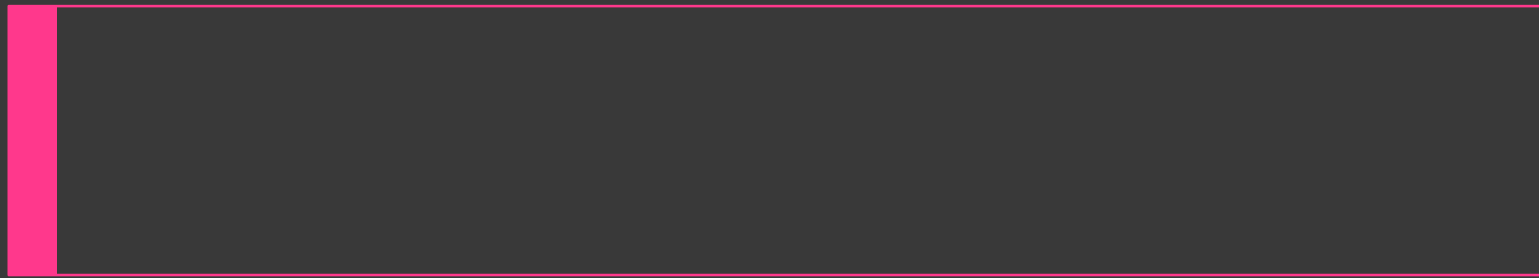


# Chemo-radiation in bladder cancer



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# Introduction

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- ▶ Radiotherapy used to treat muscle invasive bladder cancer
- ▶ Organ preservation
- ▶ Radical or palliative
- ▶ Vs surgery outcomes historically inferior by 10-20%, no RCT
- ▶ ?Patient selection - preserved for elderly or those with co-morbidity

QuickTime<sup>®</sup> and a decompressor are needed to see this picture.



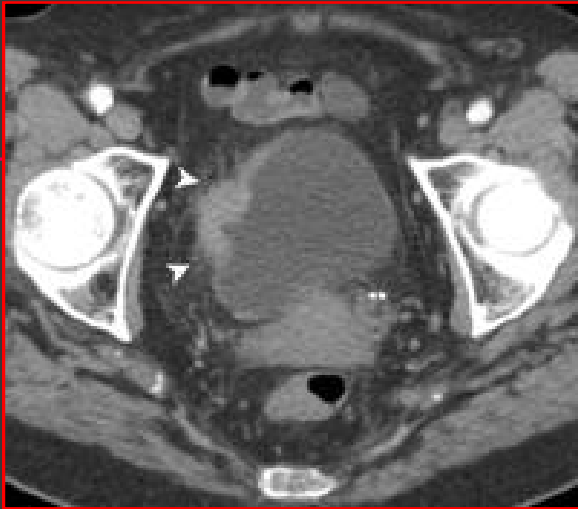
# Radiotherapy

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- ▶ CT planned, empty bladder
- ▶ Bladder outlined and grown by 1.5-2cm margin
- ▶ Daily treatment on a linear accelerator in a cancer centre







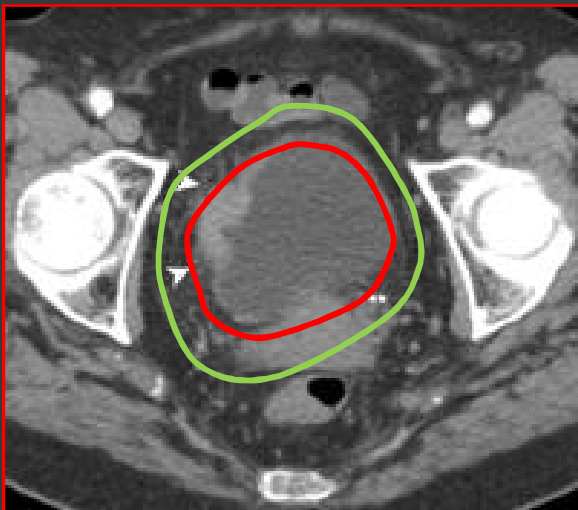
Planning CT of pelvis



Bladder outlined



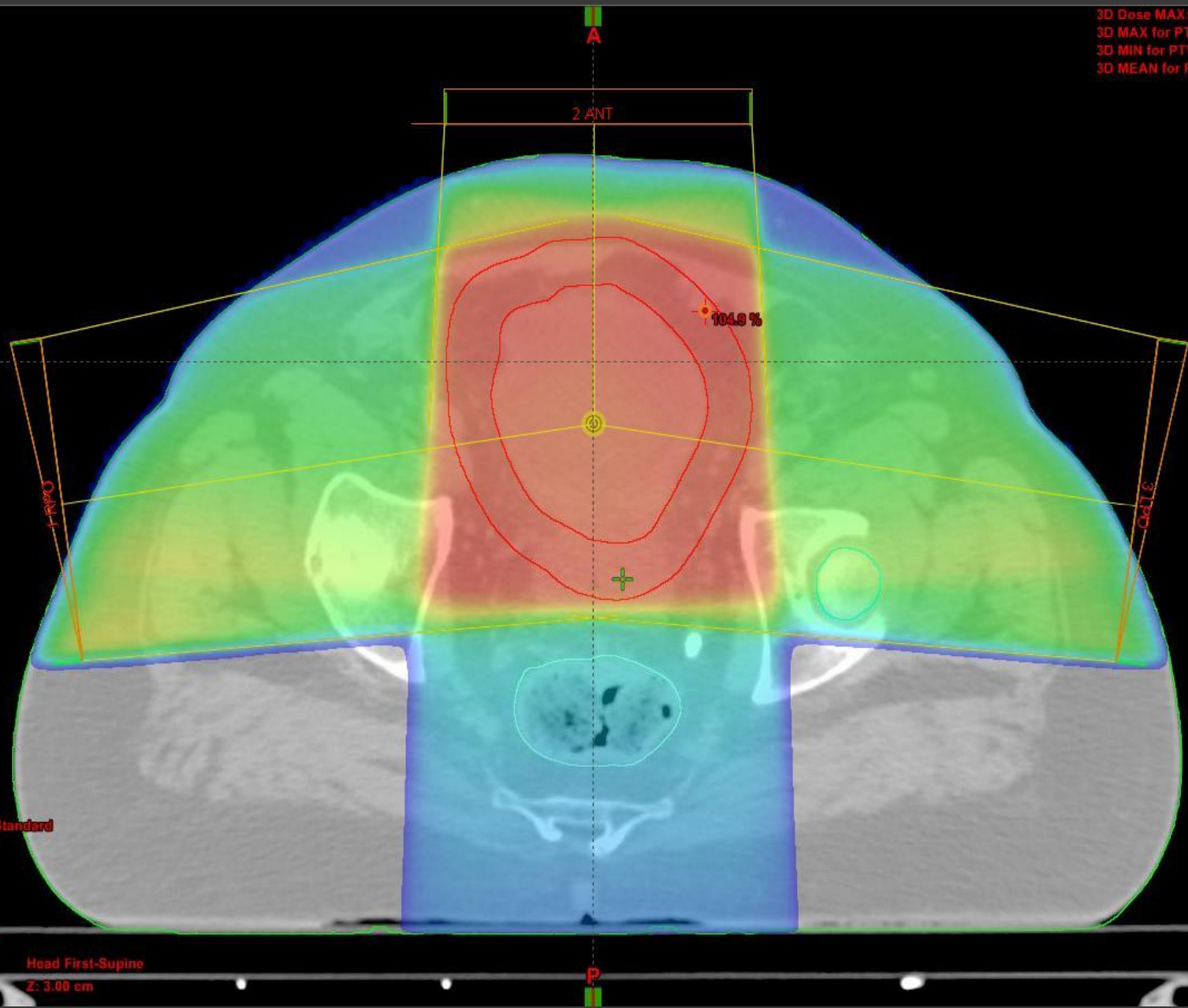
Grown by 1.5-2cm circumferentially







3D Dose MAX: 104.9 %  
3D MAX for PTV BLADDER: 104.9 %  
3D MIN for PTV BLADDER: 95.0 %  
3D MEAN for PTV BLADDER: 101.0 %



# Radiotherapy

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- ▶ Different fractionation regimes: 64Gy/32#, 55Gy/20#, 36Gy/6#, 21Gy/3#
- ▶ 5-year reported loco-regional control rates are 40-55% for daily fractionation regimes, 30% for weekly hypofractionated regimes (*Pos et al, IJROBP 2005*)
- ▶ Significant bladder movement: 'plan of the day', composite volumes



# Side-effects of radiotherapy

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## ▶ Acute

- ▶ Cystitis
- ▶ Lethargy
- ▶ Diarrhoea
- ▶ Skin inflammation

## ▶ Late

- ▶ Reduced bladder capacity, telangiectasia
- ▶ Change in bowel habit
- ▶ Impaired sexual function
- ▶ Second tumours



# Radiotherapy vs. surgery

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- ▶ Cochrane review (2002): overall survival benefit for surgery
- ▶ No randomised controlled trial
- ▶ Three trials comparing pre-operative radiotherapy + cystectomy vs radiotherapy with surgical salvage
- ▶ Small numbers, and surgical pt received radiotherapy
- ▶ Mean 5-year survival 36% vs 20%, low for radiotherapy
- ▶ Outdated radiotherapy techniques



# Radiotherapy vs. surgery

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- ▶ TURBT followed by RT or CRT (*Rodel et al, JCO, 2002*)
  - ▶ 10-y CSS of 42% with 80% retaining bladder
- ▶ RT vs cystectomy retrospective (*Kotwal et al, IJROBP, 2007*)
  - ▶ Overall survival 41% (cystectomy) vs 35% (radiotherapy) at 5years,  $p>0.05$
  - ▶ Local and distant recurrence rate 37% (cystectomy) vs 34% (radiotherapy).
  - ▶ Older age in RT arm



# Why are radiotherapy outcomes improving?

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- ▶ Increasing evidence that radiotherapy improving  
?equivalent to surgery
- ▶ Radiotherapy techniques improved;
  - ▶ Use of conformal sparing radiotherapy techniques sparing normal tissue with more penetrating radiotherapy
  - ▶ Cone beam CT to monitor organ motion
  - ▶ Plan of the day, composite volumes
- ▶ Chemotherapy: Neoadjuvant, concomitant, ?adjuvant



# Chemotherapy

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# Chemo-radiation

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- ▶ Neoadjuvant : before radical treatment
- ▶ Concomitant: with radical treatment
- ▶ Adjuvant: after radical treatment



# Neoadjuvant chemotherapy

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- ▶ Purpose;
  - ▶ Reduction of primary tumour volume (prognostic)
  - ▶ Treatment micrometastatic disease
- ▶ More likely to tolerate *before* radical treatment than after



# Neoadjuvant chemotherapy

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- ▶ Meta-analysis comparing neoadjuvant chemo + surgery/radiotherapy vs local treatment alone  
*(Cochrane 2008)*
- ▶ 5% survival benefit prior to surgery or radiotherapy
- ▶ 3000 patients, 11 RCTs
- ▶ OS improved by 5% from 45 to 50%
- ▶ Platinum-based combination chemotherapy
- ▶ Improved metastasis-free survival



# Concomitant chemoradiation

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- ▶ Improved loco-regional disease-free survival vs RT alone (*BC2001, ND James et al 2010*)
- ▶ 458 patients
- ▶ OS benefit not yet seen, too soon
- ▶ No significant difference in G3-4 toxicity
- ▶ 5FU + MMC - can be used with GFR >25ml/min
- ▶ 64Gy/32# or 55Gy/20#
- ▶ Toxicity: neutropenia, thrombocytopaenia, cystitis, diarrhoea
- ▶ Salvage cystectomy offered for persistent disease



# Adjuvant chemotherapy

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- ▶ Adding chemotherapy *after* surgery or radiotherapy
- ▶ Advantages:
  - ▶ Knowledge of pathological stage
  - ▶ Primary treatment not compromised by toxicity
- ▶ Meta-analysis 491 patients, 6 trials (*cochrane 2008*)
- ▶ Heterogeneous data with a number of trials stopping early, small numbers
- ▶ Inconclusive
- ▶ Consider Gem/Cis q4w



# Summary

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- ▶ Radiotherapy alone once considered inferior to surgery
- ▶ Evidence to suggest survival improving for radiotherapy
- ▶ Better radiotherapy techniques
- ▶ Addition of chemotherapy
  - ▶ Neoadjuvant improves metastasis-free survival
  - ▶ Adjuvant improves local control
- ▶ Surgical salvage if fails locally
- ▶ Organ preservation!!



# Conclusion

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- ▶ Chemo-radiation should be always considered as an alternative to surgery
- ▶ Benefit of organ preservation with surgical salvage if fails



