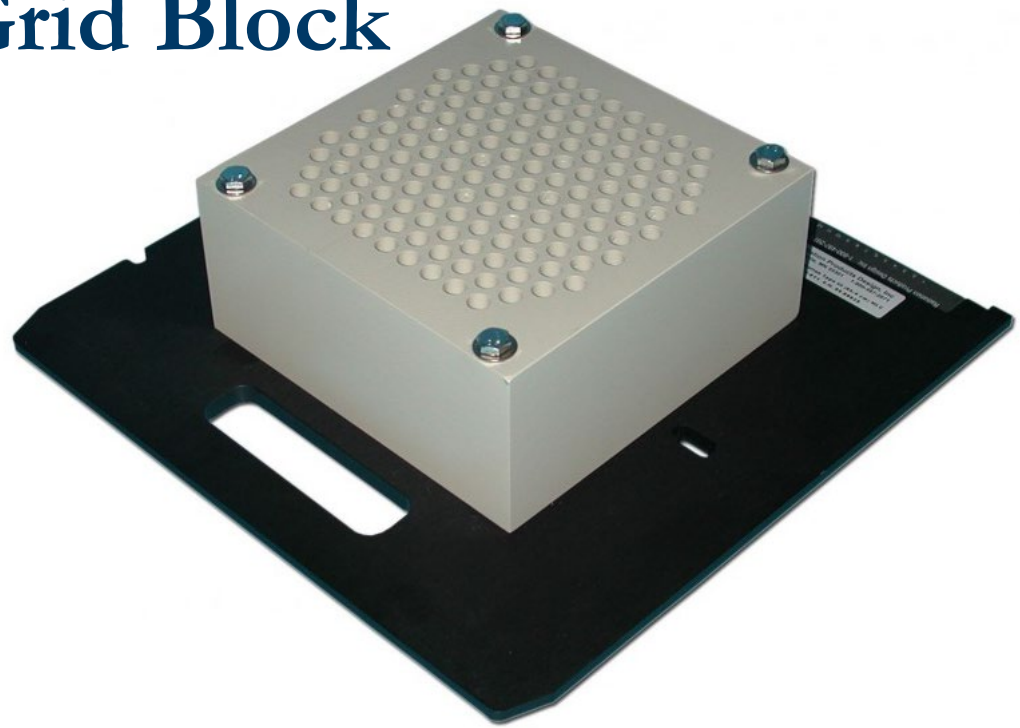
Other ways to plan: Brass/Lead Grid Block

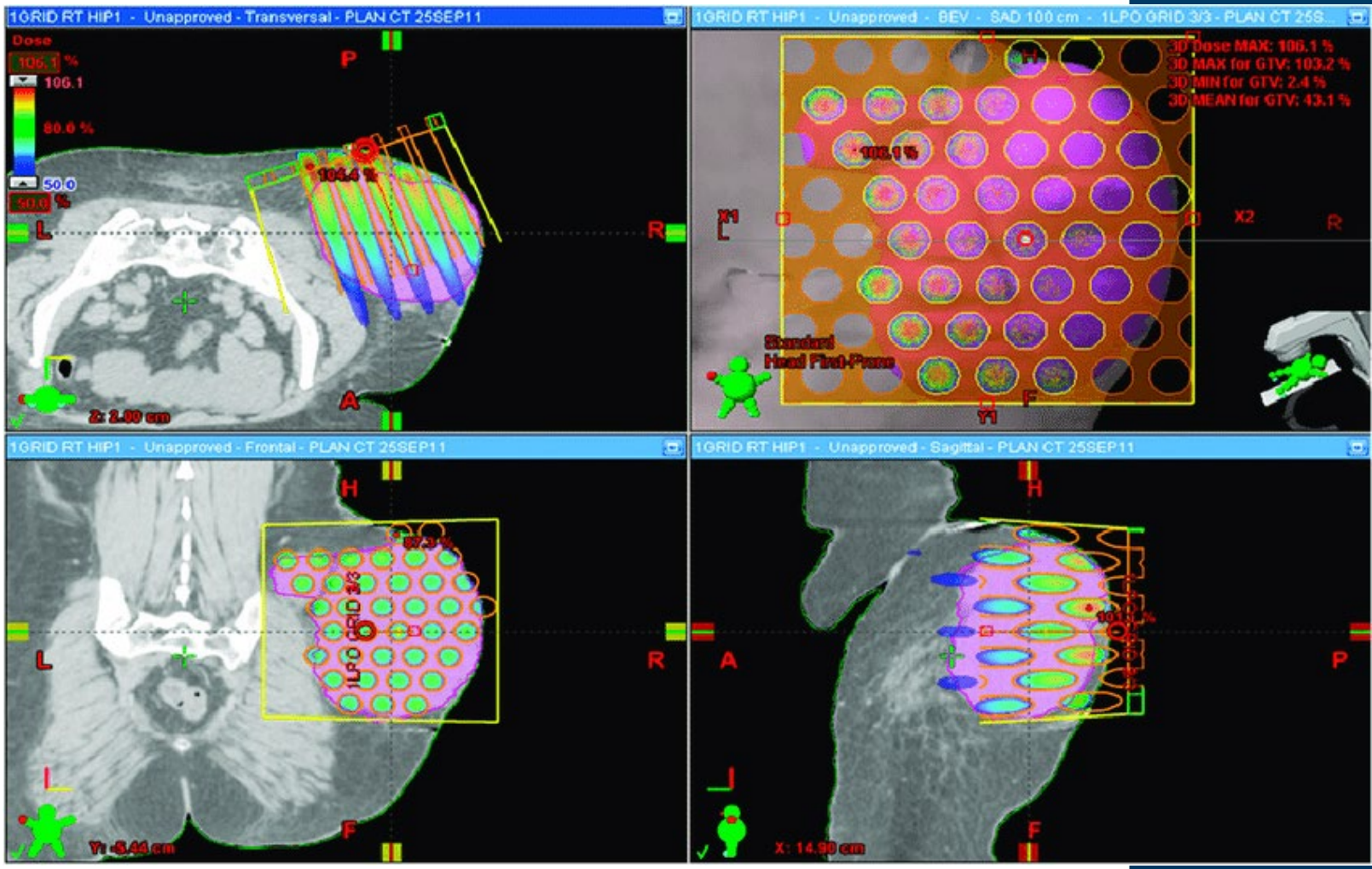




- 8cm thick block with a hexagonal array of 1.3 cm holes separated by 1.8 cm gaps
- Weighs 40 lbs

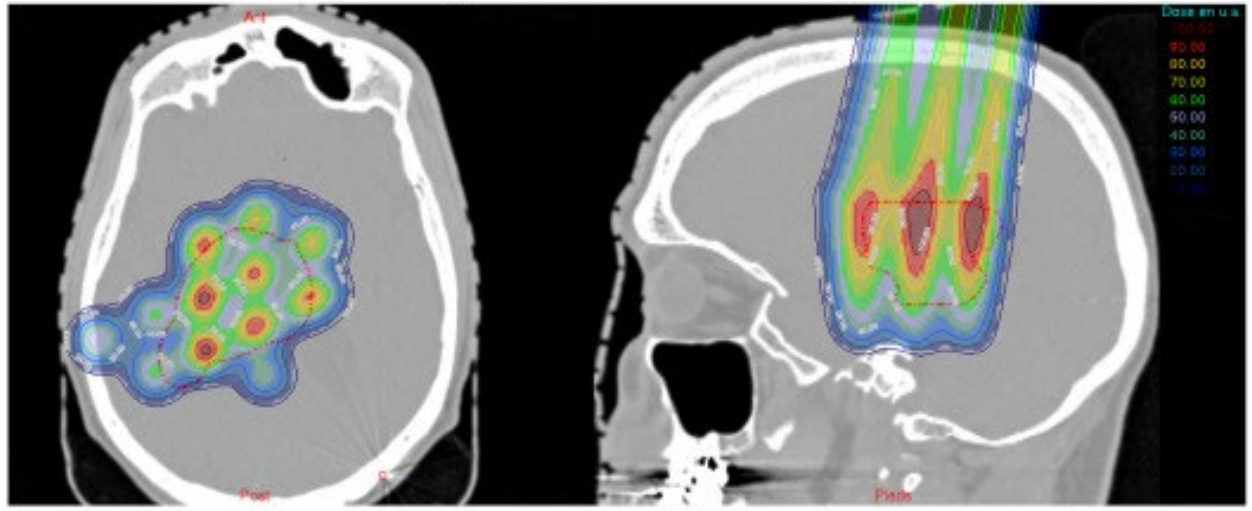
Brass Grid

- Older technique
- Relatively easy to plan
- Dose is prescribed to dmax
- Requires purchase of a grid aperture

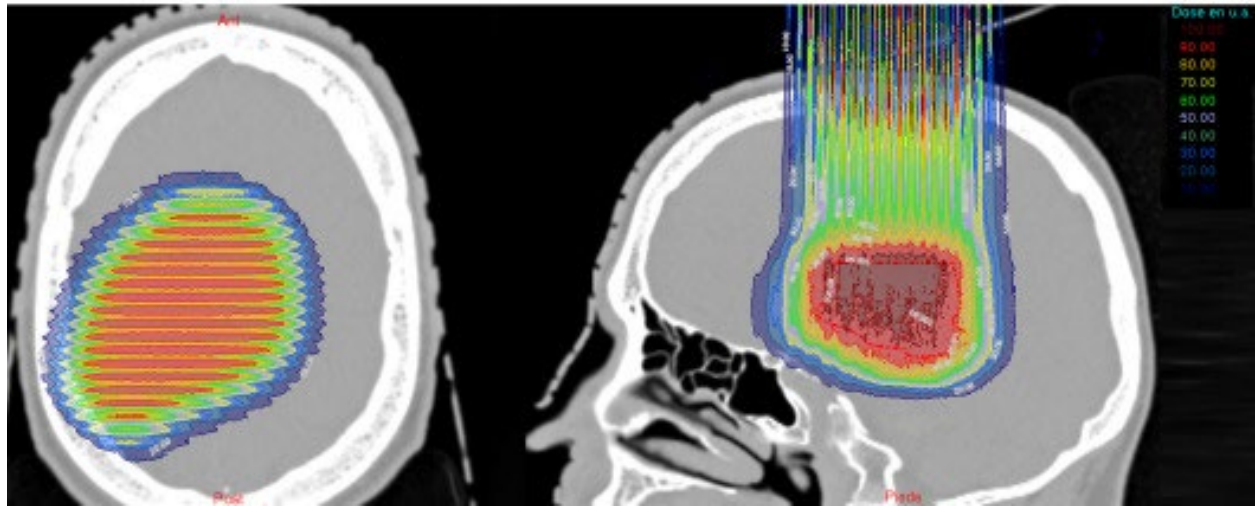


Other ways to plan: Proton Minibeam

(a) Dose distribution of GRID therapy

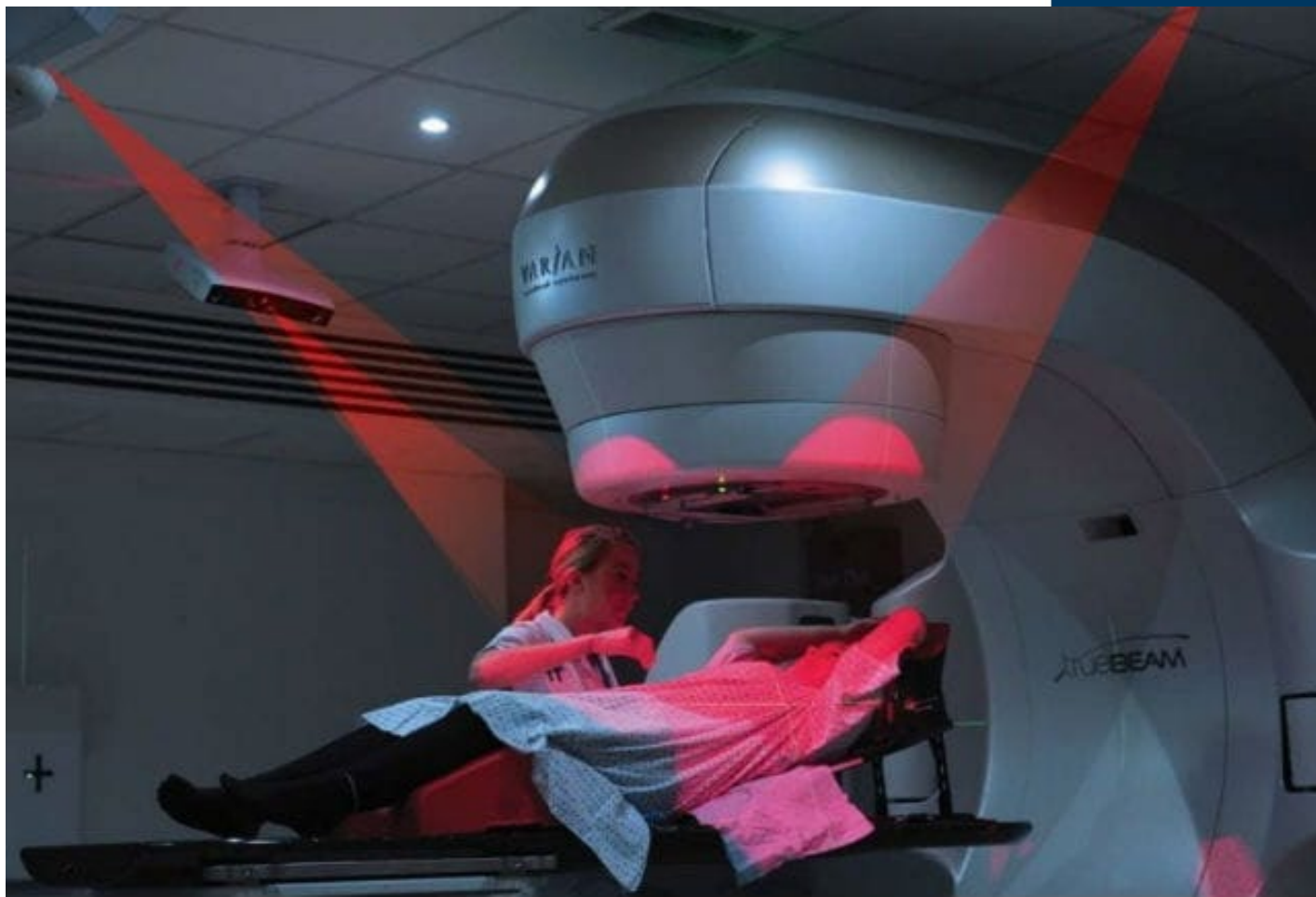


(b) Dose distribution of PMBRT



Monitoring patients during Grid

- Ensure all spheres are within tumor GTV on CBCT
- Utilize surface monitoring



Flulike Immune Reaction is Desirable

- Flulike illness from cytokine release and immune reaction is associated with improved response
- For 3 days prior to grid and 10 days after grid, we recommend:
  - No steroid use
  - Avoid NSAIDs
  - Avoid Tylenol

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Grid Therapy Outcomes

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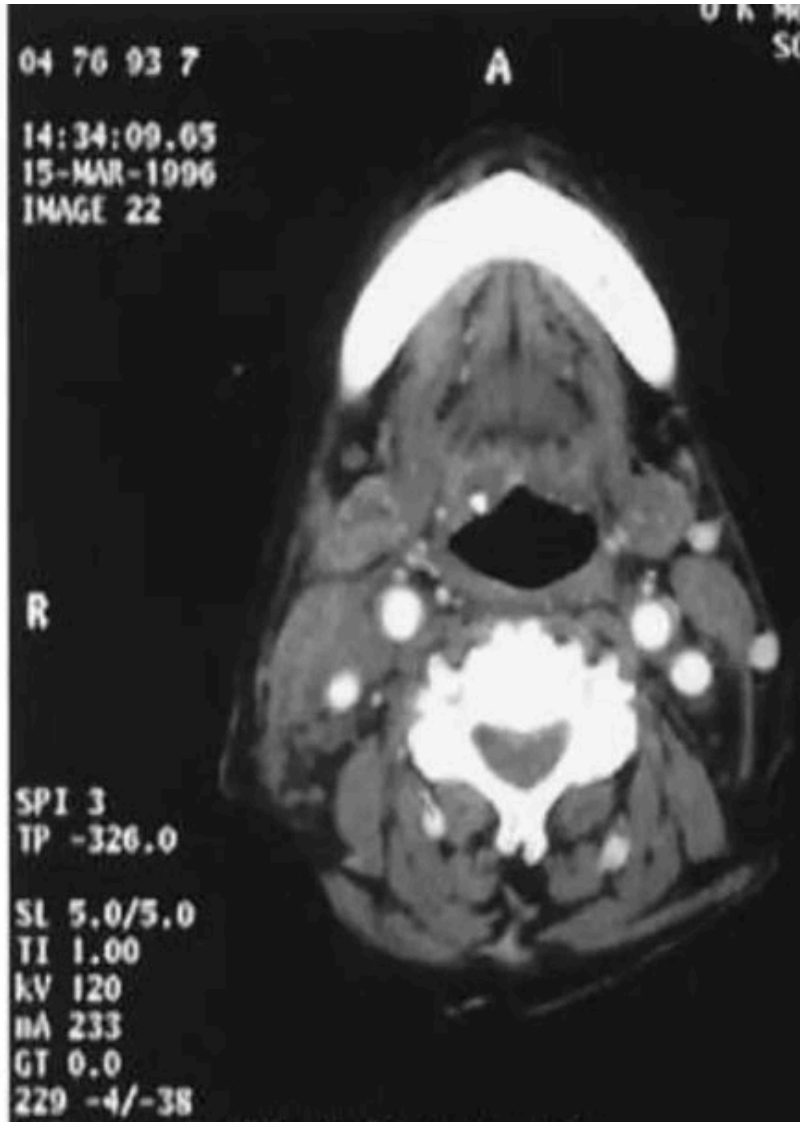
Grid: Before and After



Neowise Comet
Emerald Bay – Lake Tahoe, CA
Photo cred: The Lost Coast

Questions & Discussion

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Contact me anytime