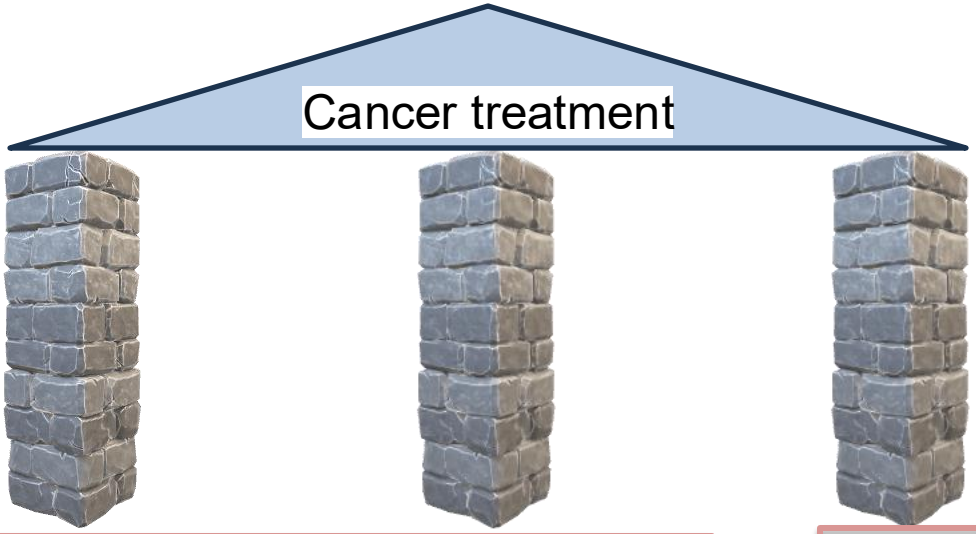
The role of radiotherapy in patients with metastatic cancer

Eduardo Urias, MD, MBA
Radiation Oncology
Joe Arrington Cancer Center
Covenant Medical Group

The pillars of cancer treatment



Surgery
- Staging/diagnostic
- Resection/dissection
- Debulking

Radiation therapy
- External beam
- Brachytherapy
- Radiopharmaceuticals

Local therapies

Medical therapy
- Cytotoxic chemotherapy
- Targeted therapy
- Hormonal therapy
- Immunotherapy
- Cellular therapy

Systemic therapy

Objectives

- Brief overview of radiation therapy (RT)
- How RT can help (and hurt) patients with metastatic cancer
- Supporting a patient with metastatic cancer undergoing RT

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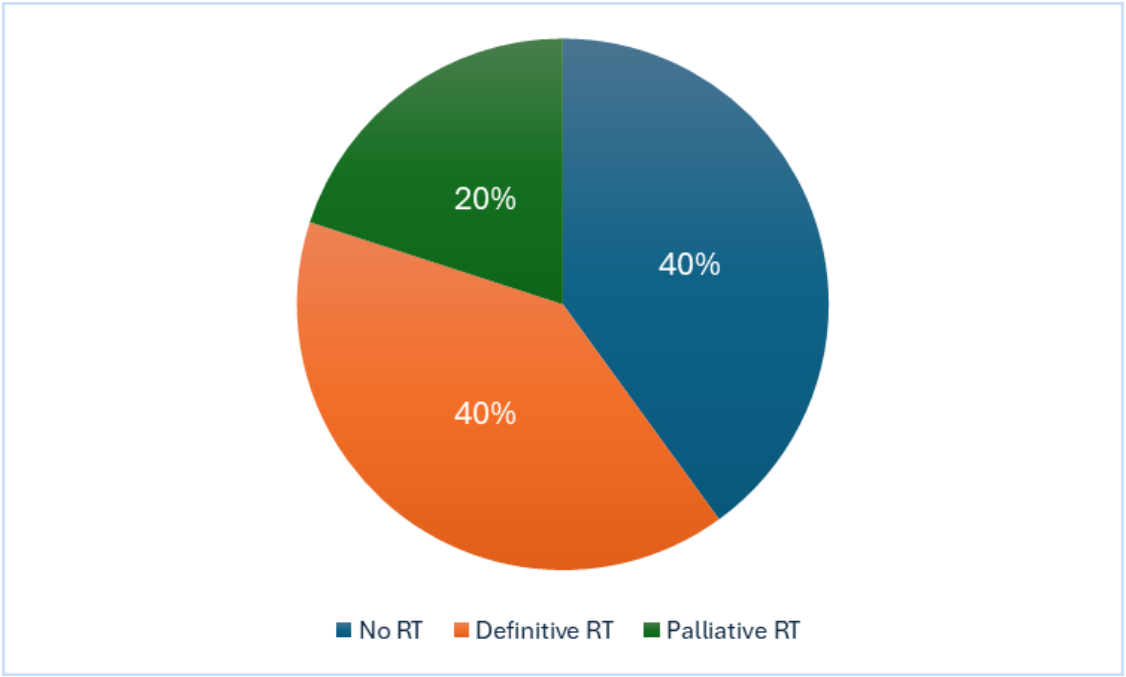
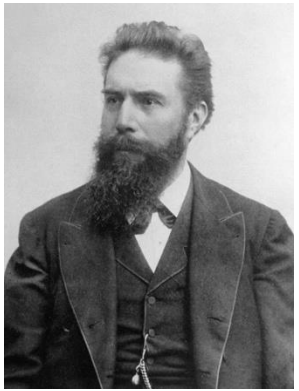
~60% of patients with cancer receive RT, mostly with definitive (curative) intent



History of RT

- **1895** Wilhelm Roentgen publishes his discovery of an “invisible light”, aka, X rays
- **1896** first medical uses of RT including treating breast tumors
- **1898** Marie Curie publishes her discovery of radioactivity in matter. Reports on its biological effects shortly after



Wilhelm Roentgen

Marie Curie

How RT works

- Causes DNA damage accumulation that leads to cell death
- Both healthy and cancer cells are susceptible to radiation damage, but cancer cells have a lesser ability to repair the damage

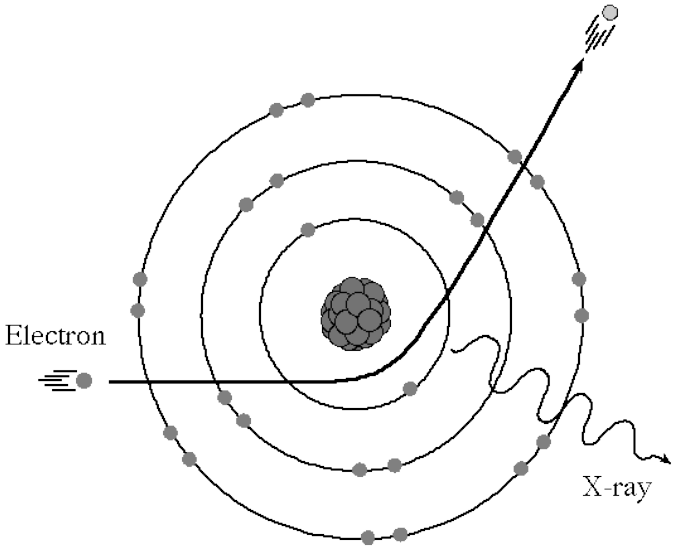
Radiosensitivity

- Different cell types in the body have different responsiveness to RT
- Organ damage is a function of dose and volume exposed

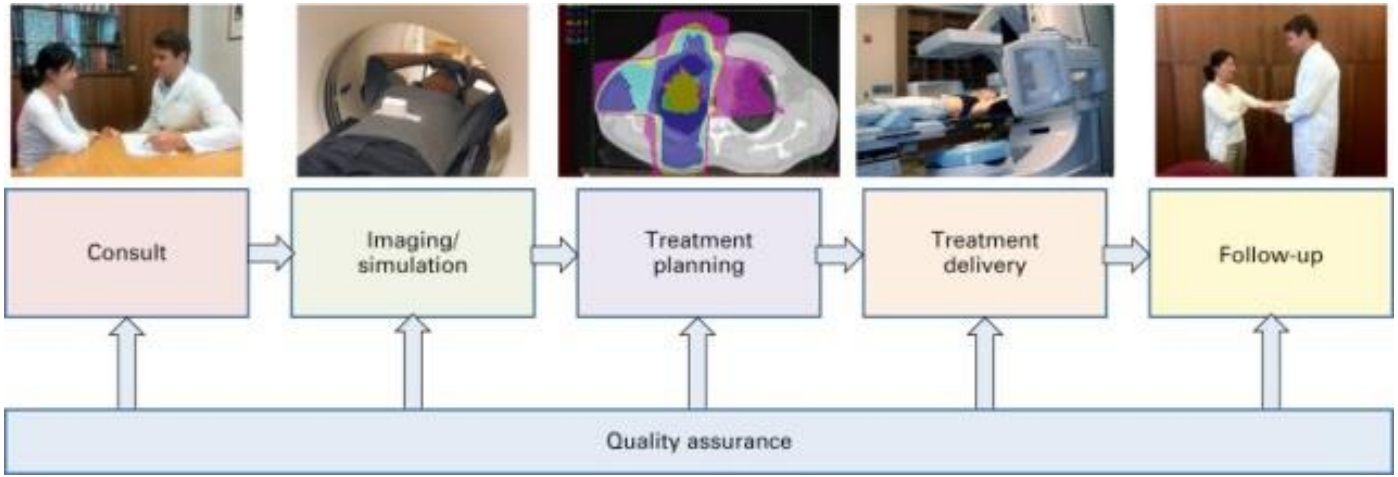
Radio-sensitivity	Tissue
Very low	Nervous system and muscles
Low	Nongrowing cartilage and bone, thyroid, pancreas, lungs, and kidneys
Medium	Growing cartilage, bone, and blood vessels
High	**Lens**, **skin**, cornea, bladder, uterus, and gastrointestinal tract (non–small intestines) • Cataracts, 0.5 Gy • Skin erythema, > 3-6 Gy
Very high	**Testes**, ovaries, bone marrow, lymphoid tissues, and small intestines • Male sterility, 0.15 Gy in one brief exposure (temporary or permanent)

How RT is delivered

- A linear accelerator accelerates an electron and smashes it into a high-density target, where X-rays are generated

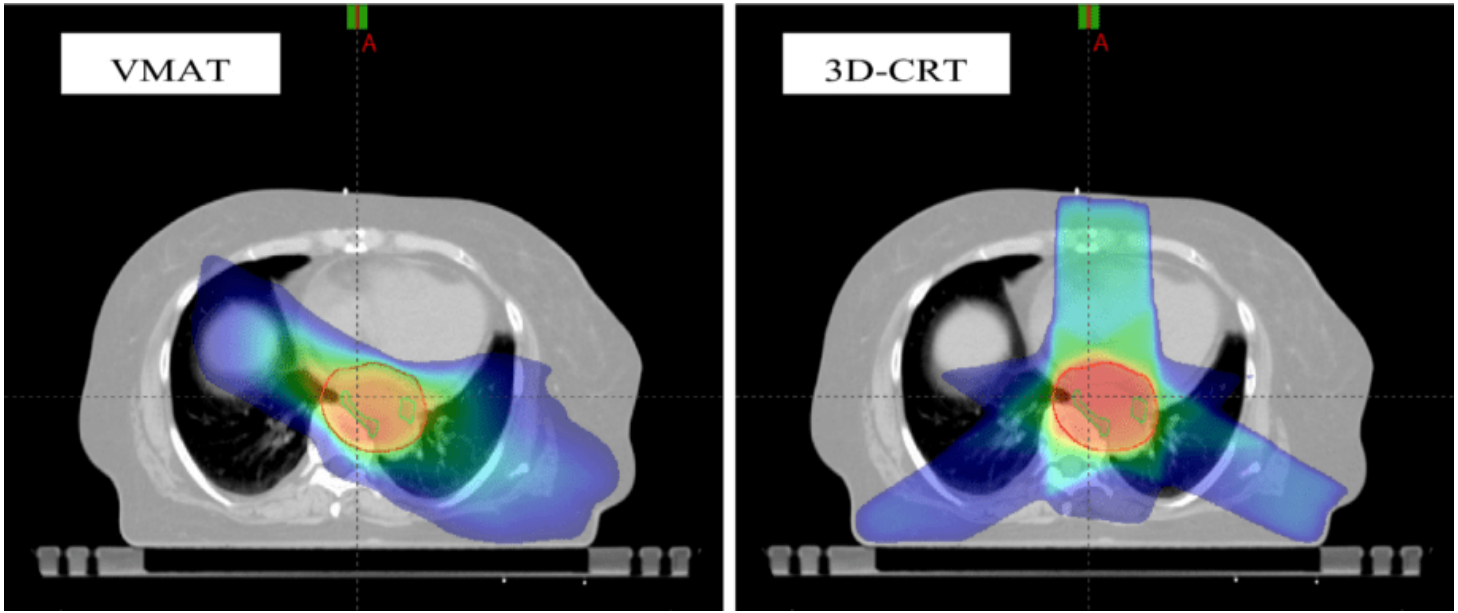


RT workflow



thoracickey.com

Different techniques for different cases



Resource intensive
Longer planning (e.g., treatment delay)
Better dose distribution, resulting in lower risk of side effects and/or higher doses

Typical prescriptions

- Gray (Gy) = unit of absorbed dose of radiation
- Fraction (fx) = individual treatment

- Palliative treatments are mostly 1 – 5 fractions of treatment

  - E.g.:
  - 8 Gy in 1 fx
  - 12 Gy in 1 fx
  - 20 Gy in 5 fx
  - 20 Gy in 1 fx
  - 30 Gy in 10 fx

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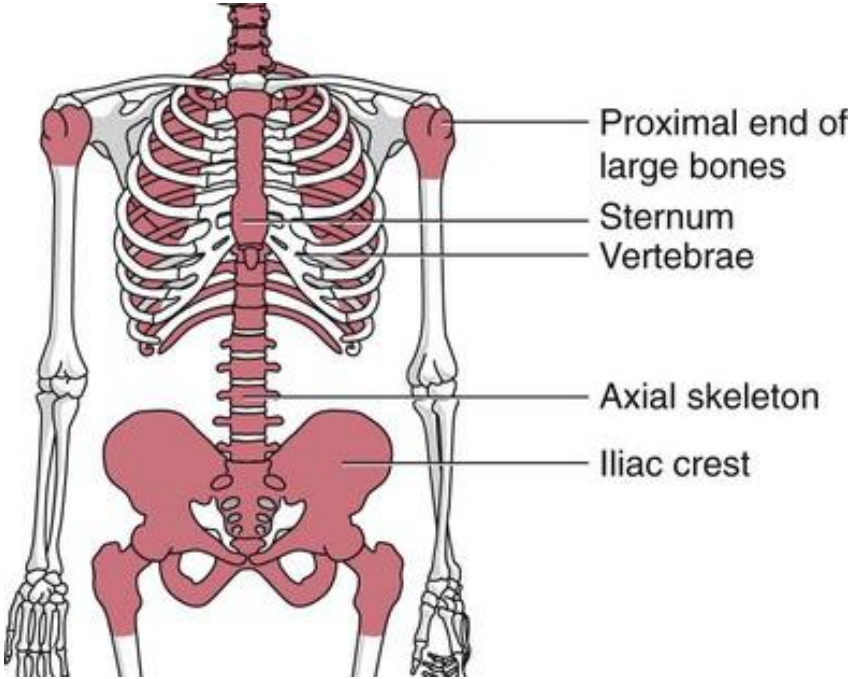
Palliative RT

- Bone pain
- Brain metastases
- Spinal cord compression / any nerve compression
- Bleeding masses
- Obstructive masses
- Other symptomatic tumors

Bone pain

- 60-80% response rates to RT
- Full palliative effect typically takes several weeks
- Pain flares are possible (may signal a good pain response)

- Special considerations: bone marrow suppression depending on the site of treatment



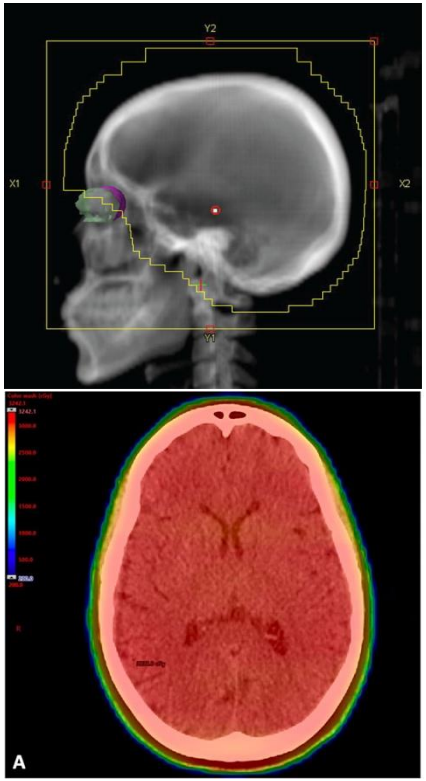
Active bone marrow distribution in adults

Oncohemakey.com

Brain metastases

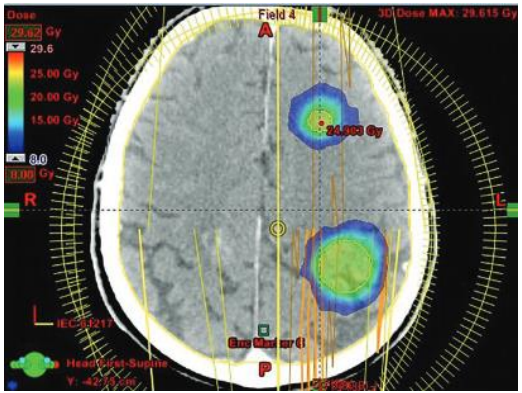
Whole brain radiotherapy

- Same-day treatment is possible
- Higher toxicity
- Reserved for multiple mets and/or patients with poor prognosis



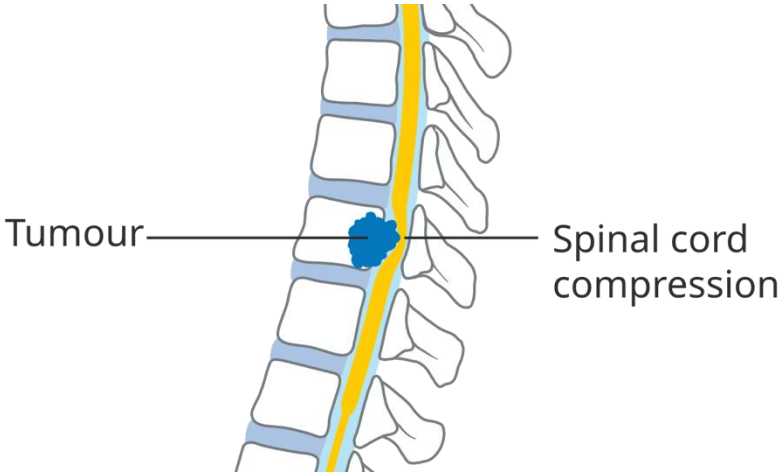
Stereotactic Radiosurgery (SRS)

- Many hurdles to doing emergently
- Resource-intensive
- May delay treatment
- Spares most of the radiographically *uninvolved* brain



Nerve compression (mostly spinal cord)

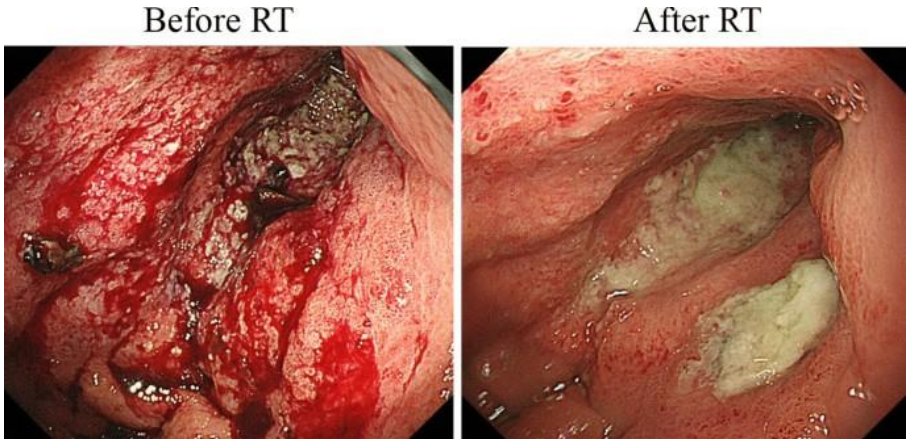
- Could be an emergency if sudden onset of neurologic deficits
- If diagnosis is known, always start steroids first while plan for surgery or radiotherapy is decided
  - If the type of cancer is not known, steroids could compromise pathologic confirmation



Hemostasis

- 80-90% response rates
- Decrease in bleeding as early as first treatment

- Considerations:
  - Alternatives: embolization by IR, surgical resection
  - Radiosensitivity of tumor



Effect of RT in a patient with hemorrhagic gastric cancer.
Sugita, et al, J of GI Cancer, 2021

Obstructive masses

- Examples: esophagus, bowel, airway

- Typically, mild-moderate and temporary response to palliative RT
- Patients without widespread metastatic disease should be considered for more aggressive course, potentially chemo-RT

Other symptomatic tumors

Amini, et al, Front Onc, 2014

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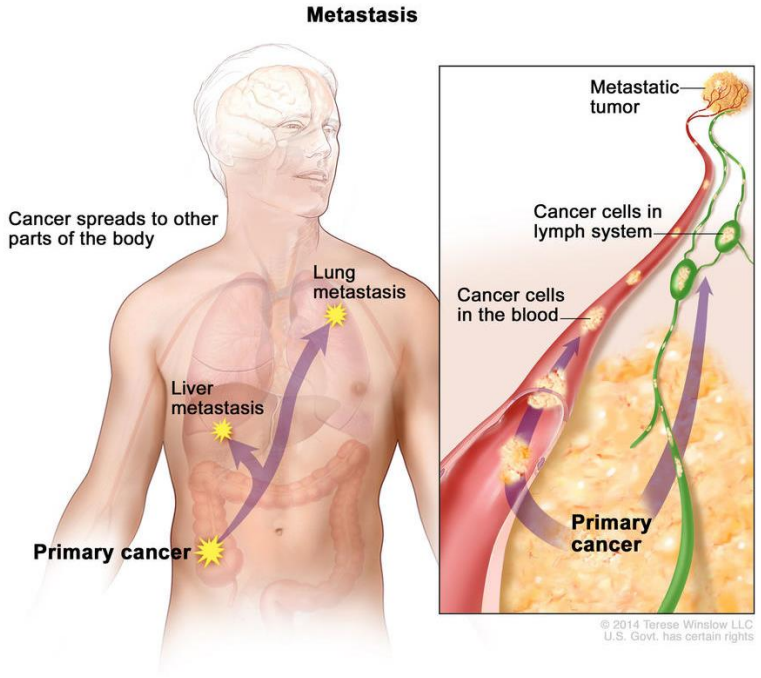
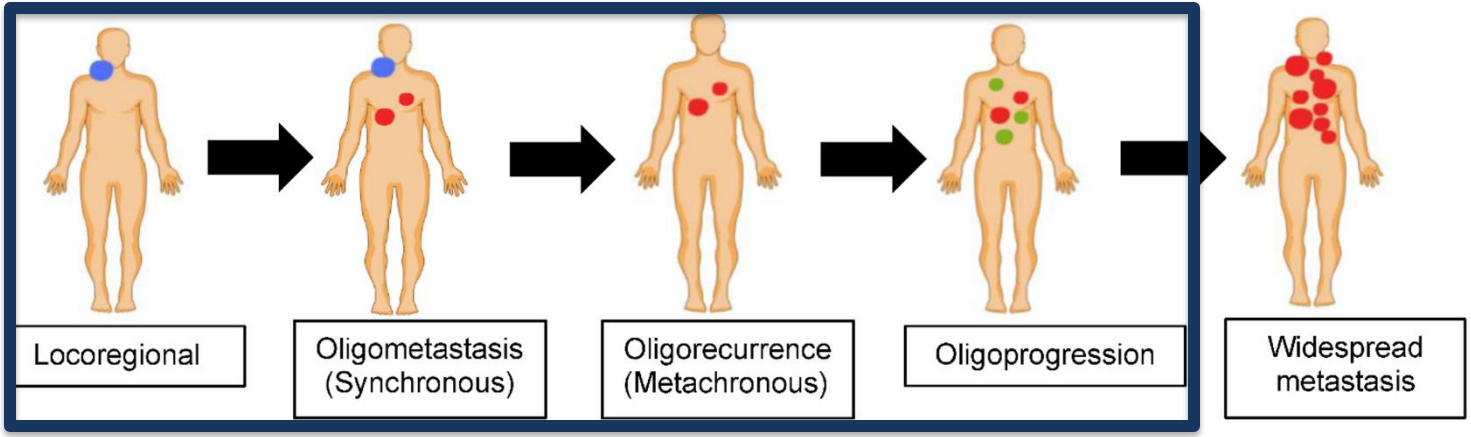
Hematogenous spread of cancers

- Once a patient develops metastatic cancer, there are, potentially, innumerable microscopic reservoirs of tumor deposits as well as persistent cancer cells in circulation



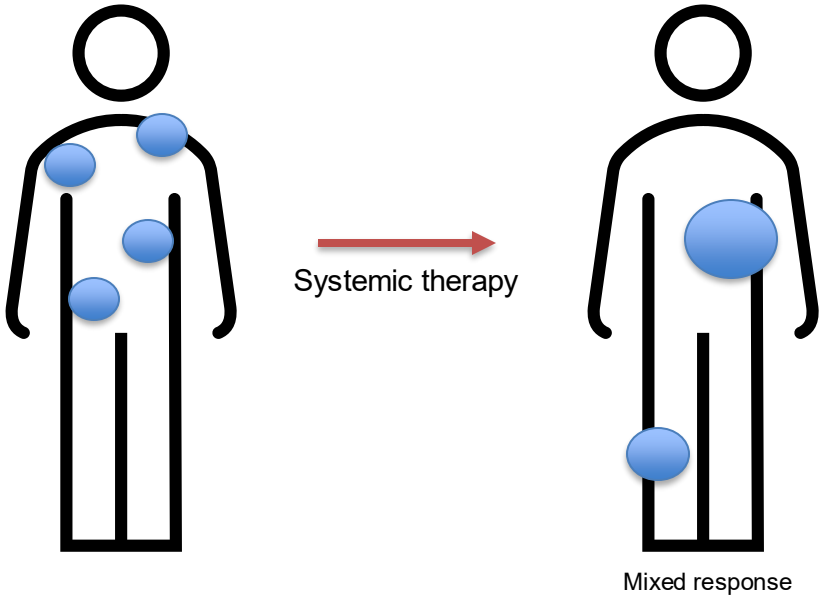
Metastasis-directed therapy

- For many cancers with ***few*** progressing lesions (typically considered ≤5), RT can improve outcomes and delay time to next systemic therapy



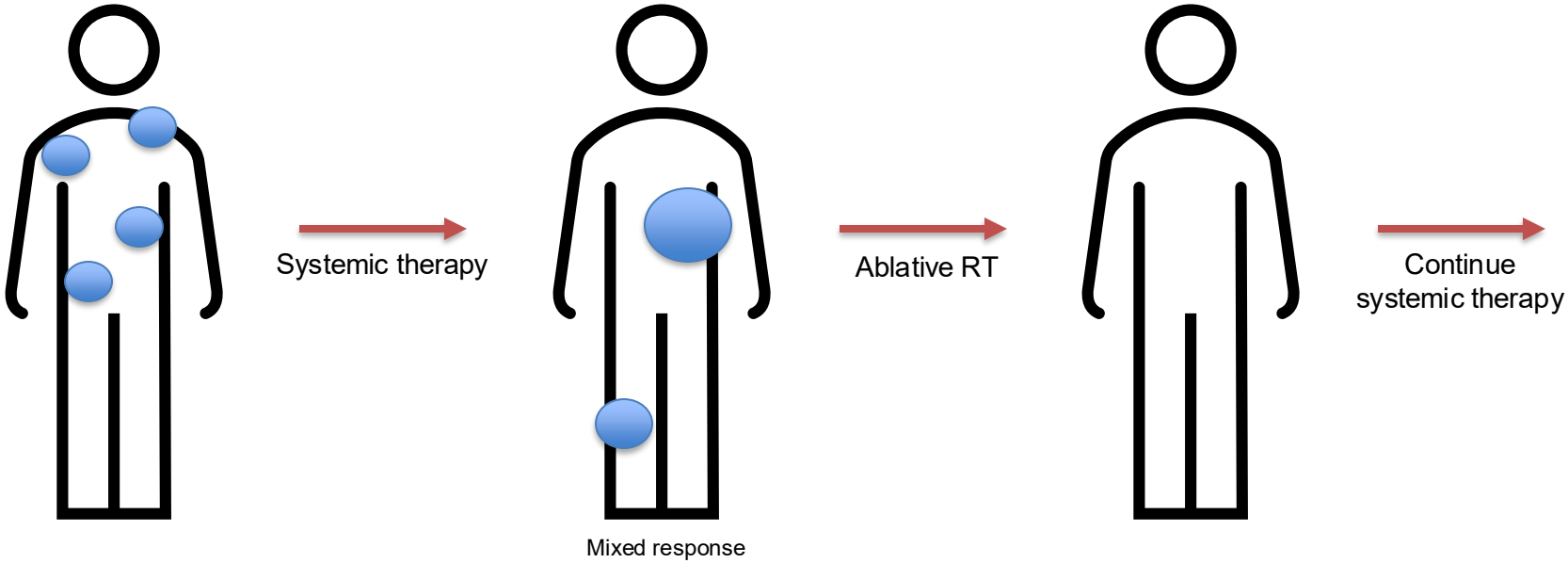
RT may delay further progression

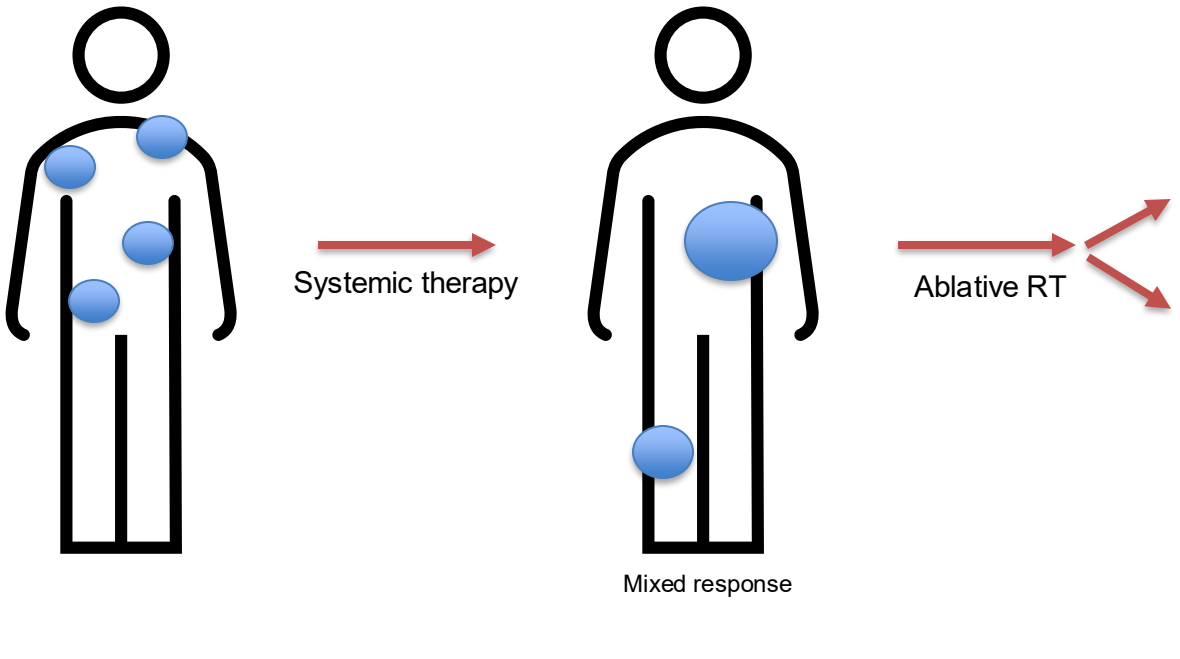
Bahig, Cancers, 2022



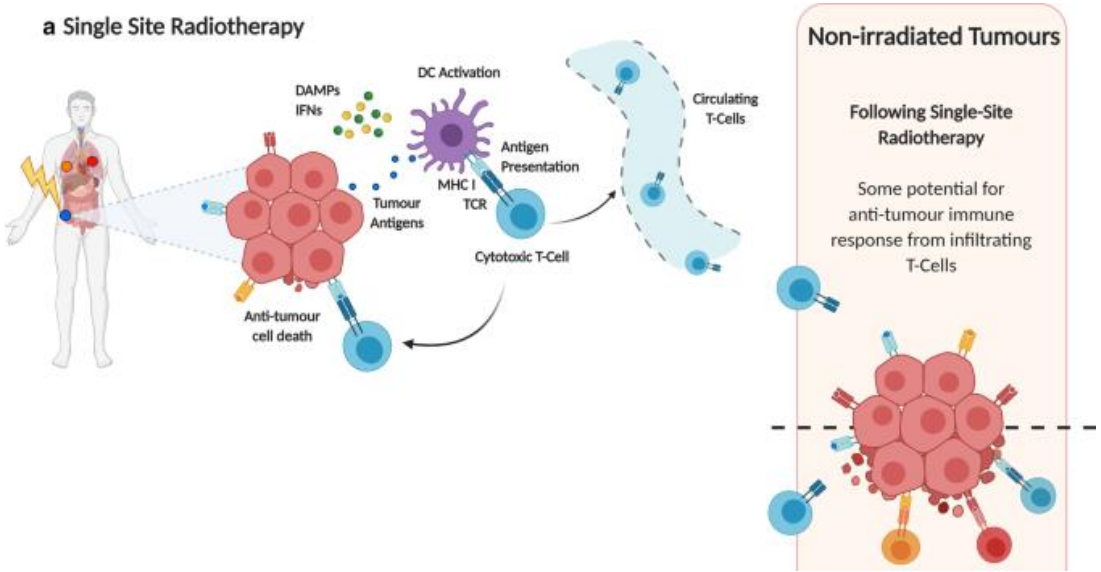
Was the treatment a failure?
What's the next step?


ONLY A SITH DEALS IN ABSOLUTES


Systemic therapy
Mixed response
Ablative RT
Continue
systemic therapy

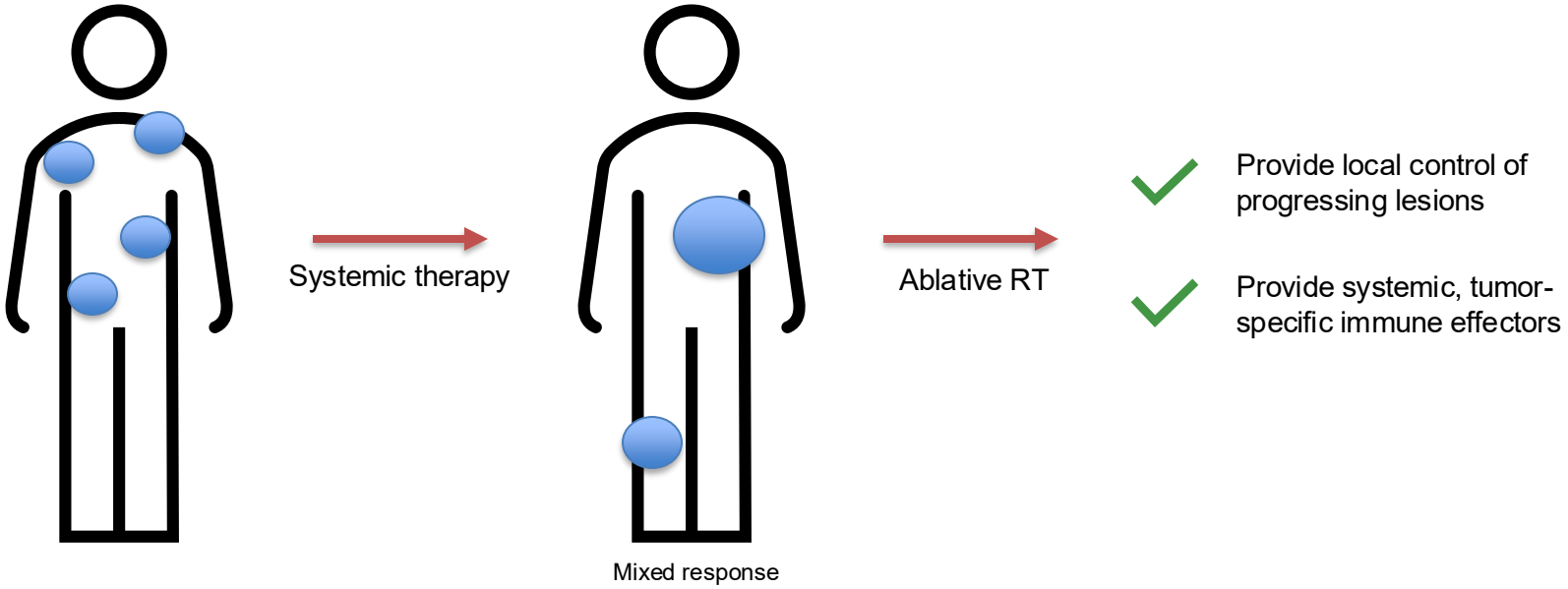

Systemic therapy
Mixed response
Ablative RT
Success! Pt may continue the same systemic therapy
Out-of-field progression. Side effects from RT for, essentially, no oncologic benefit

Radiotherapy as an immune-modulator



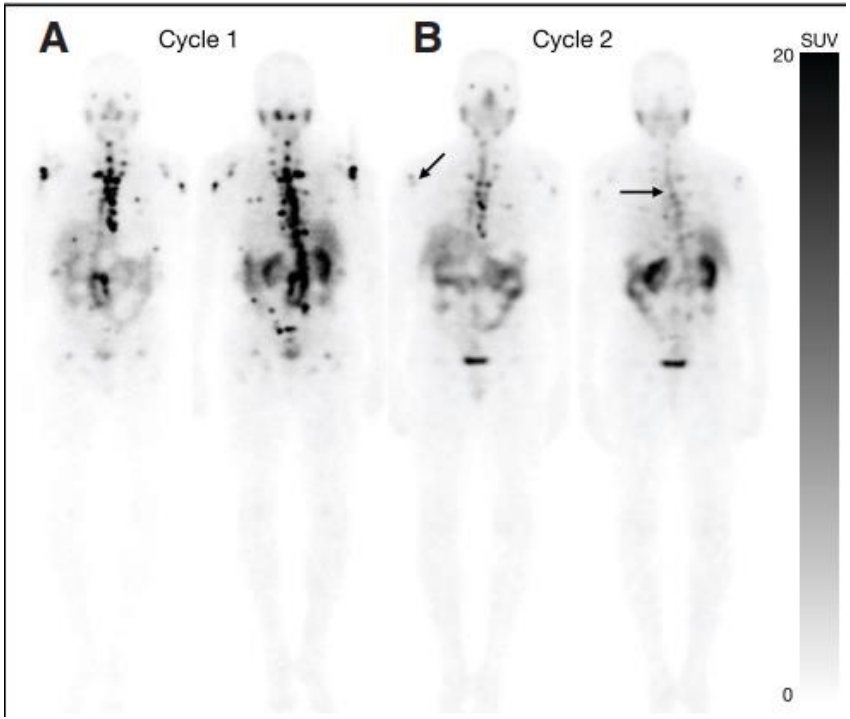
Colton, et al, Radiation Oncology, 2020

Radiotherapy as an immune-modulator



Radiopharmaceuticals

- Cancer-specific ligands bound to a radioactive source, injected IV.
- E.g., Pluvicto, Xofigo, Lutathera.
- Requires extensive coordination and radiation safety protocols.



SPECT showing disease response to Pluvicto in a patient with metastatic prostate cancer. Yadav, J Nucl Med, 2024

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  - Case studies

How to support a patient with metastases receiving RT

- Factors influencing toxicity: area being irradiated, overlapping prior RT, concurrent systemic therapy, volume of organs exposed to radiation, dose of radiation.

- Should we hold systemic therapy?
- Should we hold RT?

- Steroids (pain flare, mass effect in CNS, esophagitis), blood transfusions, neutropenic precautions, antiemetics, antidiarrheals, skin care (Aquaphor, barrier creams, Silvadene, Mepilex).

Case #1

- 38 year old female presents to the ER with 3 month history of worsening vaginal bleeding. Hemoglobin 6 at presentation; she has symptoms of anemia including dizziness and excessive fatigue. Transfused 2 units of blood.
- Pelvic exam notable for bright red blood in the vaginal vault and a 7 cm friable mass at the cervix.
  - Exam under anesthesia was performed and bleeding sources were cauterized. Vagina was packed extensively.
- PET/CT scan shows multiple pulmonary, hepatic, and nodal mets.

Case #1

- Not recommended:
  - Start systemic therapy – hemorrhaging primary tumor is unlikely to have a sufficiently rapid response
  - Surgery – morbidity likely not be justified in the setting of widely metastatic disease; could delay time to start systemic therapy
- Hospitalist consults IR and patient is taken to OR for feeding artery embolization. Unable to locate specific feeder; patient continues to bleed.
- Radiation Oncology is consulted. Patient starts treatment the next day. Bleeding improves after second treatment.

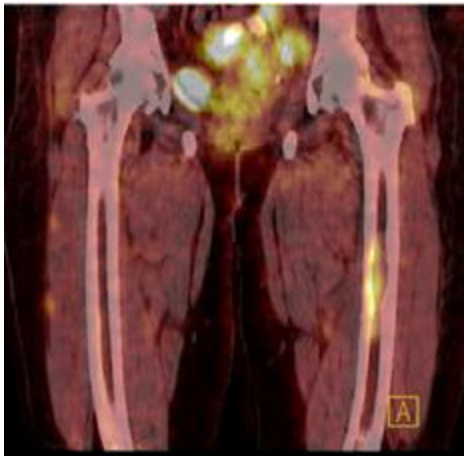
Case #1

- Patient completes 10 fx of RT. Bleeding is reduced to occasional spotting.
- Develops dysuria and mild diarrhea

- Next: rule out UTI. May give Azo and/or tylenol for relief. Consider Imodium for diarrhea; may consider temporary low-residue diet if severe.

Case #2

- 68 year old man with widely metastatic prostate cancer on hormonal deprivation therapy. Worsening left thigh pain for several weeks, now limiting mobility and increasing opioid use.
- Not a candidate for Pluvicto due to underlying CKD.



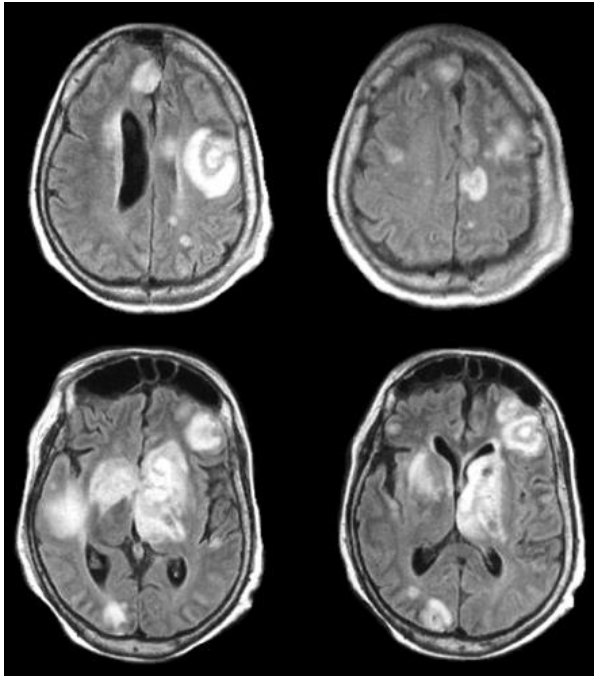
Ozdemir, MedNuc Im Mol, 2012

Case #2

- Evaluated by Ortho who determines patient to be a poor candidate for surgery.
- RO sees patient. Starts treatment a couple of days after; 5 fx planned
- Severe increase in pain after fx 3.
- Next: start steroids (dexamethasone 4mg bid). Counsel on low weight bearing.

Case #3

- 69 year old man with history of metastatic NSCLC on 3rd line of systemic therapy. He presents to the hospital with a 3-day history of headaches, confusion, and right hemiparesis.
- CTs of his body also show progression of disease.

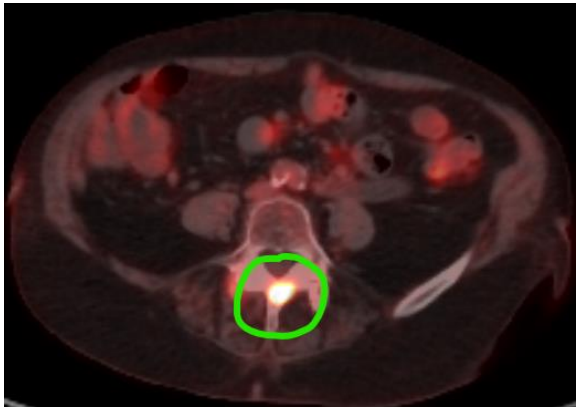


Case #3

- What to do?
  - Start steroids
  - Consult Neurosurgery?
  - Consult Radiation Oncology?
  - Discuss hospice?
- RO consulted. Whole brain radiotherapy was started on the same day.
- The patient struggled with nausea, vomiting, fatigue, and severe headaches.
- 2 weeks after treatment his neurologic symptoms improved, including left-sided hemiparesis.

Case #4

- 86 year old man with history of locally advanced rectal adenocarcinoma treated 10 years prior. Incidentally found to have a lung nodule and L5 lesion; lung biopsy confirms metastatic rectal adeno.
  - No targetable mutations, low PD-L1 expression, low tumor mutational burden.



- Next step?
  - Chemo-immunotherapy?
  - Surgery?
  - RT?
  - Hospice?
- Patient elects for *definitive* RT. Develops fatigue that improves 3 weeks after finishing treatment.
- Remains disease free 6 months after RT.

When seeing a patient undergoing RT

- Always confirm whether concurrent systemic therapy is appropriate.
  - Radiosensitizing systemic therapy could increase the risk of toxicity.
- Don't forget to rule out important complications, potentially non-RT related: UTI, skin infections, metabolic/infectious encephalopathy.
- In palliative cases, steroids are your friends.

- Always feel free to reach out to treating Radiation Oncologist.

Thank you

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