Solitary Plasmacytoma

Bryce Beard PGY4
Faculty advisor: Shahrokh Iganej, MD
Kaiser Permanente Los Angeles Medical Center
Los Angeles, California

Case:

65 year old man presents to PCP with progressively worsening lower extremity weakness x 8 weeks. Associated symptoms include subacute on chronic worsening low back pain.

Past medical history: Hypertension, GERD, chronic low back pain.
Past surgical history: None.
Social history: Former smoker. No EtOH. Retired waiter.
Family history: None.
Allergies: No known drug allergies.
Medications: Losartan, omeprazole.

Case:

65 year old man presents to PCP with progressively worsening lower extremity weakness x 8 weeks. Associated symptoms include subacute on chronic worsening low back pain.

Physical exam:

- General: Well-nourished, well-developed. No distress.
- Neurological:
  - Motor: ⅗ strength left arm, ⅗ strength left leg, ⅘ strength right arm, ⅘ strength right leg
  - Sensory: Sensation to light touch is globally intact.
  - Reflexes 1+ and symmetric
  - Gait is sluggish and has difficulty standing on tips of toes.
- Extremities: Clubbing of fingers.
- Skin: Intact. No rash.
- Other: No thyromegaly, no hepatosplenomegaly.

Case: Work-up

Basic labs

CBC shows mild thrombocytosis (478k) otherwise normal.

Electrolytes, BUN/Cr, LFTs normal.

Neuropathy studies:

Vit B12, folate, MMA, homocysteine, ANA, RF, CRP are normal.

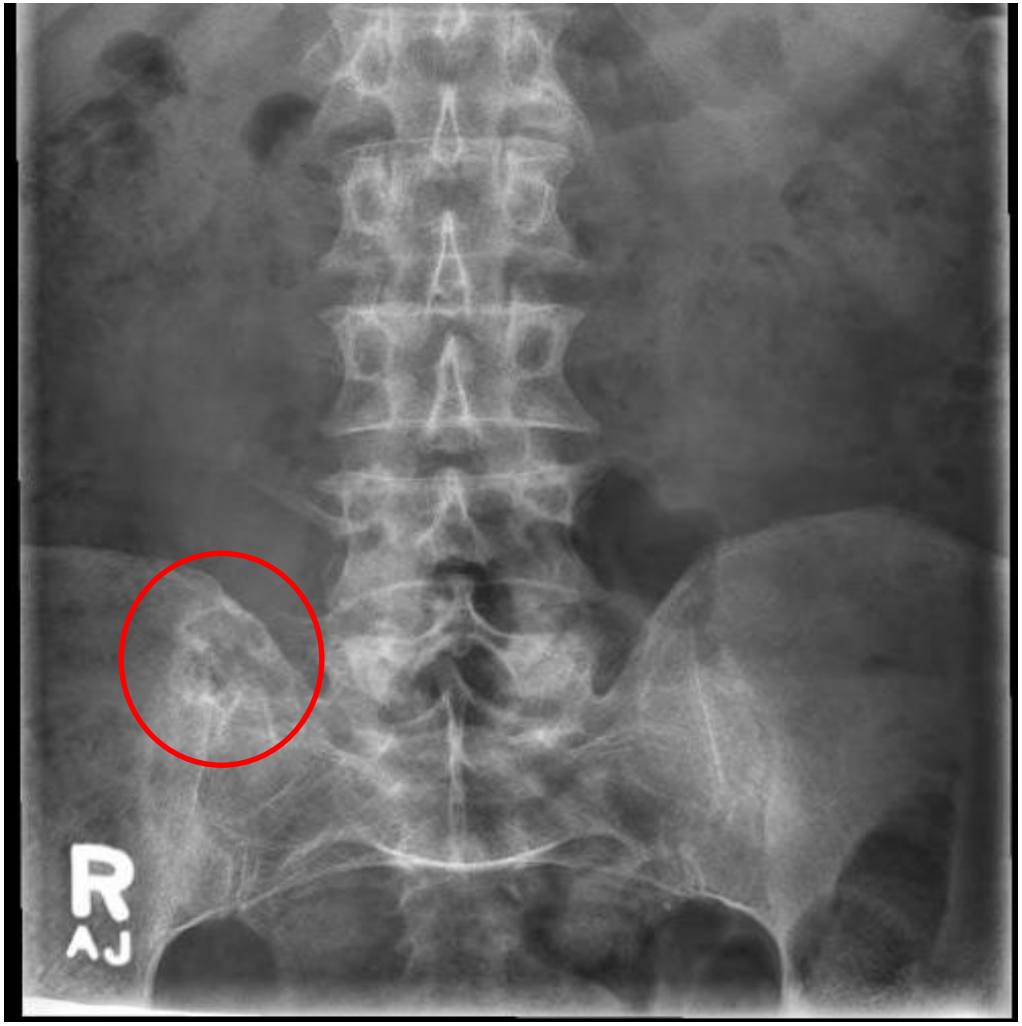
SPEP:

- Total protein: 7.2 (nl)
- Albumin: 4.3 (nl)
- Alpha1 globulin: 0.3 (nl)
- Alpha2 globulin: 0.7 (nl)
- Beta globulin: 1.13 (elevated)
- Gamma globulin: 0.9 (nl)
- M-protein: 0.55 (elevated)

Immunofixation: IgG lambda monoclonal gammopathy

Kappa light chains: 29 (elevated)
Lambda light chains: 36 (elevated)
K/L light chain ratio: 0.8 (nl)

Case: Imaging



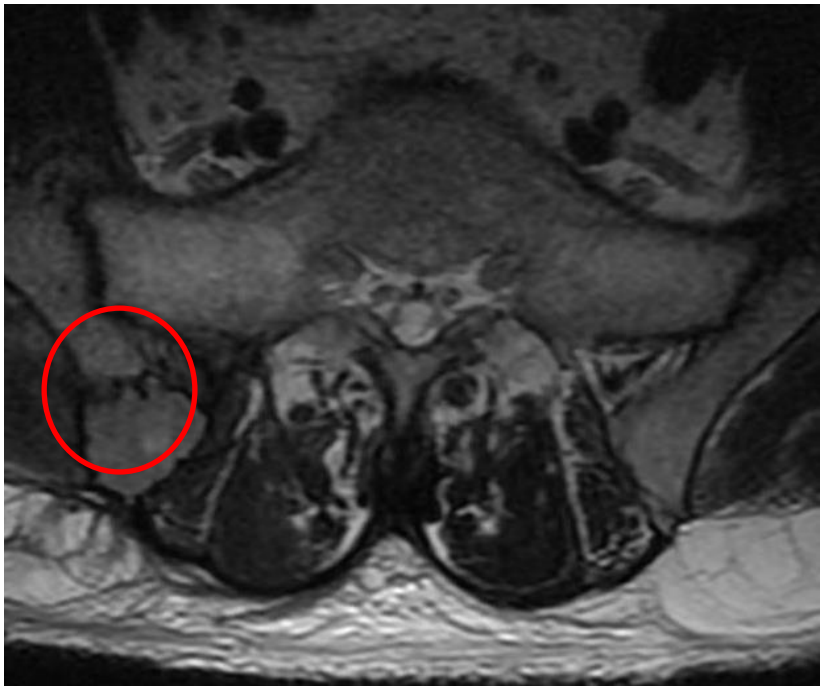
Plain film lumbosacral spine

No fracture or acute pathology of the bone. There is an irregular lucency in the right superior sacroiliac joint region.

Case: Imaging

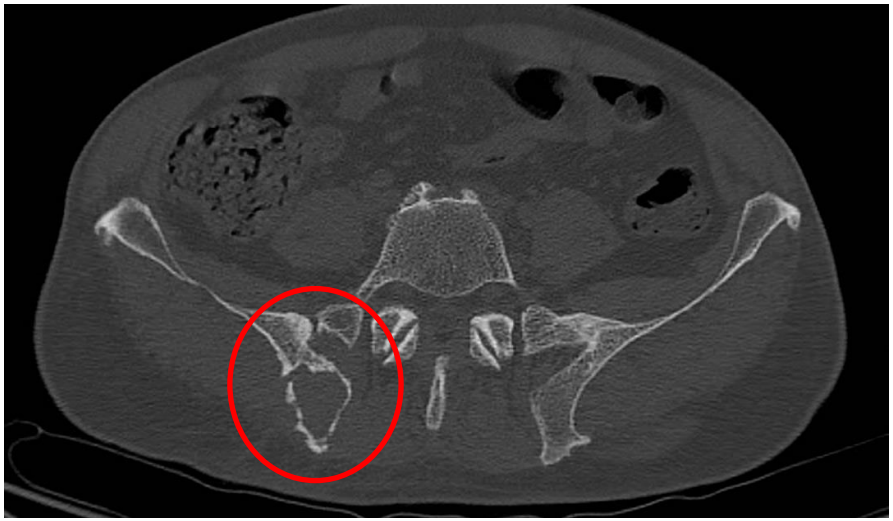
MRI cervical and lumbar spine:

Visualized spine is normal. Irregular linear low T2 signal lesion in the right posterior iliac without marrow edema.



CT chest, abdomen, pelvis

3.2 x 2.5 x 3.7 cm irregular cortical expansile lucency in the right posterior iliac bone.

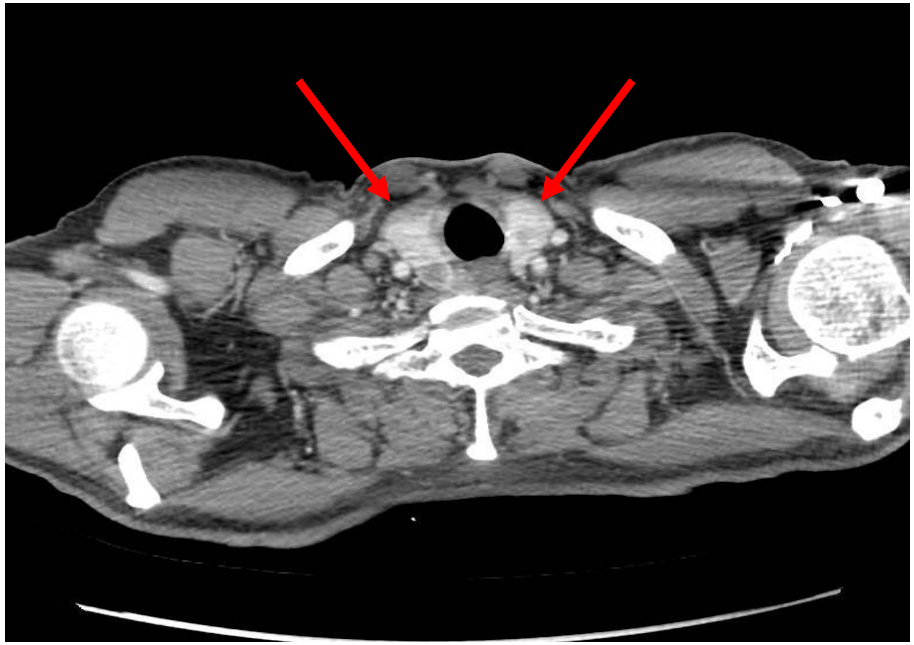


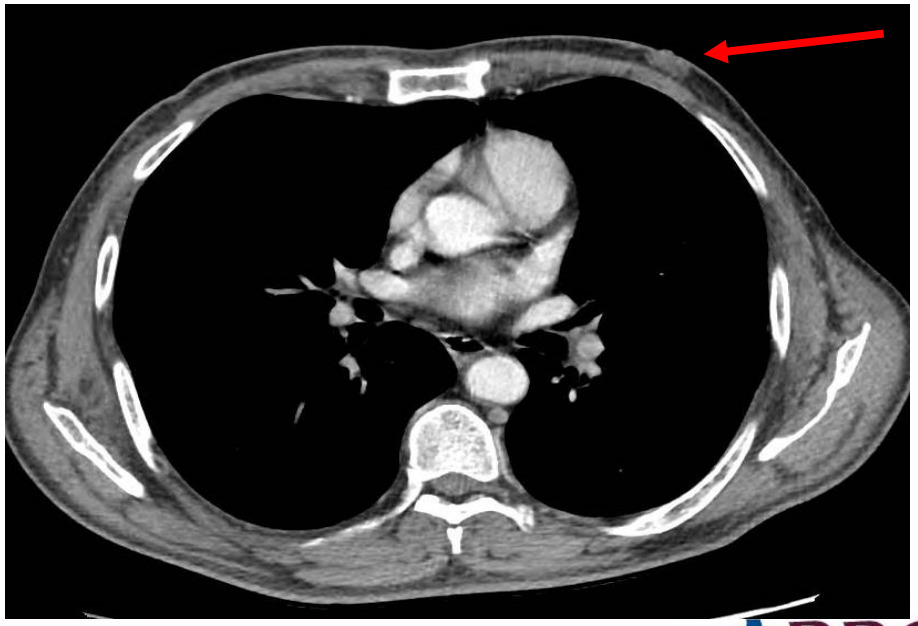
Case: Imaging

CT chest, abdomen, pelvis

Mild thyromegaly and gynecomastia.

No additional suspicious lesions or organomegaly.





Case: Work-up

Nerve conduction studies: Evidence of demyelinating motor neuropathy in 4 limbs with secondary axonal changes in the legs with sparing of the sural nerves consistent with **chronic inflammatory demyelinating polyneuropathy**.

Biopsy of right posterior iliac tumor:

- Microscopic: bone partially replaced by sheets of plasma cells with strong lambda staining
- Diagnosis: **plasmacytoma (clinically correlate to rule out multiple myeloma)**

Suggested work-up for plasma cell neoplasms

General: H&P, CBC with differential and blood smear, chemistry panel (with Ca and Cr), albumin, LDH, uric acid

Other labs:

- Unilateral bone marrow aspirate or biopsy of mass if solitary lesion
- Serum B2 microglobulin
- M-component measurement
  - Serum protein electrophoresis and immunofixation
  - Urine protein electrophoresis and immunofixation
  - Free light chain measurements if conventional M component is negative or equivocal

Imaging

- Whole-body low-dose CT scan or FDG PET/CT
- Skeletal survey acceptable under certain circumstances (ie pt unable to get CT or PET)
- If solitary plasmactyoma is suspected, whole body MRI is preferred imaging. (PET/CT is also acceptable, however MRI has better sensitivity for diffuse marrow infiltration.)

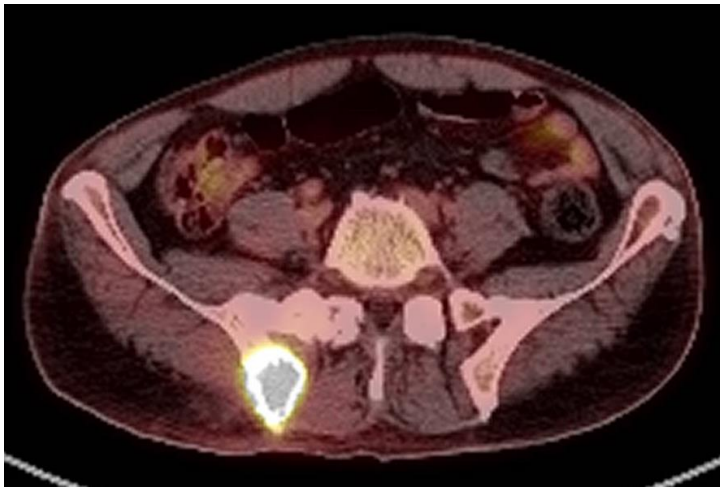
Halperin *et al*. 2019.
NCCN Guidelines Multiple Myeloma v3.2020

Case: Additional work-up

Bone marrow aspirate: normocellular bone marrow with no evidence of lymphoma/myeloma (2-3% plasma cells).

PET scan showed no additional evidence of disease.

Endocrine panel:
- Testosterone 190 ng/dL (low)
- Prolactin 21 ng/mL (elevated)
- FSH, LH, PTH, TSH normal



Diagnosis: Solitary bone plasmacytoma with suspicion for POEMS syndrome.

Multiple Myeloma (MM)

- Arises from malignant transformation of a post-germinal center B cell
- Incidence of MM in US in 2020: 32,270 (12,830 estimated deaths)
  [Siegel *et al.* 2020]
- Exists on clinical spectrum:

  pre-MM → smoldering MM → MM → plasma cell leukemia

- Pre-MM entities [Rajkumar *et al*. 2014]
  - Non-IgM MGUS
  - Light-chain MGUS
  - Solitary plasmacytoma
  - Solitary plasmacytoma with minimal marrow involvement
  - POEMS syndrome

Multiple Myeloma Diagnosis

Clonal bone marrow plasma cells > 10% OR biopsy proven plasmacytoma, PLUS

- Any presence of end-organ damage due to myeloma ("CRAB")
  - **C**alcium high
  - **R**enal insufficiency
  - **A**nemia
  - **B**one lesions (CT, plain radiograph, PET)
- If "CRAB" not present, "SLiM" criteria can fulfill
  - **S**ixty percent plasma cell bone marrow involvement
  - **Li**ght chain ratio > 100
  - **M**RI: > 1 focal lesion

Smoldering MM = 10-60% clonal plasma cell involvement and/or M-protein > 30 g/L and absence CRAB/SLiM criteria and absence of amyloidosis

Solitary Plasmacytoma (SP)

- SP constitute < 6% of MM [Halperin *et al*. 2013]
- 2 varieties of SP:
  - solitary bone plasmacytoma (~70%)
  - solitary extraosseous plasmacytoma (~30%) [Thumallapally *et al*. 2017]
- Diagnostic criteria
  - single bone or extraosseous lesion histologically proven to be plasmacytoma
  - < 10% bone marrow plasma cells
  - absence of end-organ damage (CRAB/SLiM)
- 3-year incidence of progression to MM [Rajkumar *et al*. 2013.]
  - SP no marrow involvement: 10%
  - SP with minimal (<10%) marrow involvement:
    - Bone: 60%
    - Extraosseous: 20%

POEMS Syndrome

Polyneuropathy

Organomegaly

Endocrinopathy

Monoclonal protein

Skin changes

<u>International Myeloma Working Group diagnostic criteria</u>

Both: Polyneuropathy

Monoclonal plasma cell proliferative disorder (almost always lambda)

Plus: at least 1 of 3 major criteria

- Sclerotic bone lesion
- Castleman's disease
- Elevated level of VEGFA

Plus: at least 1 of 6 minor criteria

- Organomegaly
- Extravascular volume overload (edema, ascites, pleural effusion)
- Endocrinopathy
- Skin changes
- Papilledema
- Thrombocytosis/polycythemia

Rajkumar *et al*. 2014.

POEMS Syndrome

Polyneuropathy

Organomegaly

Endocrinopathy

Monoclonal protein

Skin changes

Neuropathy and other symptoms can resolve with treatment. [Dispenzieri *et al*. 2003]

Treatment is determined by extent of disease.

- Limited (solitary plasmacytoma or up to 3 lesions) → ISRT
- Widespread disease → systemic therapy

Management of Solitary Plasmacytoma

- No RCTs due to rarity of diagnosis
- RT is the mainstay of treatment based on retrospective series showing excellent local control (79-97%) [Ozsahin *et al.* 2006; Reed *et al*. 2011]
- Surgery alone (ie s/p excisional biopsy) leads to high (~60%) local recurrence rate [Ozsahin *et al*. 2006]
- Surgery may be indicated for structurally unstable lesions or neurologic compromise (ie cord compression)

RT for Solitary Plasmacytoma

RT dose:

- No consensus
- Generally accepted range: 35-50 Gy
  - Early report by Mendenhall *et al* suggested > 40 Gy for optimum LC
    - >40 Gy → 94% LC
    - <= 40 Gy → 69% LC [Mendenhall *et al*. 1980]
  - There is no evidence of dose response above 40 Gy [Tsang *et al*. 2018]
  - Tsang suggested dose of 35 Gy is likely adequate for small (< 5 cm tumors) [Tsang *et al*. 2001]
  - Later report by Ozsahin suggested 30 Gy to be adequate regardless of tumor size [Ozsahin *et al*. 2006]

RT for Solitary Plasmacytoma

RT dose:

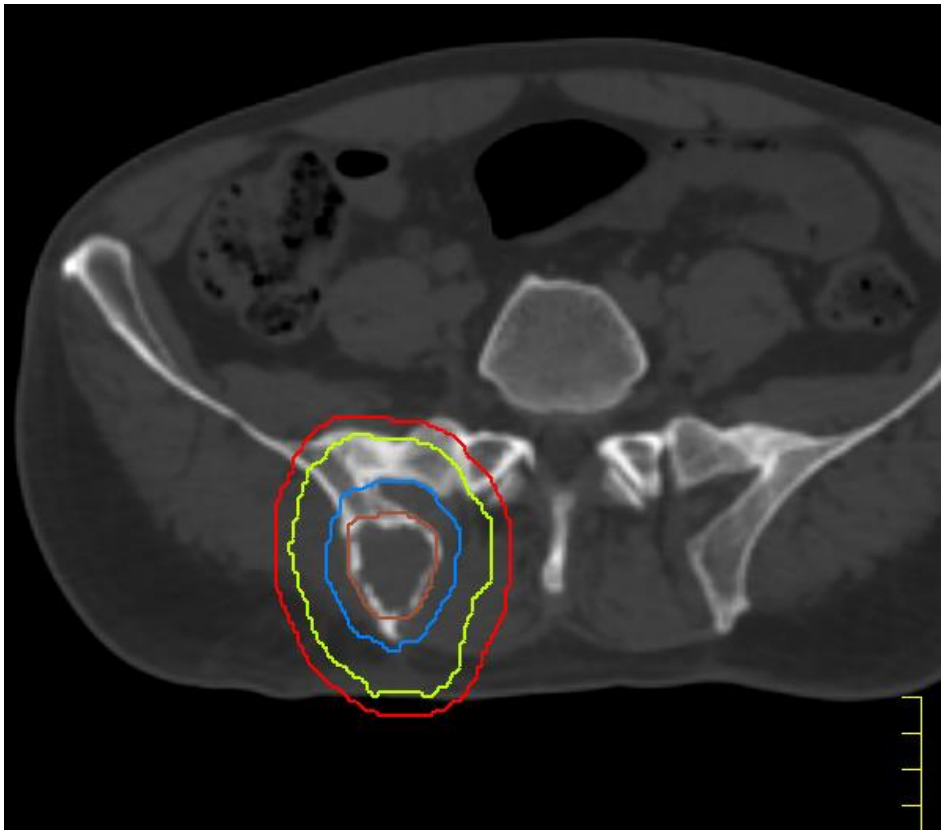
- ILROG Guidelines [Tsang *et al*. 2018]
  - SBPs < 5 cm: 35-40 Gy
  - SBPs >= 5 cm: 40-50 Gy
  - SEPs: 40-50 Gy

RT for Solitary Plasmacytoma

RT volumes:

- SBP: treat radiographically appreciable gross tumor with margin
- SEP:
  - Treat radiographically appreciable gross tumor with margin
  - Include adjacent suspicious nodes
  - No elective nodal coverage
- ILROG guidelines [Tsang *et al*]
  - GTV based on imaging
  - CTV = GTV + 0.5-3 cm in all directions respecting anatomic boundaries

Case: Pt underwent EBRT to the right iliac bone to dose of 5000 cGy in 200 cGy fractions using wedge pair technique.



GTV (brown): gross tumor based on CT bone window
CTV (blue): GTV + 6 mm adjusted for barriers to spread
PTV (yellow): CTV + 8 mm
Block edge/dose build-up (red): PTV + 5 mm

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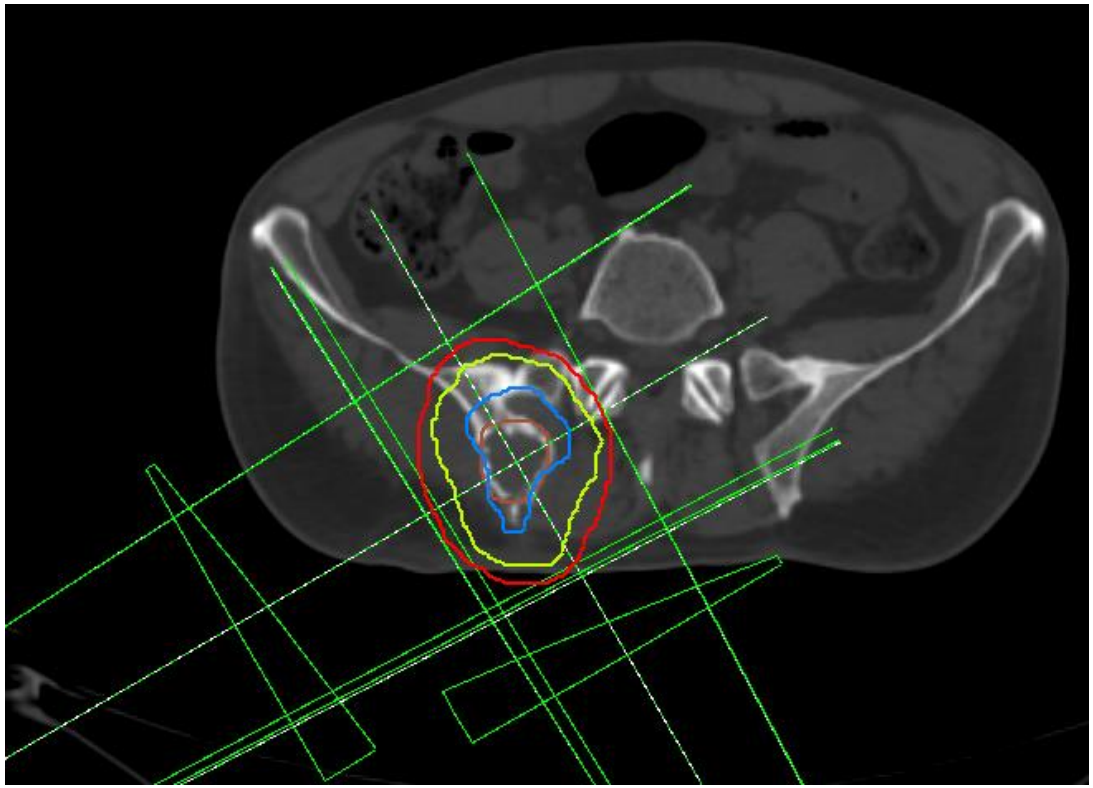
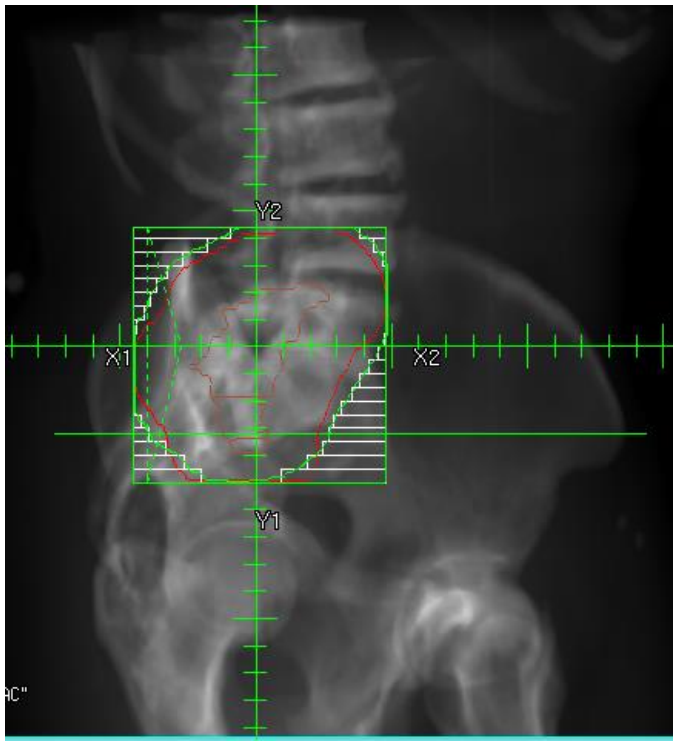


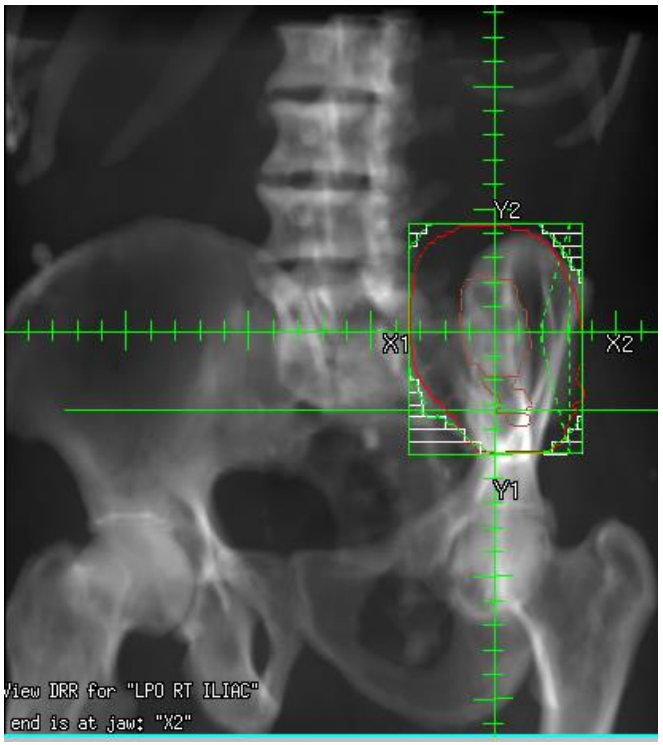
Right posterior oblique/left posterior oblique beam arrangement

Case: Pt underwent EBRT to the right iliac bone to dose of 5000 cGy in 200 cGy fractions using wedge pair technique.

RPO DRR

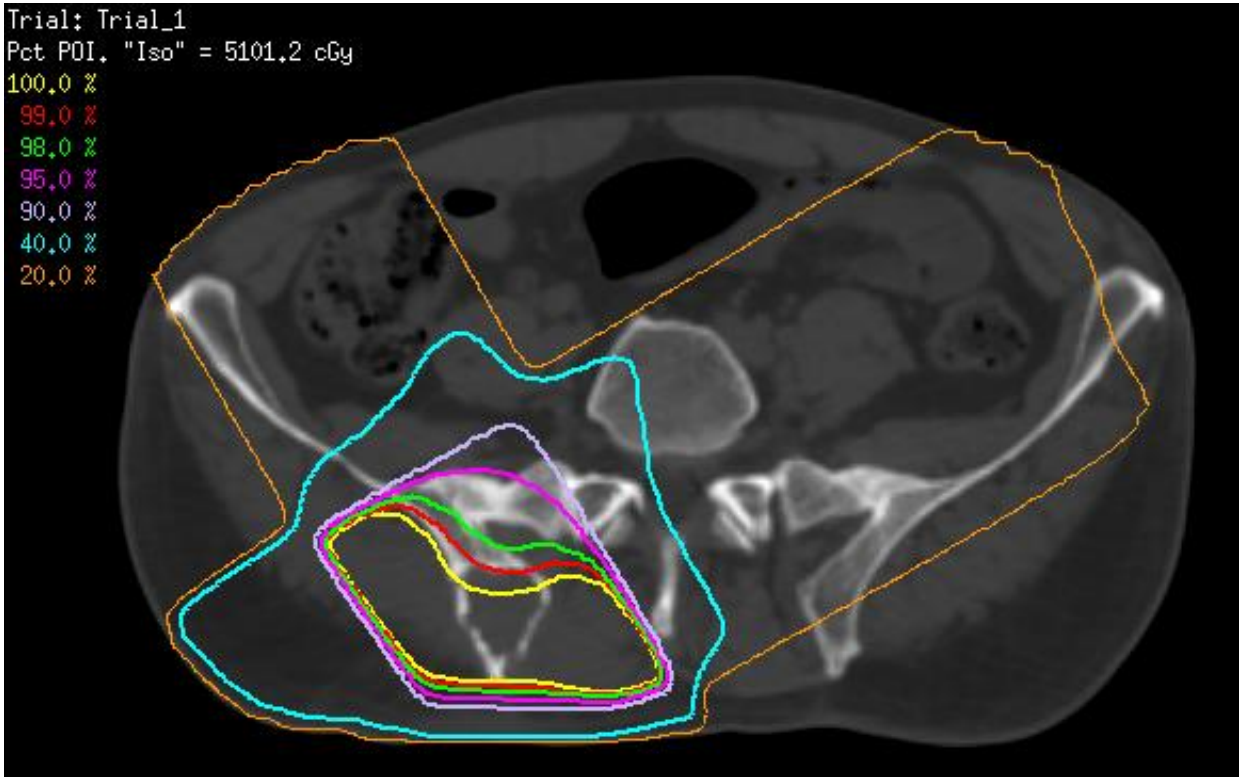


LPO DRR



Brown = GTV
Red = Block edge

Case: Pt underwent EBRT to the right iliac bone to dose of 5000 cGy in 200 cGy fractions using wedge pair technique.



Dose (5000 cGy) was prescribed to the 98% isodose line.

Case: Pt tolerated treatment well with anticipated grade 1 dermatitis.

Recommended follow-up: H&P q 2-4 months for first 2 years, then 6 q 6 months SPEP, UPEP, CBC, Cr, Ca q 4-6 months x 1 year and then annually.

2 month f/u, pt reported mild improvement in LE weakness. Ambulating with cane.

4 month f/u, pt reported resolution of weakness. 5/5 strength in all extremities on exam. Ambulating without assistive device.

Now 2 years post-RT: M-protein undetectable, normal free light chains, no myeloma signs/symptoms.

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