

Radiotherapy in Plasmacytoma and Myeloma

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Multiple Myeloma NSSG Annual Meeting

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Contents

- Indications for radiotherapy:
 - Palliation in Multiple Myeloma
 - Solitary Bone Plasmacytoma
 - Solitary Extramedullary Plasmacytoma
- Expected outcomes
- Developments in radiotherapy

Multiple Myeloma

- Indications for palliative RT:
 - Painful bone lesions
 - Spinal or cauda equina compression
 - Cranial or peripheral nerve compression
 - Impending or actual pathological fracture
 - Other symptomatic soft tissue plasmacytoma
- Dose:
 - Single 8 Gy fractions
 - Fractionated regimens (typically 20 Gy in 5#s)
- Can re-treat areas to tolerance of normal tissues

RT for bone pain - Mechanism

- Incompletely understood
- Rapid analgesic effect:
 - Immediate obstruction of mediators (substance P and cytokines) at myeloma-bone matrix interface
 - RT apoptosis in 72 hours – Tumour shrinkage
- Longer term:
 - Induction of re-calcification

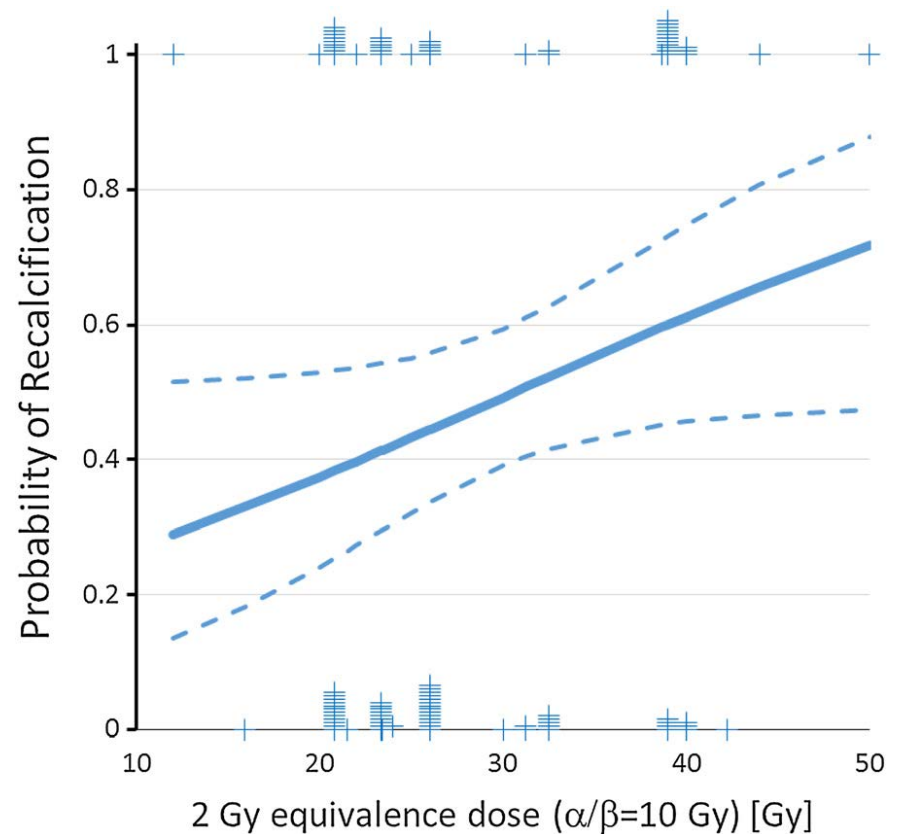
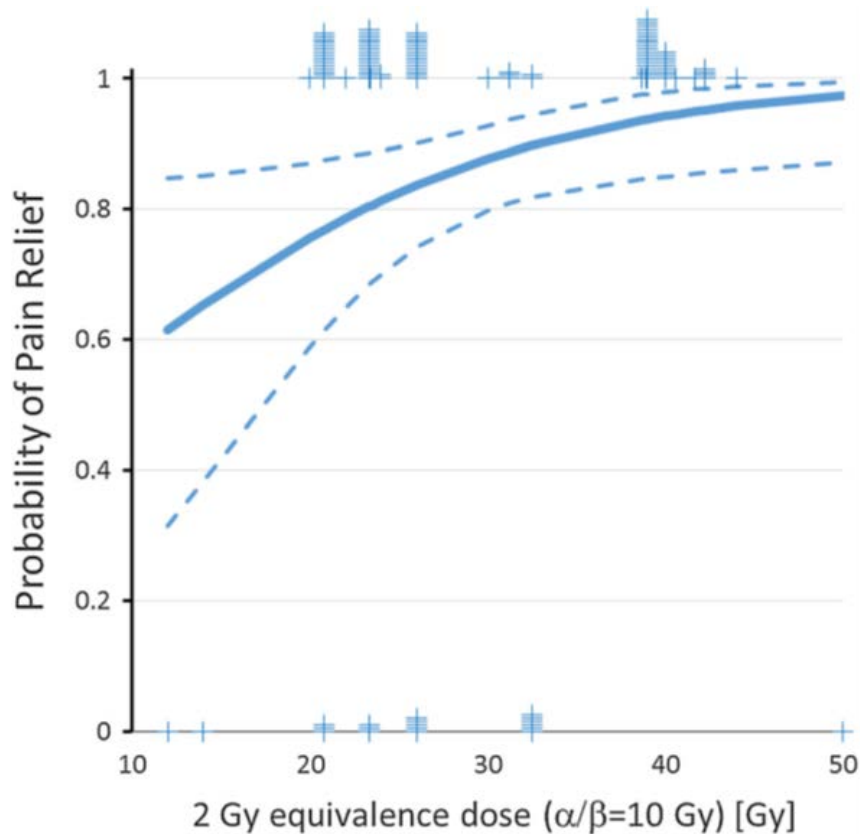
RT for bone pain - Effectiveness

- Matuschek *et al*, Radiat Oncol 2015:
 - Analysis of 107 patients treated 1989-2013
 - Symptomatic response rate 85% (Range 75-95%)
 - Complete local pain relief 31%
 - Partial local pain relief 54%
 - No change 12%, progression 3%
 - Re-calcification in 48% (23% full, 25% partial)
 - Side effects generally mild (1 grade 3 dysphagia)

RT for bone pain – Effect of dose

- Matuschek *et al*, Radiat Oncol 2015, reported:
 - Increasing the dose from 20 to 30 Gy (EQD2) increased the probability of response and re-calcification by 12%
 - Probability of symptomatic relief and re-calcification increased up to doses of 50Gy

RT for bone pain – Effect of dose



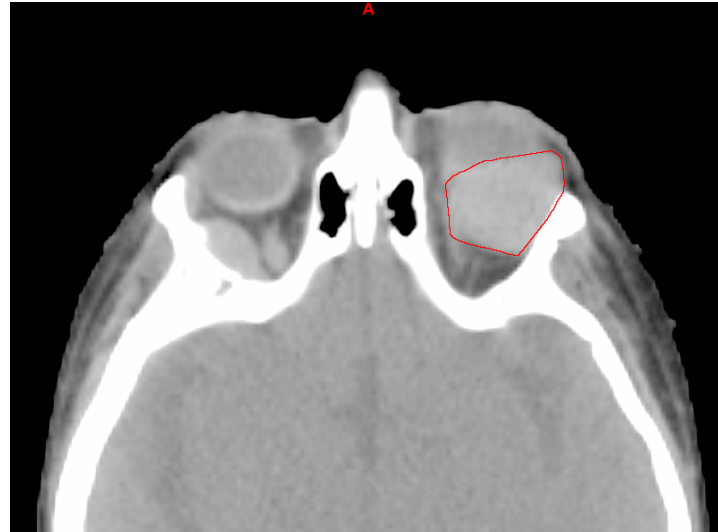
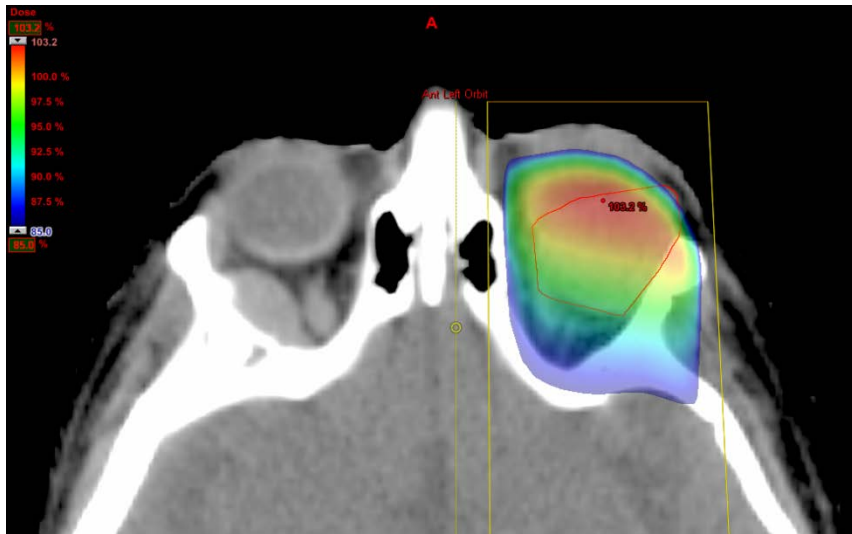
Matuschek *et al*, Radiat Oncol 2015

RT for bone lesions

- Should we be considering higher doses?
- E.g. 30 Gy in 10#s or even 40 Gy in 20#s
- Perhaps in certain circumstances:
 - Younger and good performance patients
 - Pre-dominant lesions
 - Life expectancy of >1 year
 - Fracture risk (with no plan for surgery)
 - Severe pain despite analgesia/bisphosphonates
 - Where side effects would be tolerable

Palliative RT for soft-tissue plasmacytoma

- Works very well...



Solitary Plasmacytoma

- Biopsy proven plasmacytoma with no evidence of MM on staging
- <5% of plasma cell neoplasms
- Most commonly bone
- Less often 'extramedullary'
- Treatment = Radiotherapy (+/- Surgery)

Solitary Bone Plasmacytoma

- c.260 cases per year in the UK
- Male:Female = 2:1
- Median age = 55 years (lower than MM)
- Primarily affect the axial skeletal (vertebrae 50%)
- % with M protein = 60% (24-72%)
- % developing MM = >75% (median 2-4 years)
- 10-year survival = 40-50%
(higher with PET? – Up-stages c.33-50%)

Solitary Bone Plasmacytoma

- Adverse prognostic features (progression to MM):
 - Low levels of uninvolved immunoglobulins
 - Axial disease
 - Older age
 - Lesion size >5 cm
 - Persistence of the M protein after treatment

Solitary Bone Plasmacytoma

- Adverse prognostic features (progression to MM):
 - Low levels of uninvolved immunoglobulins
 - Axial disease
 - Older age
 - Lesion size >5 cm
 - **Persistence of the M protein after treatment**
(MD Anderson, Wilder *et al*, Cancer 2002: 90% progression to MM vs. 8% if resolved)

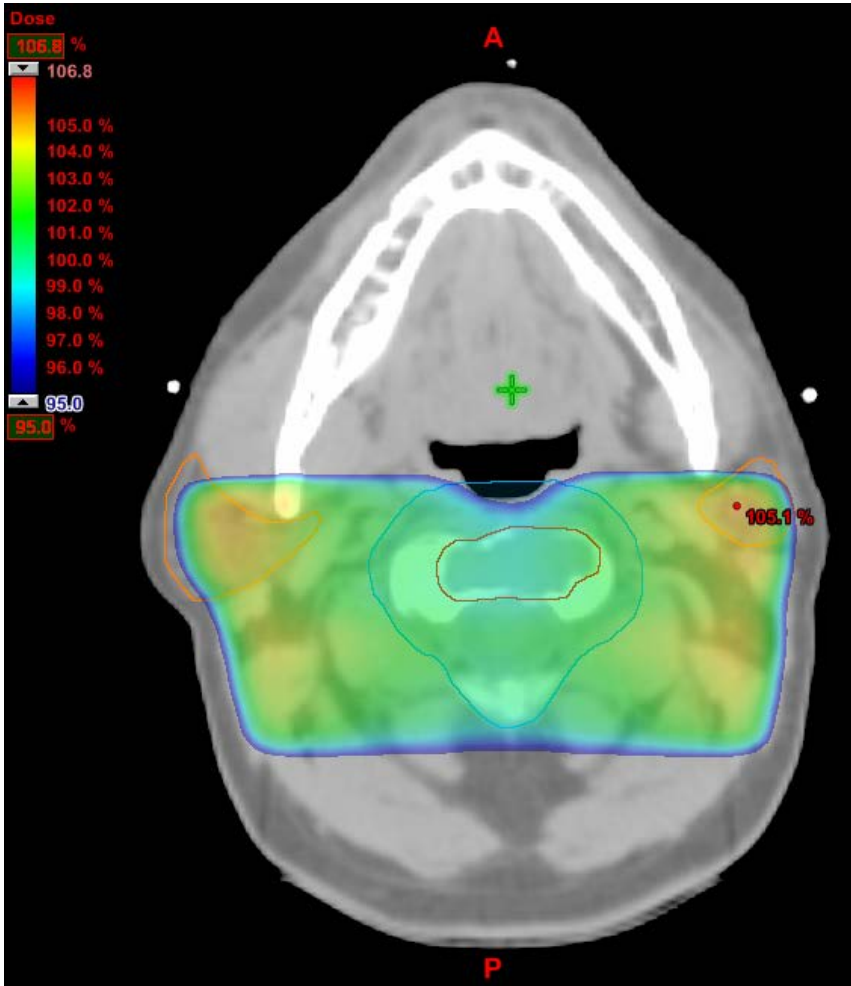
Treatment of SBP

- Radiotherapy (Surgery reserved for structural instability, rapidly progressive symptoms or cord compression)
- Dose = 40-50 Gy in 20-25 fractions (higher doses for tumours >5cm)
- Volume = Tumour plus a 2cm margin (not necessarily the whole bone)
- Local control of 85-95% (>30% failure rates for doses <40 Gy)
- Resolution of M protein in 25-50%

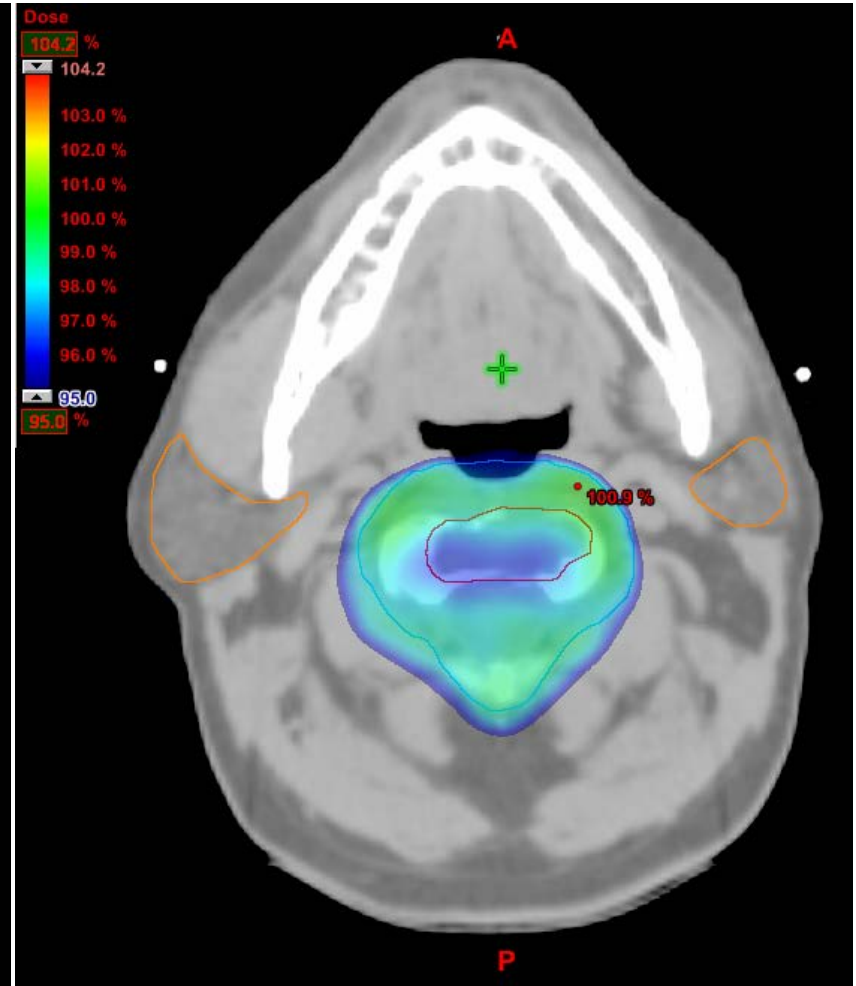
Treatment of SBP

- No trials of treatment
- Largest series = 206 patients, treated 1977-2001 (Ozsahin *et al*, IJROBP 2006)
- 83% received RT alone
- 10-year local control = 79% (95% CI 69-89%)
- 10-year OS = 53% (95% CI 43-61%)
- 10-year MM = 72% (95% CI 62-82%)

Radiotherapy for SBP



3D-Conformal Radiotherapy



Intensity Modulated Radiotherapy

Solitary Extramedullary Plasmacytoma

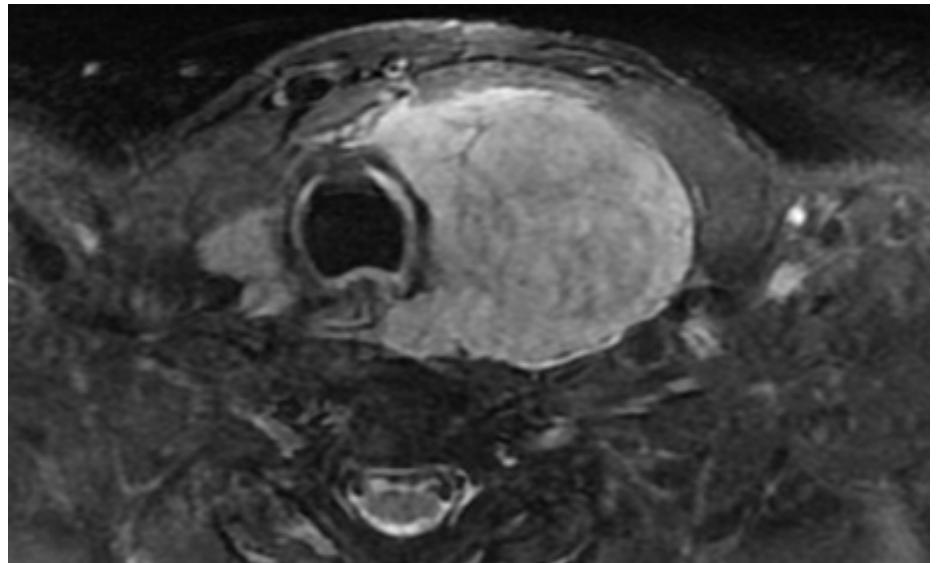
- Less common than SBP but better prognosis
- Male:Female = 3:1
- Median age = 55 years
- Primarily (80%) in the head and neck region
- % with M protein = <25%
- % developing MM = <30%
- 10-year survival = >66%

Radiotherapy for SEP

- Doses as for SBP
- Local control rates of 80-100% with RT
- Lower control with tumours >5cm (consider surgery followed by RT only if margins not clear?)
- Local draining lymph nodes may be treated if involved or at high risk of involvement

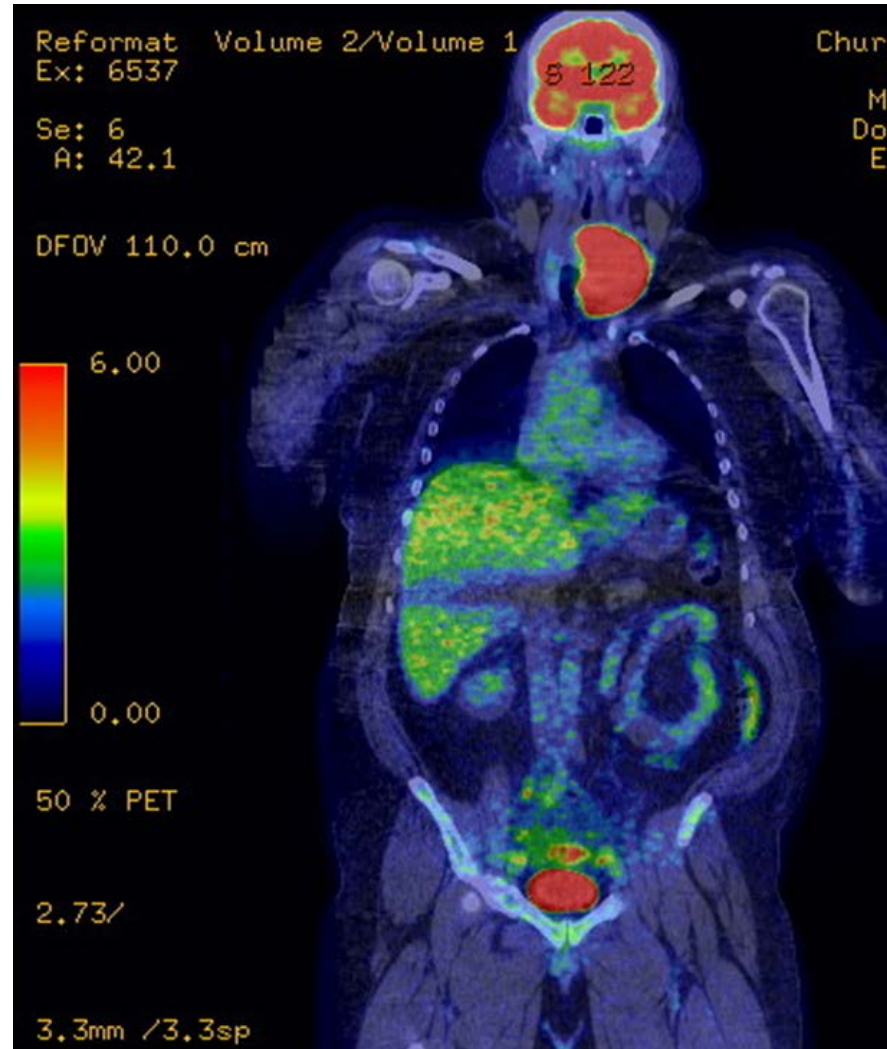
An Example of SEP - Thyroid

- 53 year old man – Hoarseness, dysphagia and neck swelling
- 6x5x9cm mass
- Bx: Plasmacytoma
- No evidence of MM



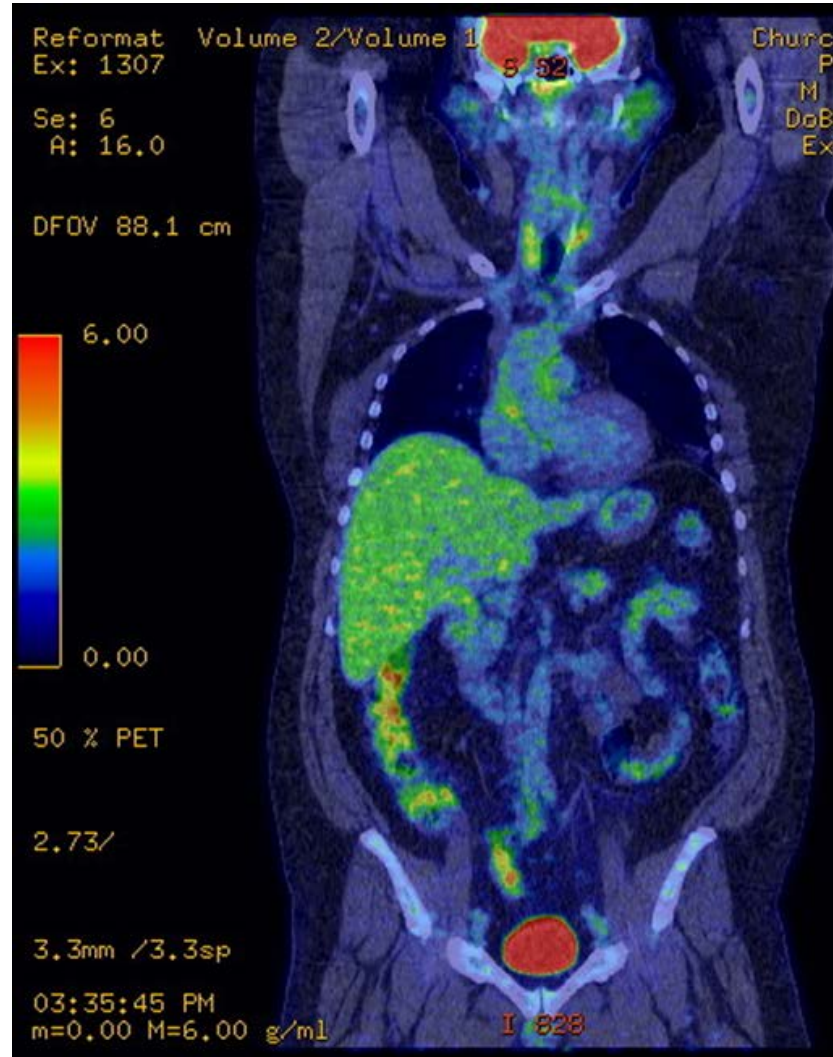
Thyroid SEP - PET-CT Pre-op

- Solitary disease
- SUVmax=24.8
- Surgery (as >5cm)
- 1/11 LNs +

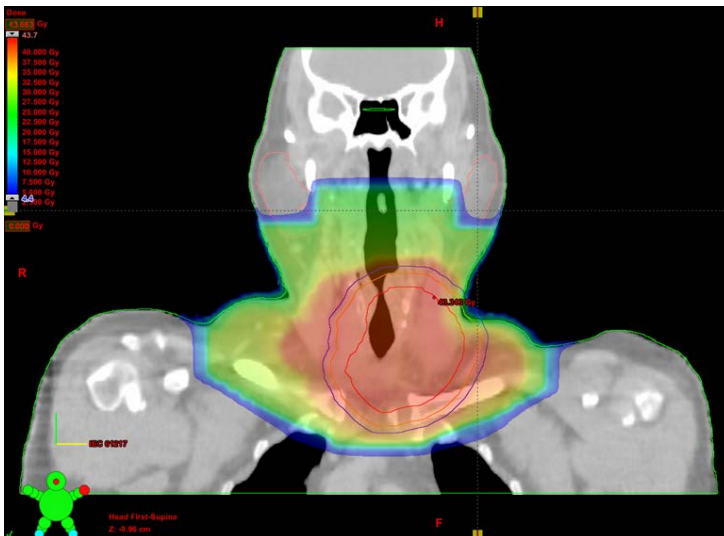
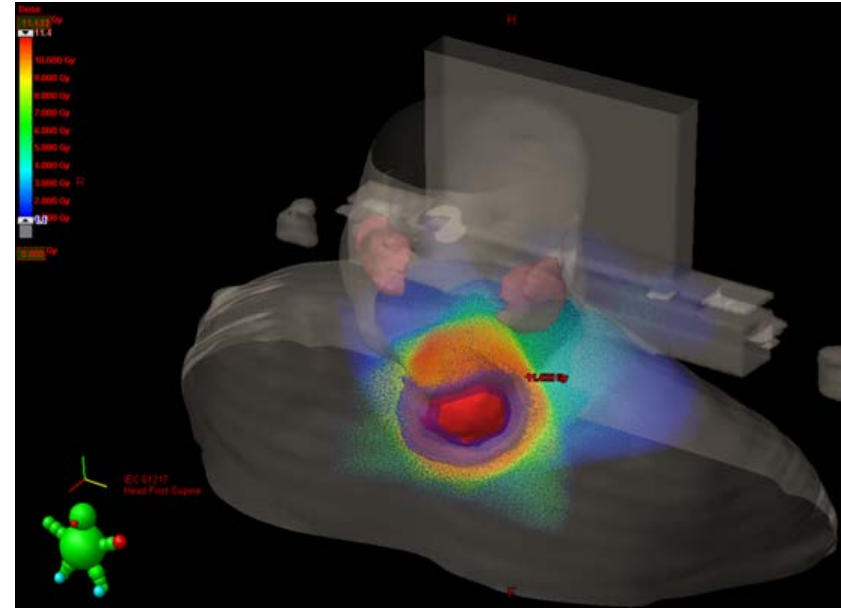
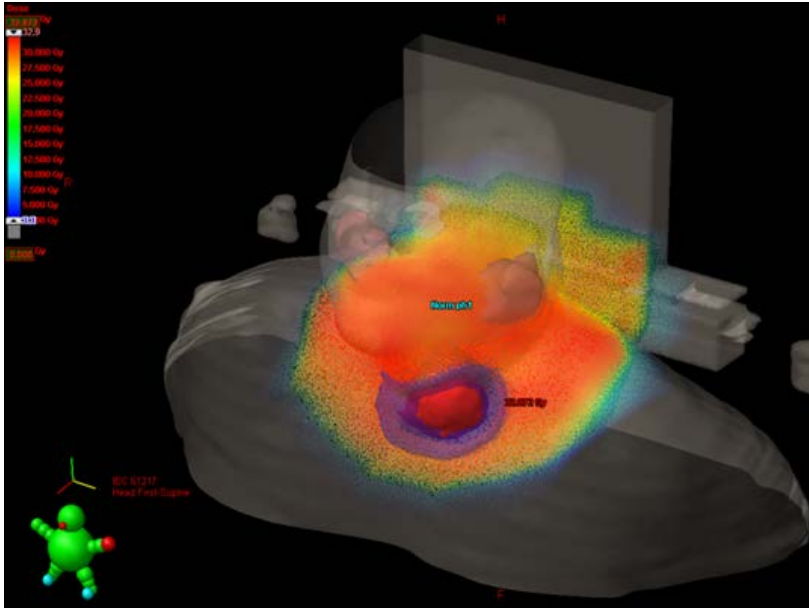


Thyroid SEP – PET-CT Post-op

- Small residuum
- $SUX_{max}=6.2$
- Free kappa light chains normalised



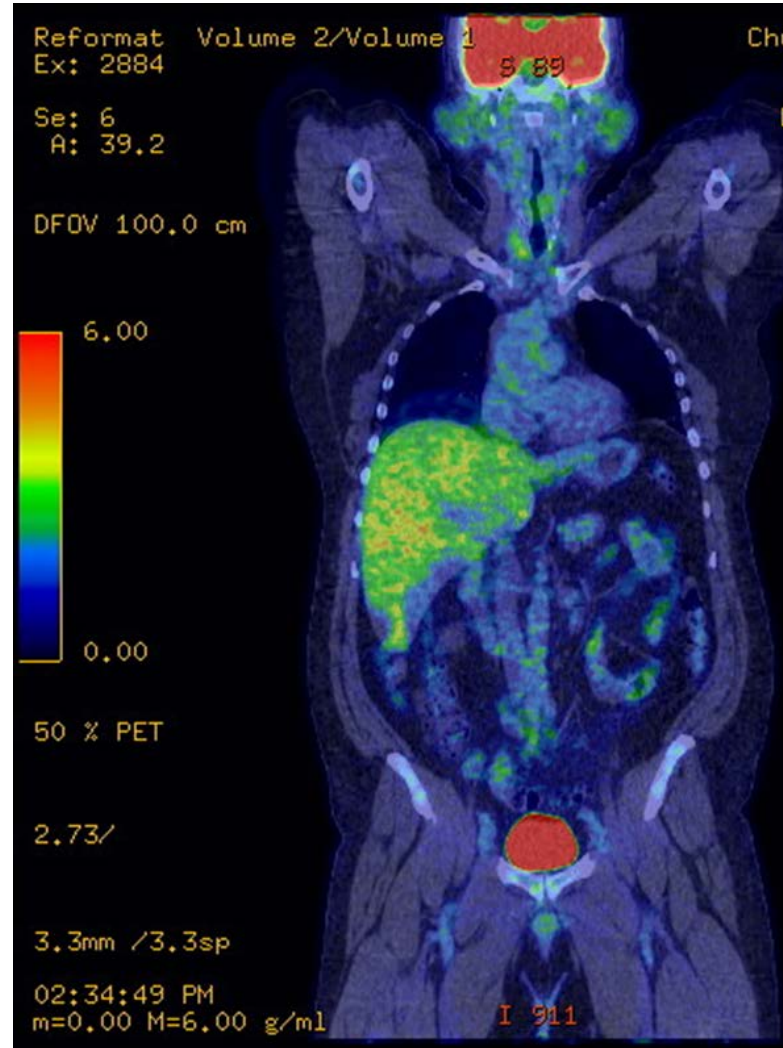
Thyroid SEP - Radiotherapy



Phase I - 30 Gy in 15 fractions to whole neck (sparing parotids)
Phase II - 10 Gy in 5 fractions to tumour bed (plus margin)

Thyroid SEP – PET-CT Post-RT

- 6 months
- No disease



Conclusions

- Effective palliative in MM (?higher RT doses)
- Effective local control for SBP/SEP
- New RT techniques reduce morbidity

Thank-you for your attention

