Solitary Plasmacytoma

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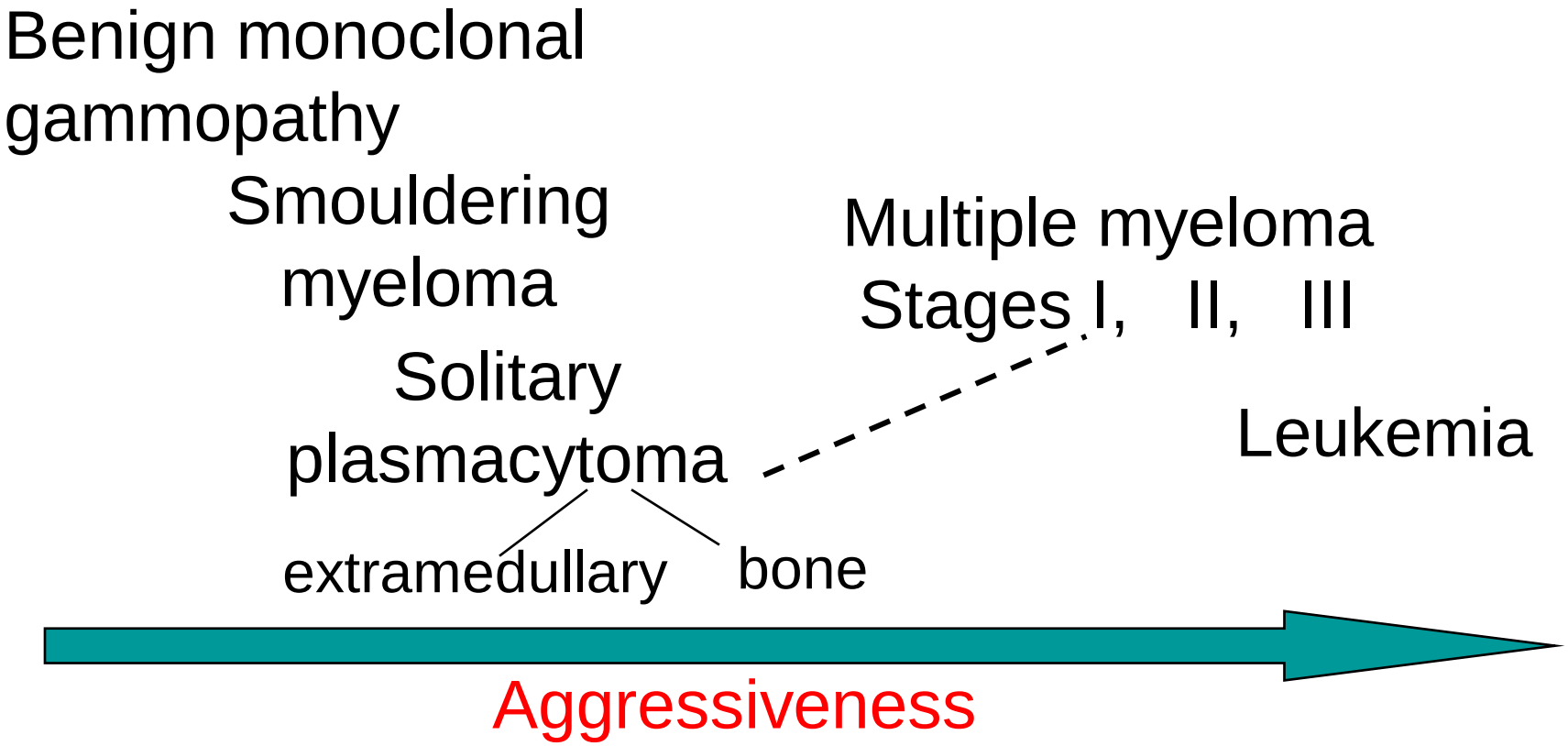
Disclosure

I have no conflicts of interest to disclose

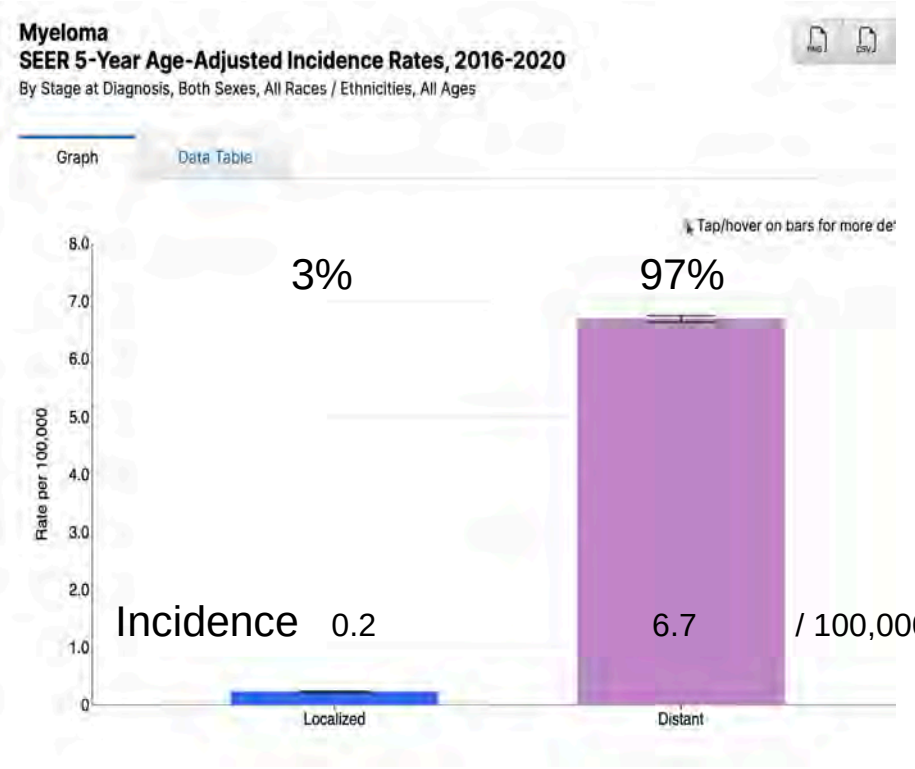
Outline

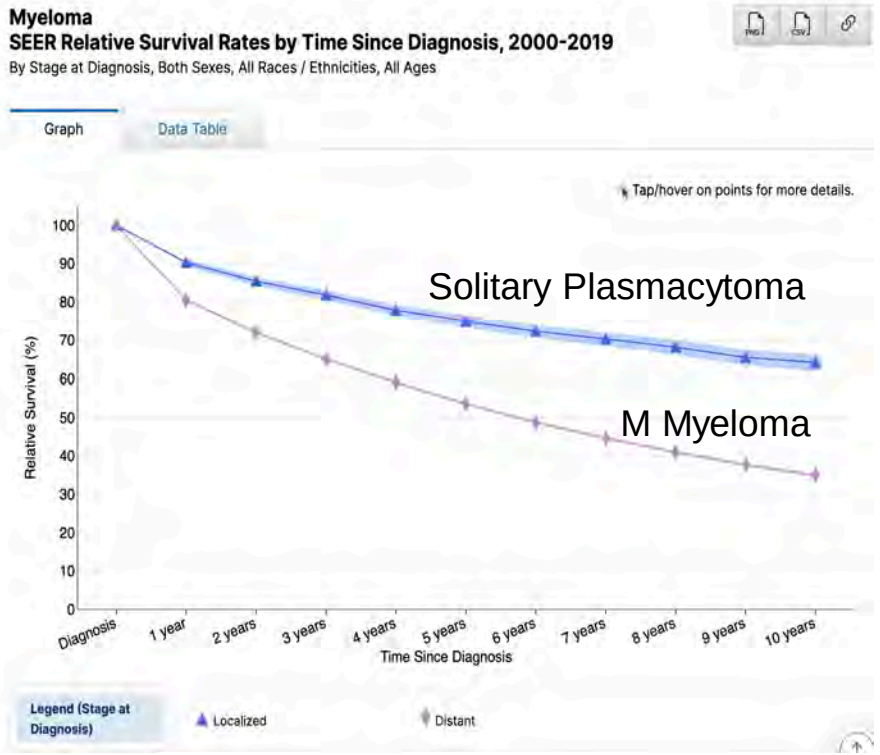
- Spectrum of plasma cell diseases
- Solitary plasmacytoma
  - Optimal staging / Imaging
  - RT issues:
    - Bone vs. EM site
    - Effect of bulk
    - Dose
  - Combined modality approach

Spectrum of Plasma cell diseases



Majority of patients have Myeloma





Diagnosing a solitary plasmacytoma

- Tissue proof from the solitary lesion
- Absence of clonal plasma cells in BM
- No other lesions by Imaging
  - Normal skeletal survey
  - FDG-PET most preferred
  - CT / MRI spine / pelvis (or whole body if PET n/a)*
- Absence of myeloma-defining features (CRAB: Calcium, Renal, Anaemia, Bone leisons)
- Qualifier: minimal BM involvement (if clonal plasma cells < 10%)

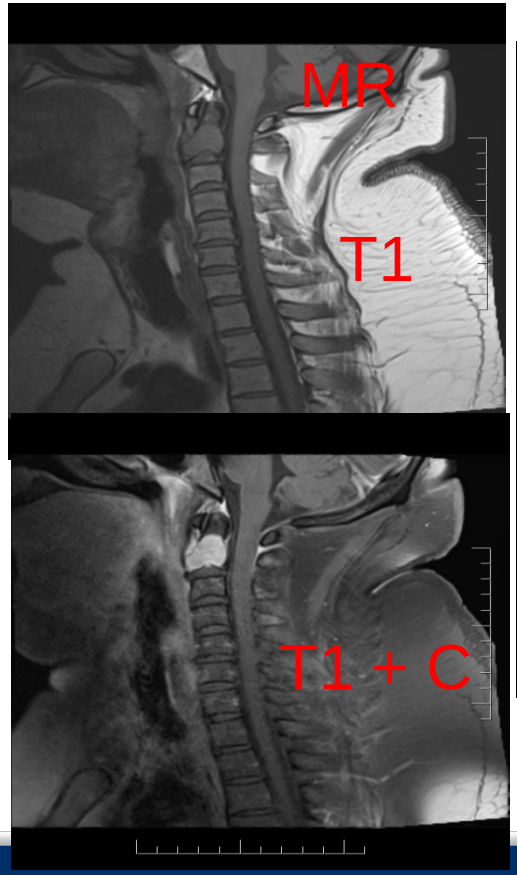
** European Expert Panel: Caers et al J Hematol Oncol 11: 10, 2018*

Localization (RCN* Study)

Vertebrae	103	40%
Head & Neck	52	20%
Pelvis	26	10%
Upper extremities	18	7%
Ribs	18	7%
Skull	14	5%
Lower extremities	12	5%
Sternum	10	4%
GIS	3	1%
Lung	2	1%

** Rare Cancer Network: Ozsahin et al IJROBP 64: 210-7, 2006*

MRI findings of C2 lesion



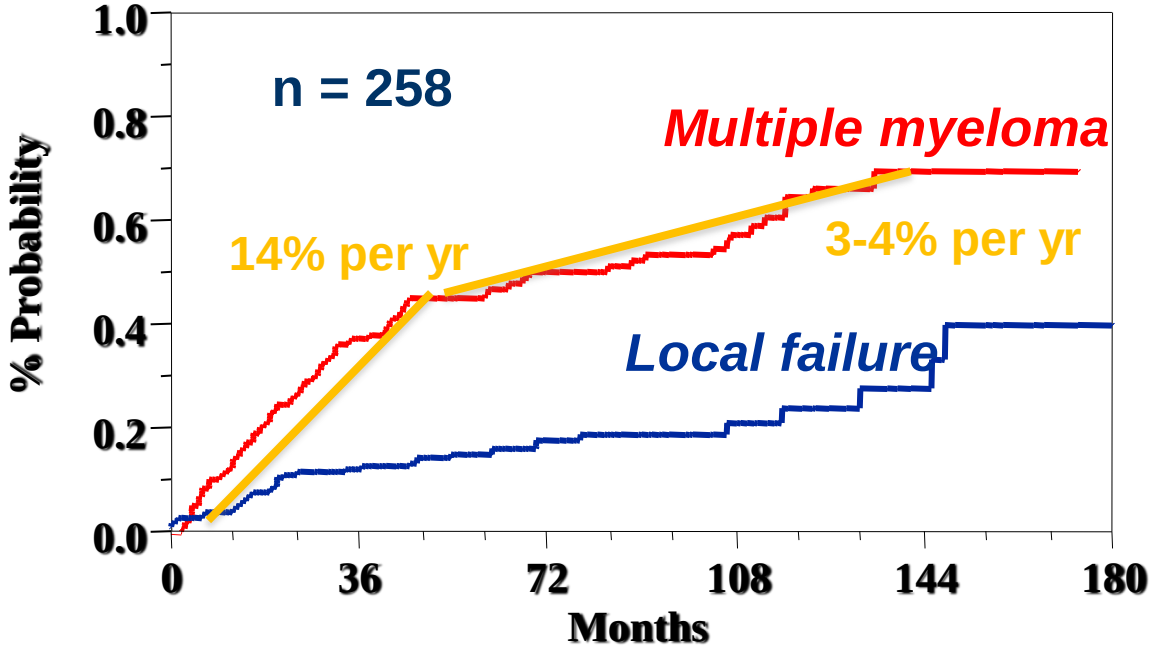
STIR for whole spine

Stage Migration Effect

Sensitive tests will diagnose multiple myeloma in up to 30-40%

- FDG-PET
- Routine MRI of whole spine / pelvis
- Other sensitive assays of BM (flow cytometry)
- ***Therefore:*** incidence decreasing, and results of treatment *appears to improve* over time due to selection of truly solitary cases

Solitary Plasmacytoma: Multiple Myeloma development and Local Failure



Median time to MM: **21 months** **(range: 2-135)**

Ozsahin et al IJROBP 64: 210-7, 2006

Issue of minimal disease

Minimal systemic disease, or oligo lesions, treat with definitive RT (vs. chemoTx)?

- Minimal BM involvement (< 10%): RT alone still reasonable
- Two separate lesions. Same approach?

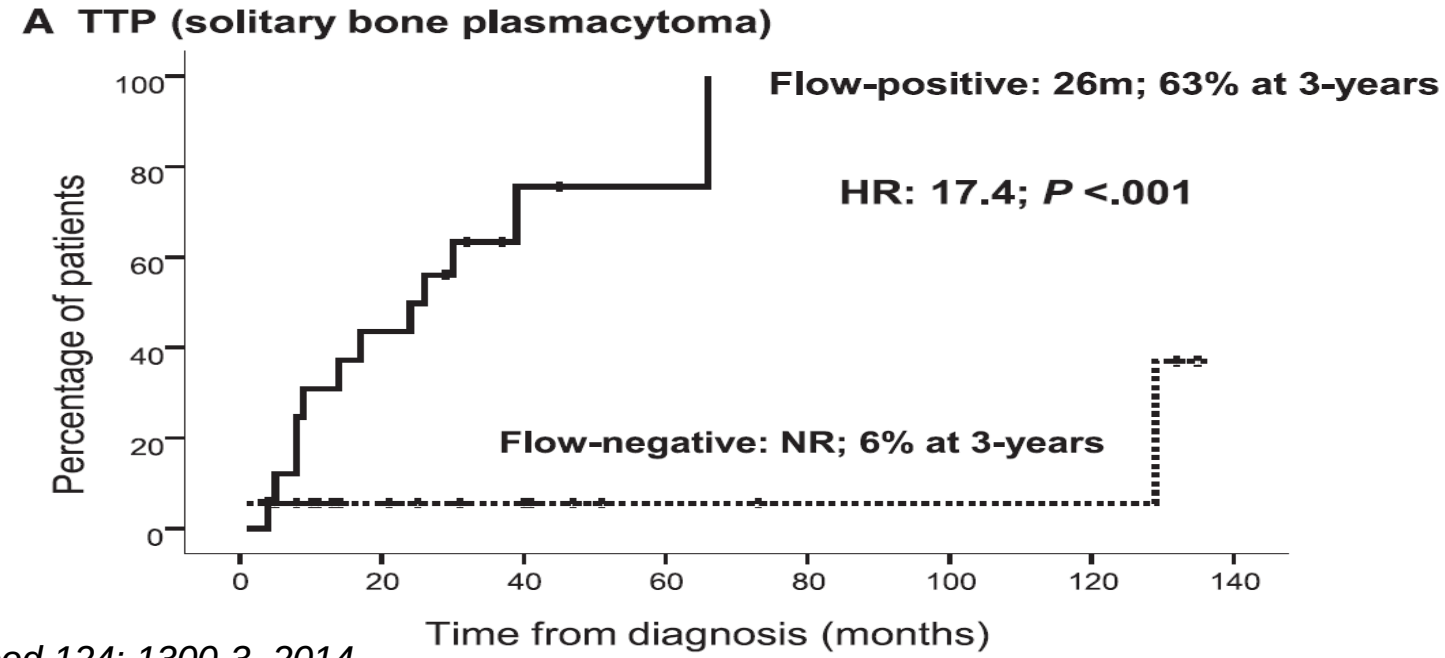
<u>Factors to consider</u>:

Local bulk, protein level, imaging, adverse cytogenetics*, tumor board discussion, overall Tx philosophy. ➡ ***Individualize***

*del(17p), t(4;14), t(14;16)

Minimal BM disease = high risk for progression to Myeloma

Good candidates for alternate strategies? eg. CMT



Paiva et al Blood 124: 1300-3, 2014

Solitary plasmacytoma – Standard Radiation Therapy

Bone

- Gross disease (MRI indispensable) + micro extent, more generous along a long medullary cavity
- No routine nodal coverage
- Surgical hardware only if contamination likely (e.g. femur IM nail)

Soft tissue (Extramedullary)

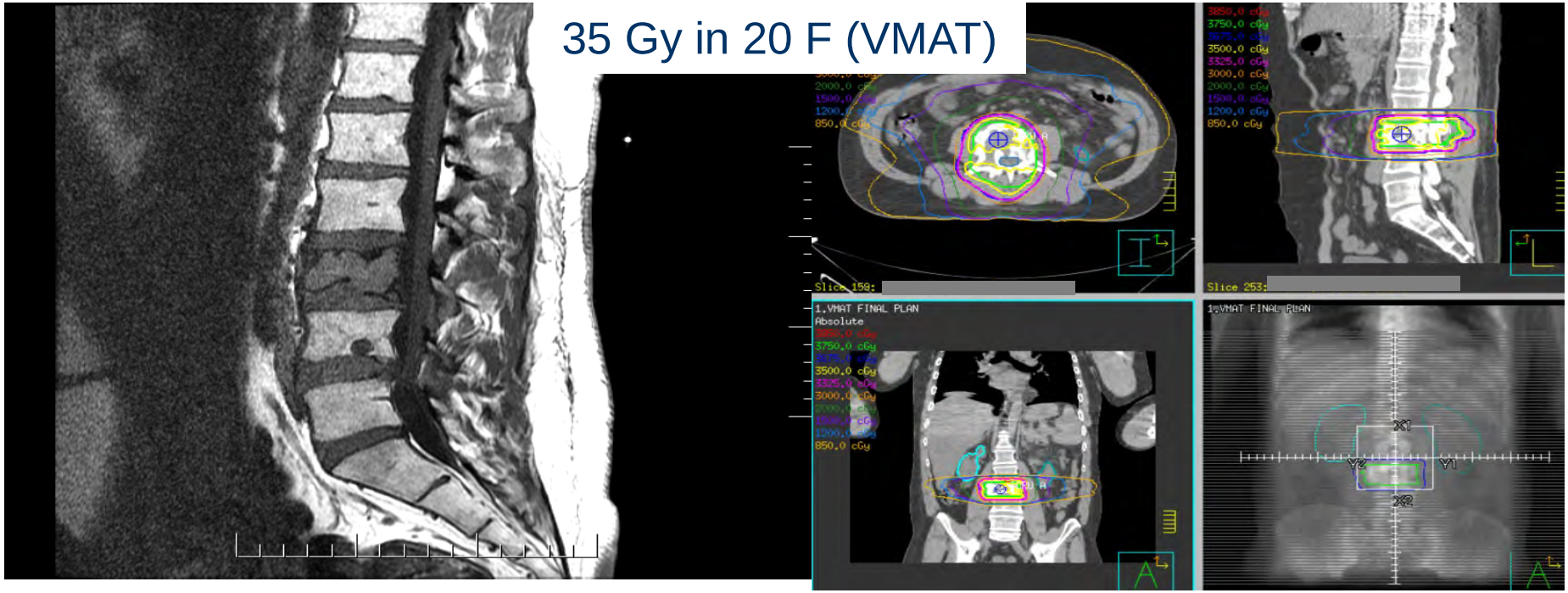
- Involved-site radiation therapy concept
- If optimal imaging obtained, no need to cover regional nodes electively (< 5% regional recurrence)*

*Nodal recurrence a rare problem (experiences at MDAH, Manchester, PMH, Japan)
Recent PMH review: Among 30 EMP, 1 had regional failure (~ 3%)

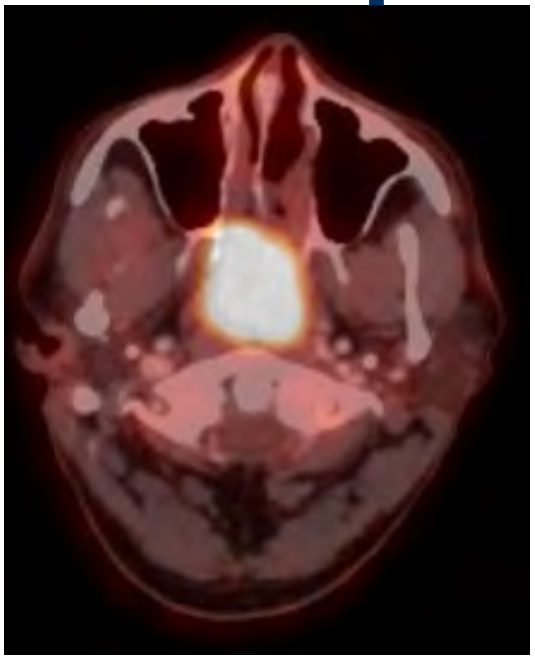
Bachar et al, Head & Neck 30: 1012-9, 2008. Sasaki et al IJROBP 82: 626-34, 2012

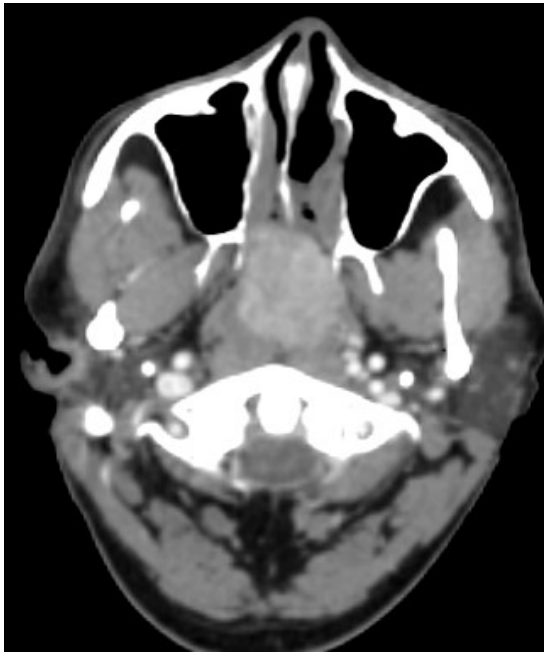
Spinal Treatment Example

Solitary plasmacytoma
L3 lesion
35 Gy in 20 F (VMAT)

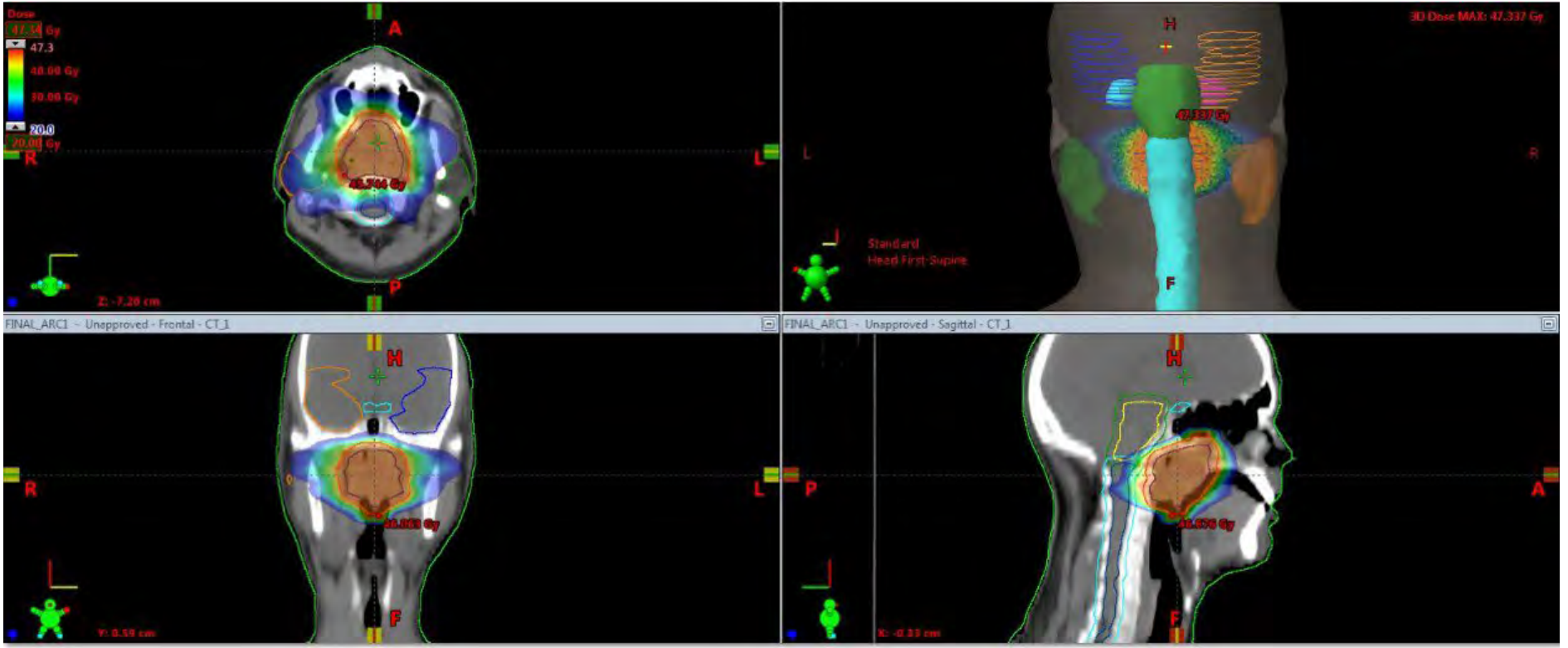


EM Treatment Example: Nasopharynx



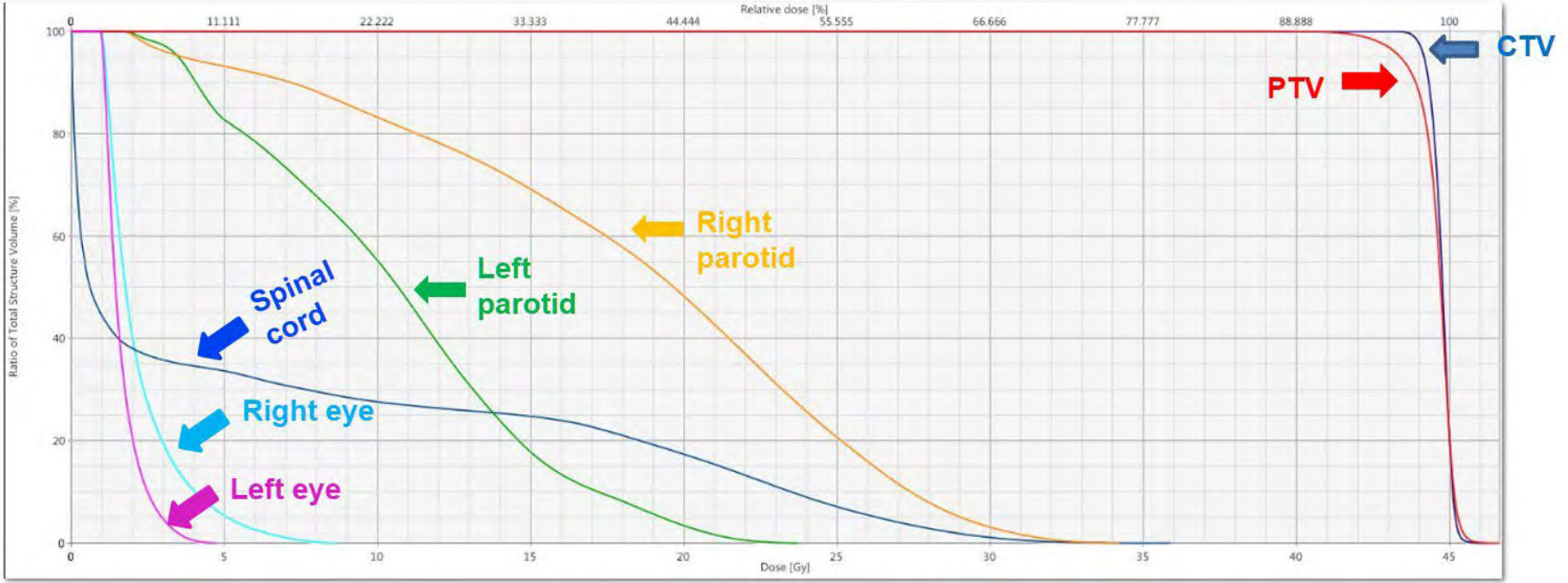


Tsang et al, IJROBP 101(4): 794-808, 2018; Slide courtesy of Dr. J. Goda



LNs were not treated electively

Tsang et al, IJROBP 101(4): 794-808, 2018; Slide courtesy of Dr. J. Goda



ALARA principles for OAR sparing

Tsang et al, IJROBP 101(4): 794-808, 2018; Slide courtesy of Dr. J. Goda

Solitary Plasmacytoma: Time-dose scatterogram

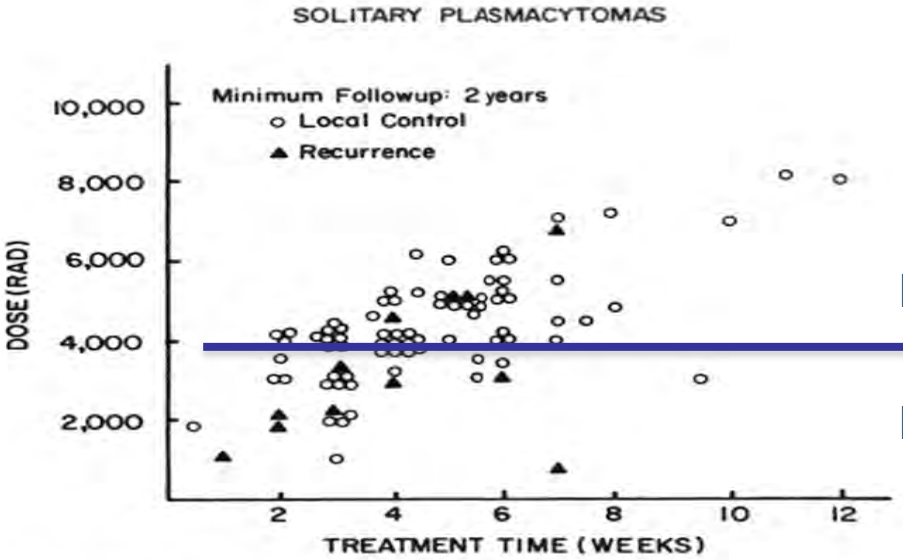


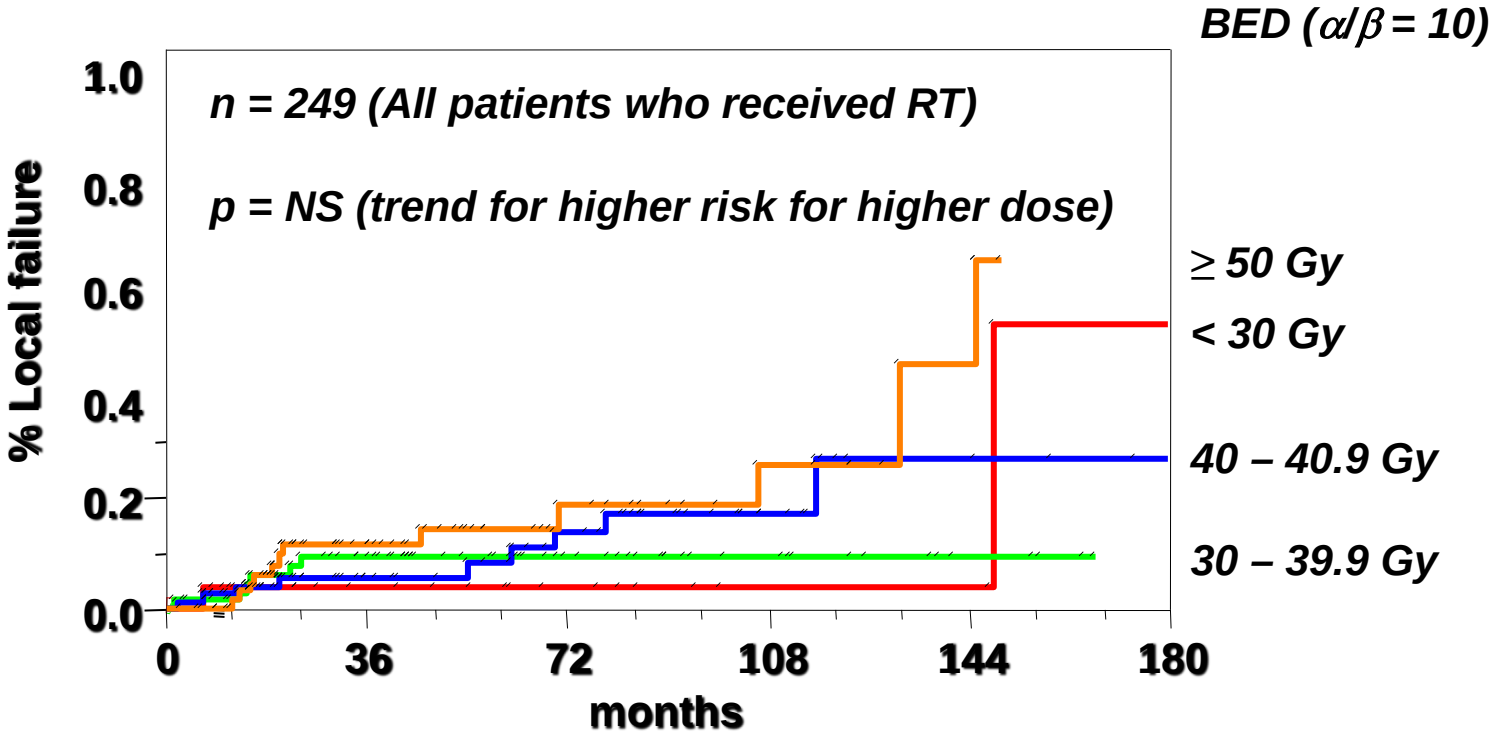
Fig. 3. Time-dose scattergram for 81 patients with solitary plasmacytoma treated by radiation therapy with a minimum of 2 years free of dissemination.

Recur = 6%

Recur = 31%

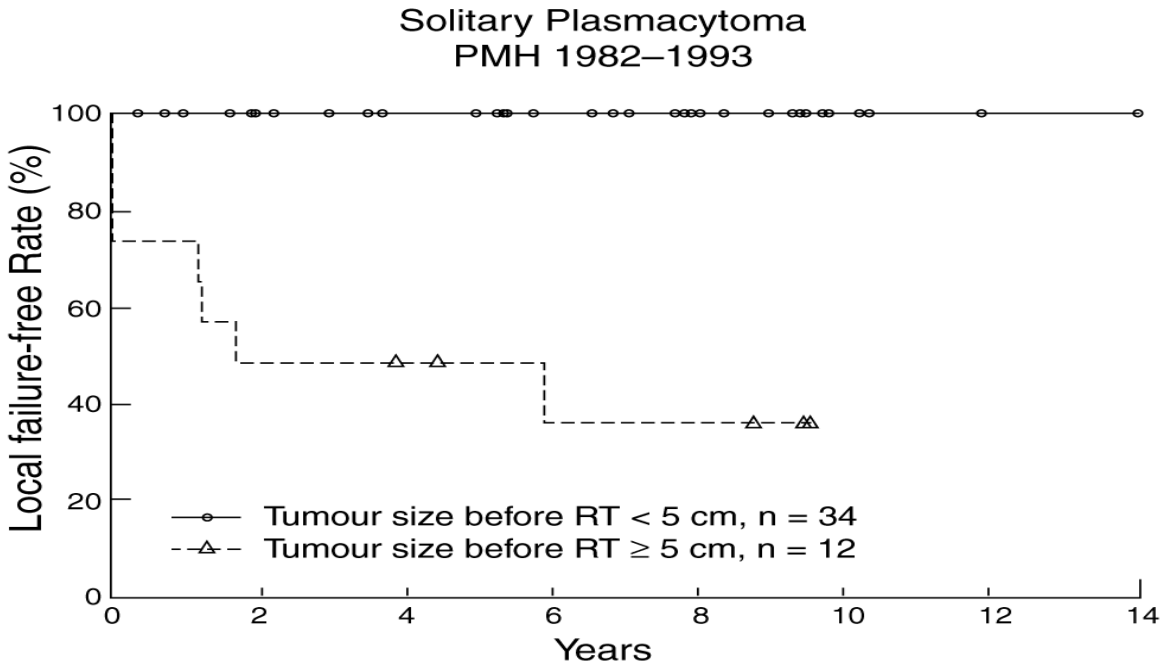
Mendenhall et al, IJROBP 6:1497, 1980

RT Dose vs. Local Failure



Ozsahin et al IJROBP 64: 210-7, 2006

Effect of tumor size on local control



Tsang et al IJROBP 50: 113-20, 2001

266G

Solitary plasmacytoma - Radiation Therapy Dose

Dose

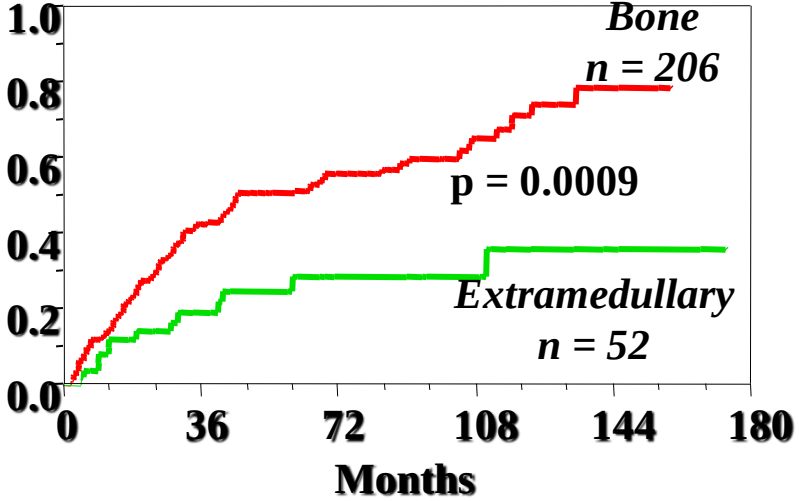
- Variation of practice
- Most authors recommend 40 – 50 Gy
- small tumors 35 – 40 Gy
- occasional failures can occur despite high dose

Dose/fraction

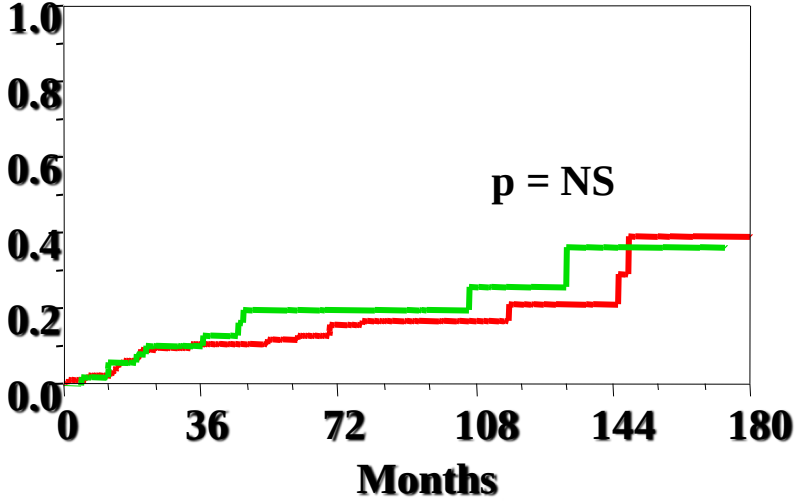
- 1.8 - 2 Gy

Solitary Plasmacytoma: Bone vs. extramedullary locations

Multiple myeloma development



Local failure



Bone site: **Inevitable progression to Myeloma**

EM site: **Potentially curable with definitive RT**

Ozsahin et al IJROBP 64: 210-7, 2006

Theoretical Advantages of CMT

- **Improve local control**
  - Specifically for bulky tumors
  - Allow smaller RT volume to spare OAR
  - Possibly dose sparing?
- **Reduce risk of Myeloma progression in high risk cases**
  - Bone cases
  - Minimal BM involvement

Solitary Plasmacytoma: RCT of adjuvant chemoTx (M/P x 3 y)

DFS

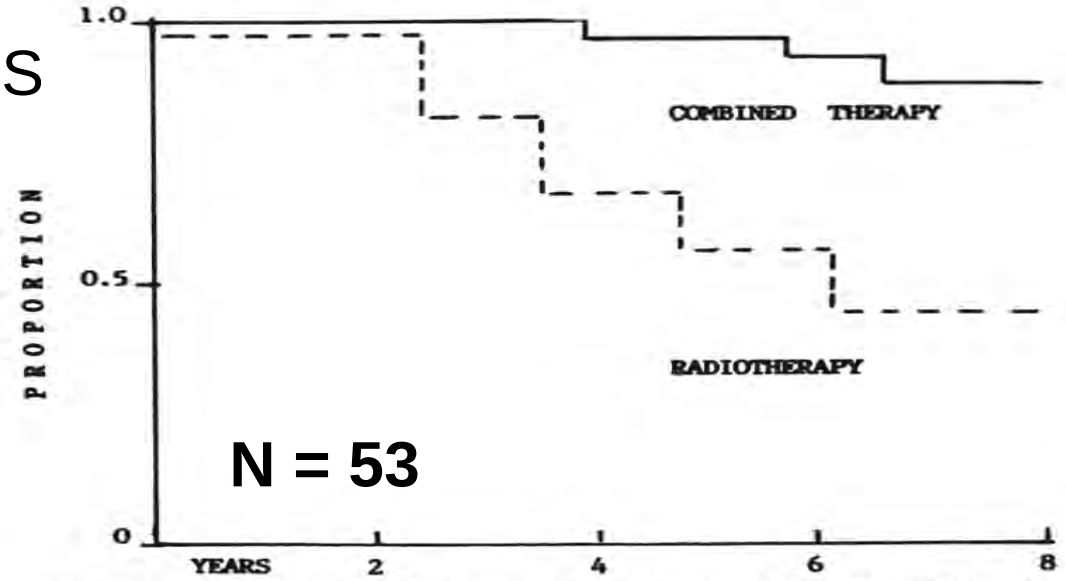
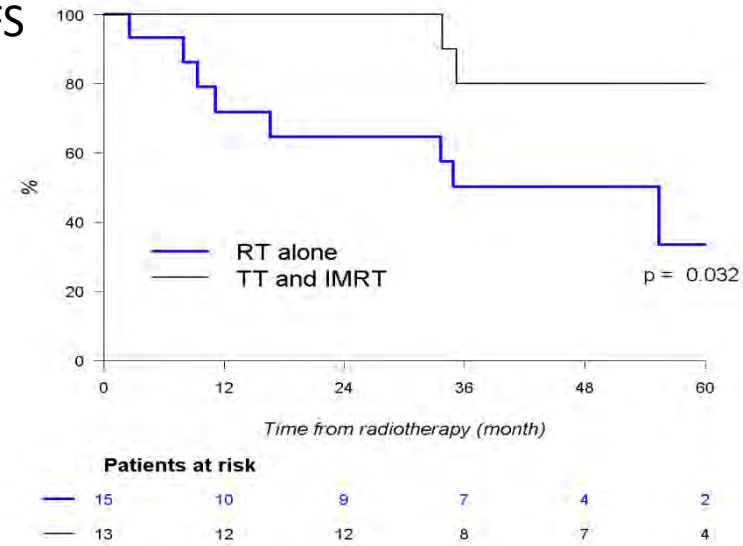


Figure 1. Actuarial curves for disease-free survival in patients treated with radiotherapy (– – –) or combined therapy (——)

Aviles et al (Mexico City), Hematol Oncol 14:111, 1996

CMT Results: Novel drugs

PFS



PFS rate at 48 months:

RT alone: 50% (CI95% 29.8 ; 84.6)

CMT: 80% (CI95% 58.7 ; 100)

p=0.032

All patients (100%) achieved local control of the plasmacytoma.

During follow-up, 10 (66%) pts in in RT group relapsed with plasma cell malignancy : 5 pts as SPB and 5 pts with MM vs. 2 pts (13%) in CMT group, one SPB and one MM.

The overall survival was 95% at 4 years [CI95% 87 ; 100] (entire cohort).

Only one patient died, from MM, in RT alone group.

<u>UK IDRIS Phase III trial</u>: Ongoing

(RT + Len/dex vs. RT alone, for SBP)

Le Ray et al Leuk Lymphoma 59: 1756-8, 2018, slide courtesy of Dr. Youlia Kirova

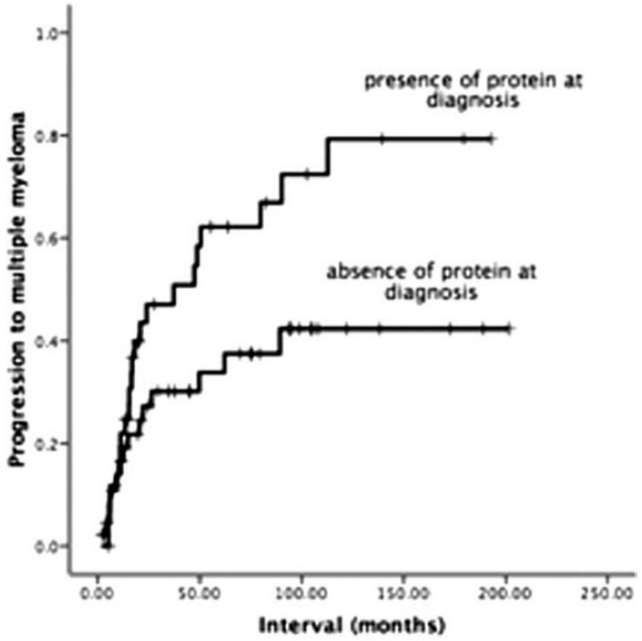
Case: EMP of Mediastinum (15 cm)

Pathology: IgA lambda, anaplastic features, Ki67 40%, MYC - TP53 - (not PL)

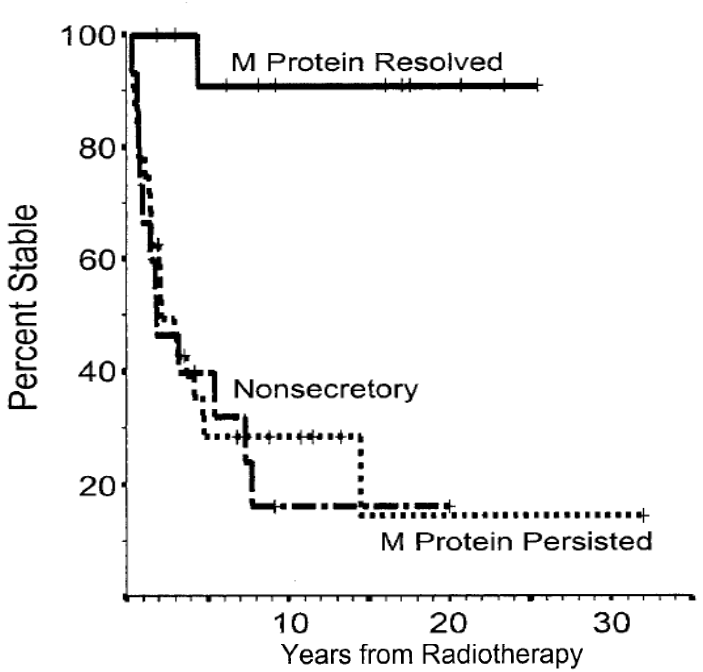
Treatment: Lenalidomide, Bortezomib, Dex (RVD regimen) ➤ ASCT +/- RT

Solitary Plasmacytoma: Follow up

High M protein pre-RT or residual post RT predicts Progression to Myeloma

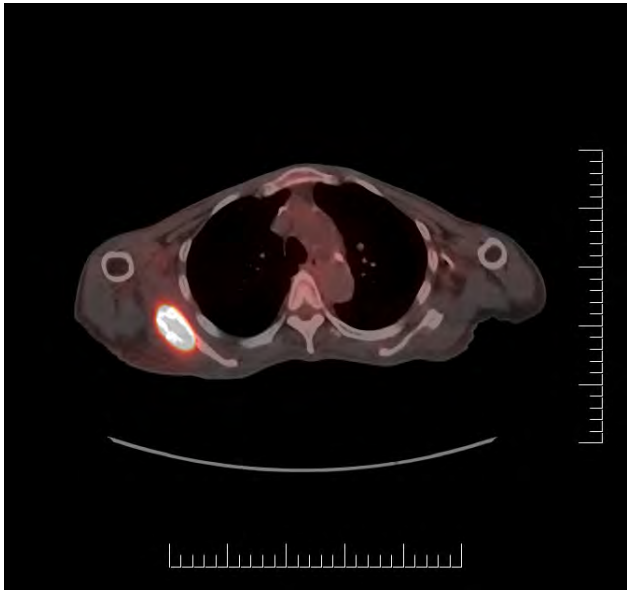


Reed et al Cancer 117: 4468-74 , 2011

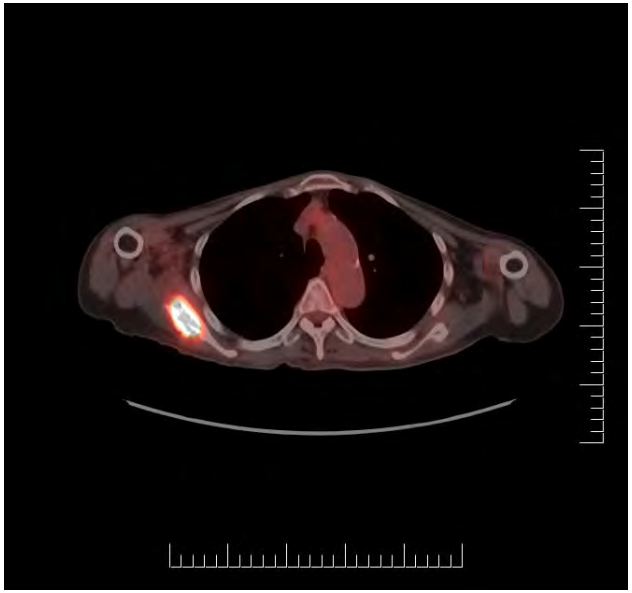


Wilder et al Cancer 94: 1532-7, 2002

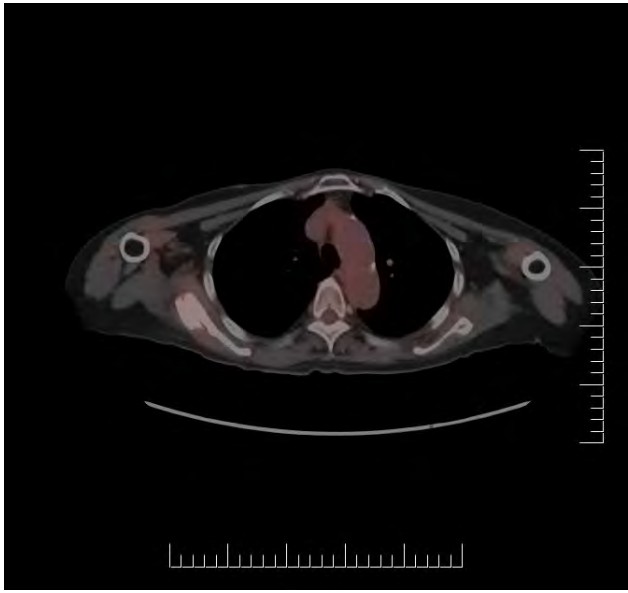
PET response after definitive RT



Before RT
SUVmax 24.3



6 months
SUVmax 10.7



16 months
CMR: SUVmax 1.4

Conclusions

- Solitary plasmacytoma potentially curable with definitive RT (EM vs. bone)
- Stage with FDG-PET / MR where appropriate
- RT doses 35 – 40 Gy in conventional fractionation
- Selective use of CMT approach for very bulky / aggressive presentations


Thank you for your attention