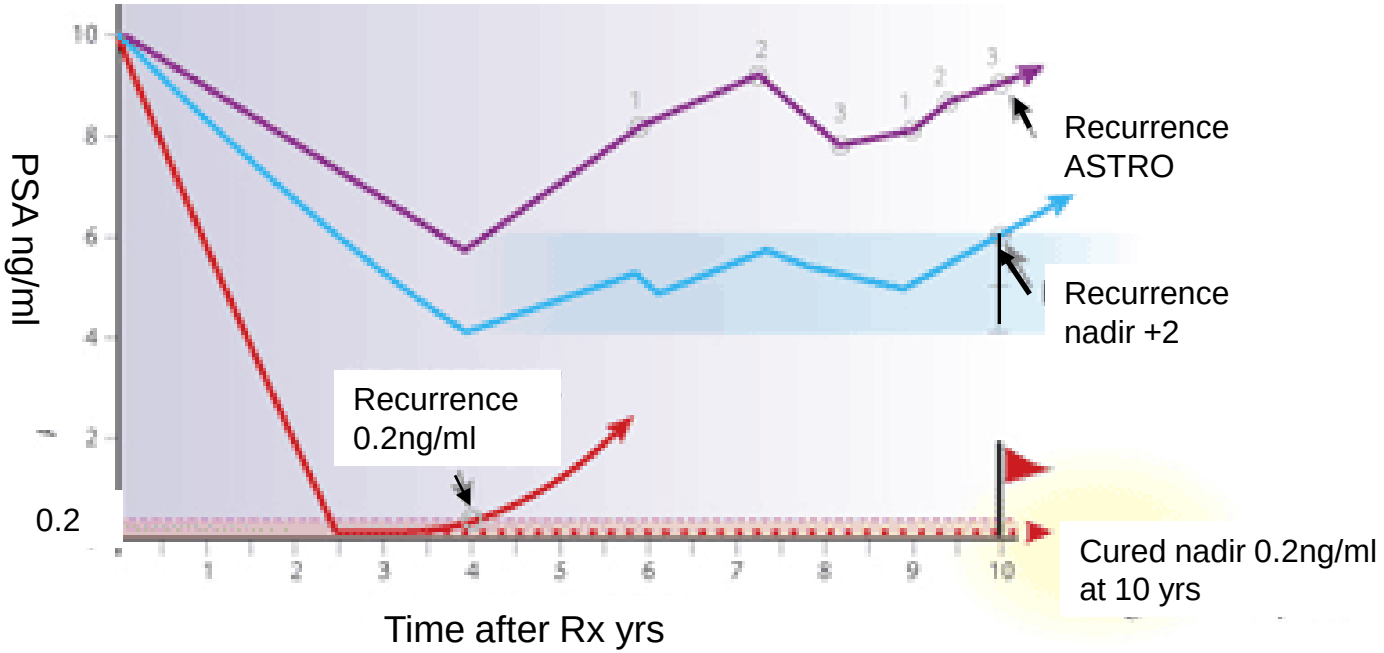
PSA nadir post LDR Brachytherapy and early Salvage Therapy

Dr Duncan McLaren

UK & Ireland Users Group Meeting 2016

Differences in PSA relapse rates based on definition used



Definitions of Recurrence

- **PSA rises above 0.2ng/ml cut point**
- **Nadir +2ng/ml rises 2.0 above lowest level**
- **ASTRO 3 consecutive rises above nadir**

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Original Article

The Importance of Prostate-specific Antigen (PSA) Nadir and Early Identification of PSA Relapse after 10 Years of Prostate Iodine125 Seed Brachytherapy in Edinburgh

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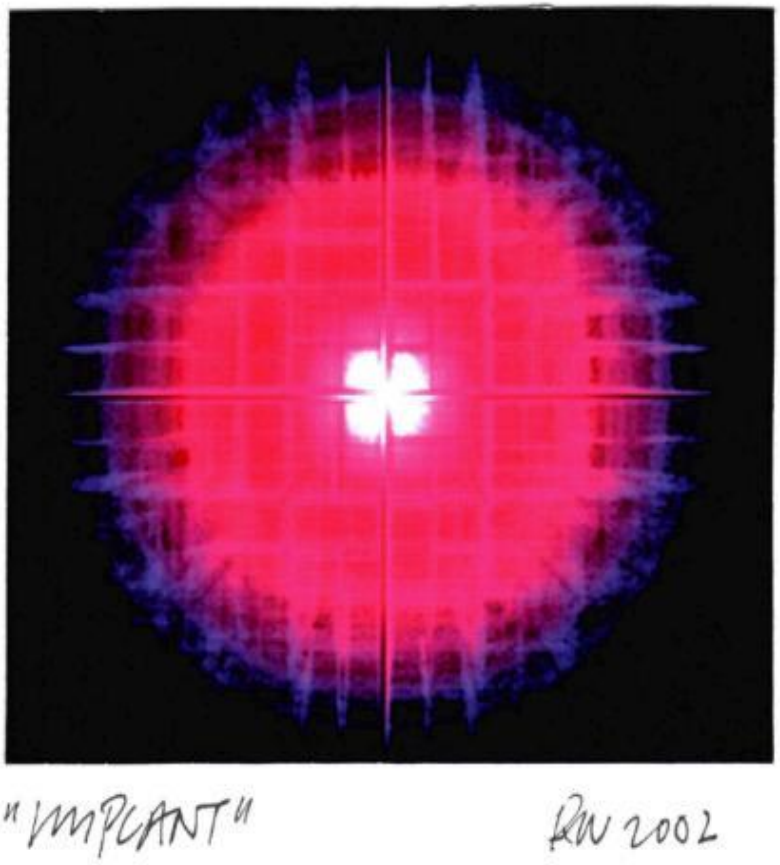
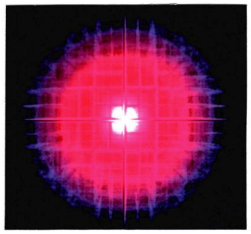
ECC Data and Patient Selection 2001

- Organ confined T1-T2 disease
- Qmax ≥ 10mls/sec & urinary residual< 150mls
- IPPS score under 15
- No TURP
- Prostate volume ≤ 50cc
- (70cc +3 months of hormones)

- Gleason score 6 PSA ≤ 20ng/ml
- Gleason score 7 PSA ≤ 15ng/ml





Edinburgh Data

2 cohorts

2001-2006

2006-2011

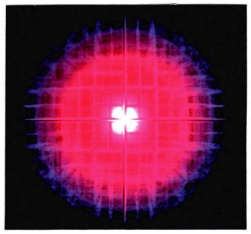
474 men with median FU 6.5 yrs

69 relapses by Phoenix definition

PSA relapse rate

9.3% @5 yr

26.4% @10yr



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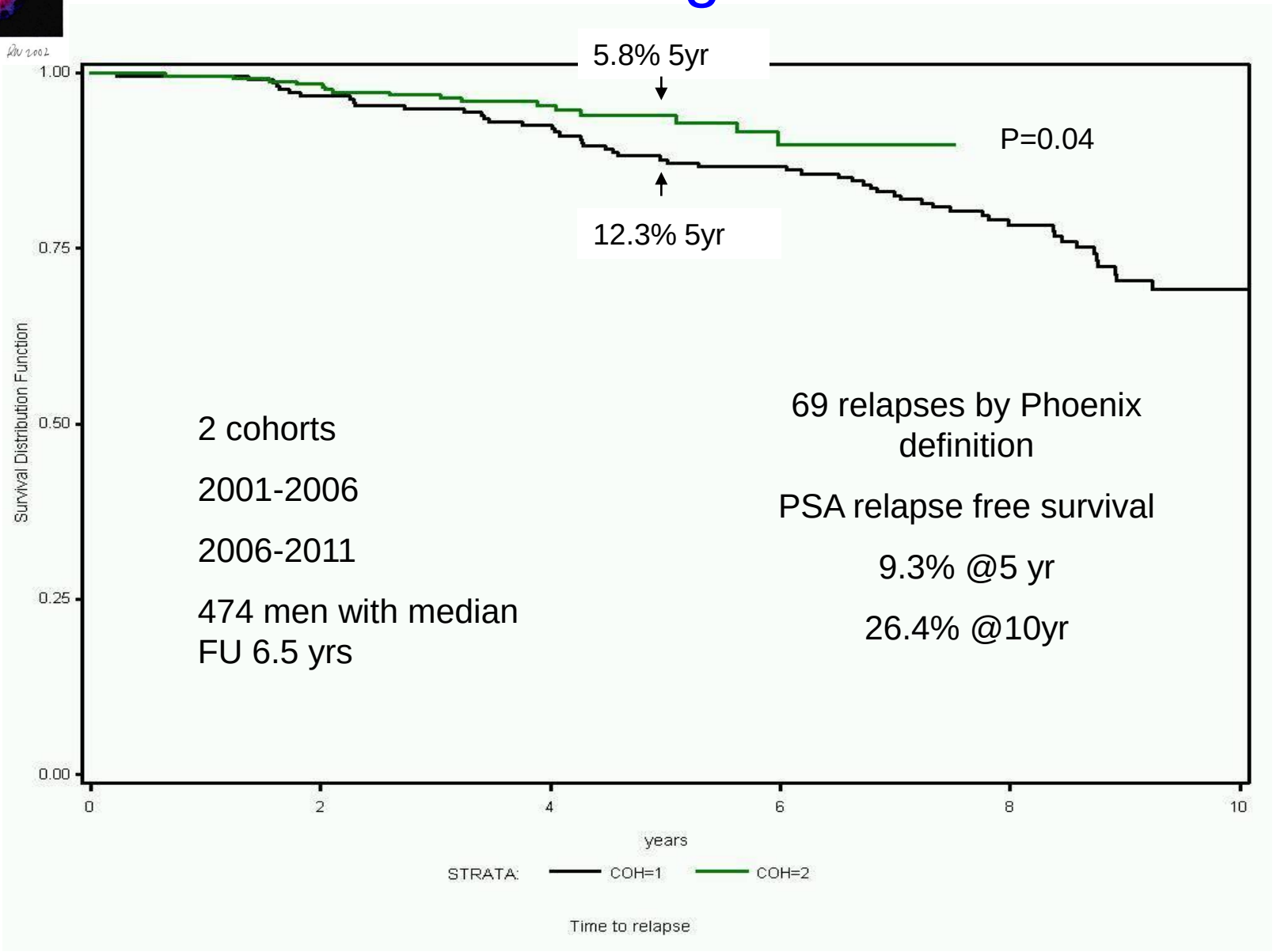


2 cohorts

2001-2006

2006-2011

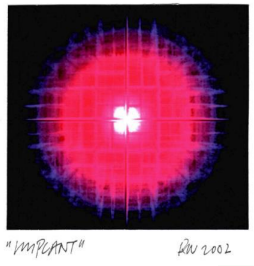
474 men with median FU 6.5 yrs

69 relapses by Phoenix definition

PSA relapse free survival

9.3% @5 yr

26.4% @10yr



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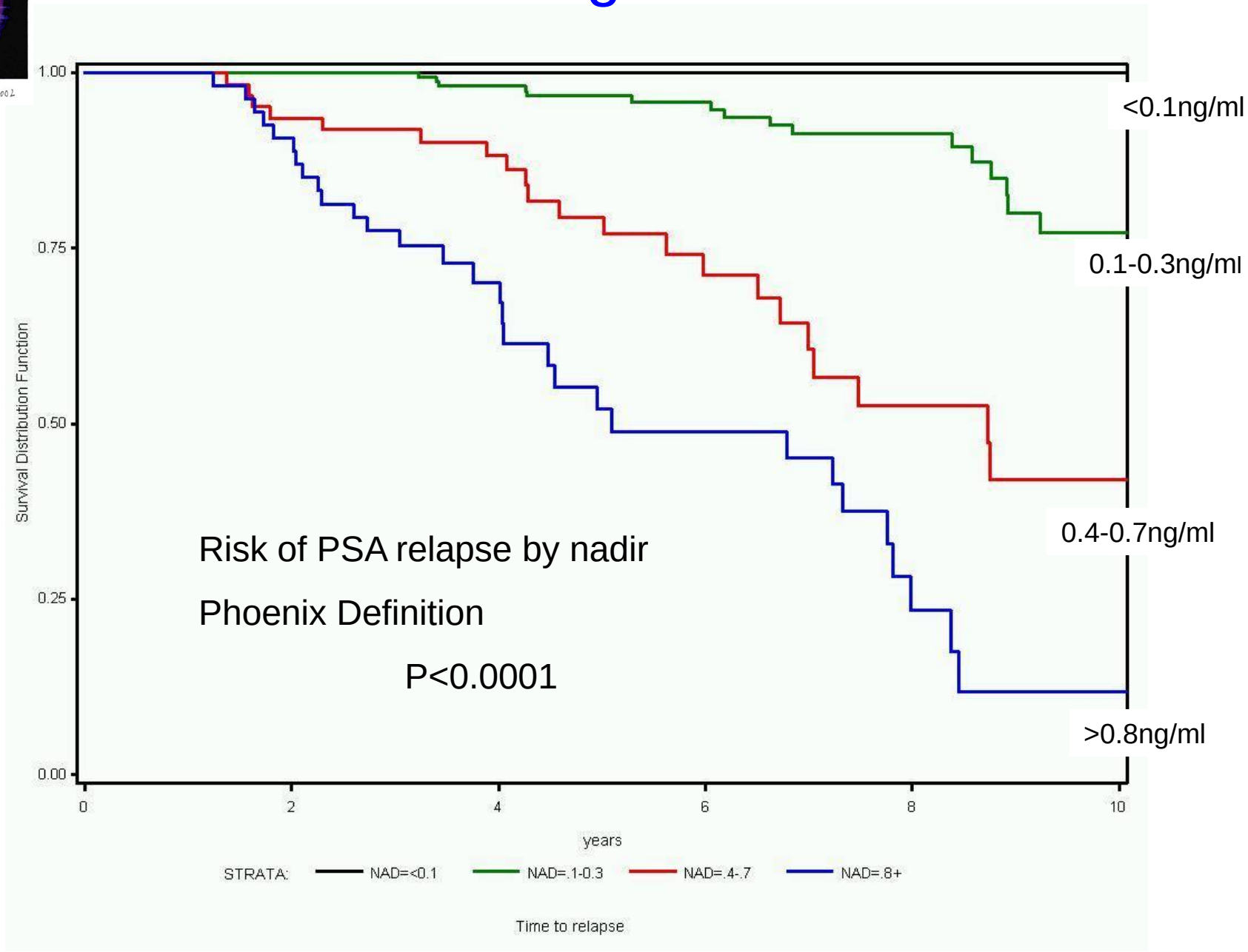


Proportional hazards analysis of prostate-specific antigen (PSA) relapse

474 men 69 PSA relapses

Cohort	ns
Age	ns
T	ns
Gleason score	ns
PSA at presentation	ns
D90	ns
Volume	0.0035
Neo-adjuvant hormones	0.0065
Bounce	<0.0001 (chi square = 25)
Nadir	<0.0001 (chi square = 127)

Is the use of the of Phoenix definition of nadir +0.2ng/ml the correct one to use following prostate brachytherapy?

Phoenix v Nadir plus 0.4ng/ml

- Nadir +2.0ng/ml
- 69 relapses
- 5yr relapse = 9.3%
- 10yr relapse = 26.4%

- Nadir +0.4ng/ml
- 94 relapse
- 5yr relapse = 13.8%
- 10yr relapse = 31%

Proportional Hazards analysis same pattern as Phoenix

(nadir remains strongest predictor of relapse)

Nadir +0.4 predicted for **all** future relapses by Nadir + 2.0ng/ml

18 months median lead time for good/intermediate risk group

6 months for high risk group

Is the Phoenix definition the optimal definition ?

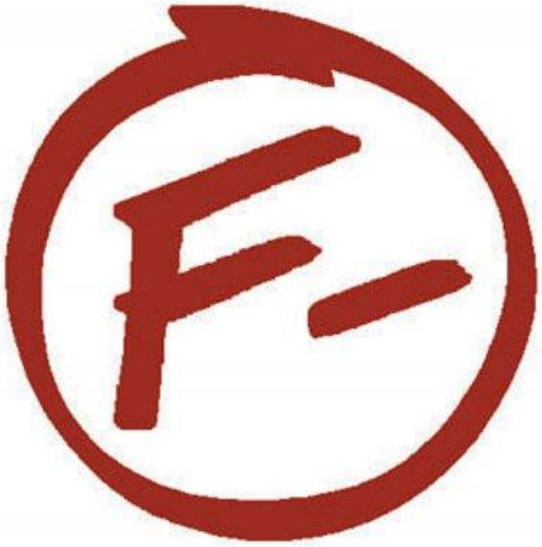
- Nadir +0.4 predicted for all future relapses with 18 month lead time for good/ intermittent patients
- Salvage therapy could have been initiated 18 months earlier
- Possible impact on outcome??
- No relapses if nadir <0.1ng/ml

Rationale for Salvage Therapy
Pros

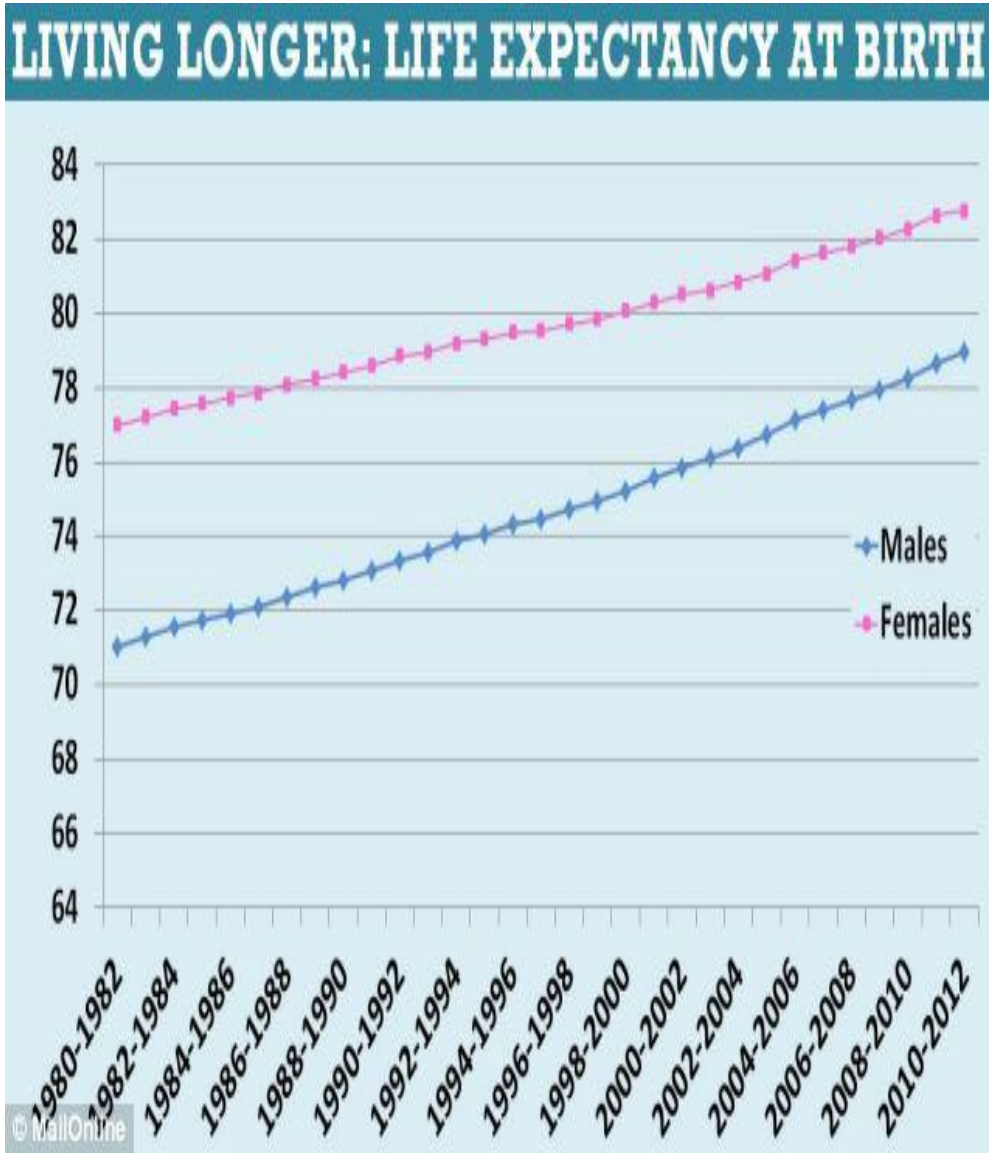
- Second chance of cure
- Improved cancer specific survival
- Potential significant cost saving
- Potential QoL gain

Rationale for Salvage Therapy
Cons

- Is there a proven survival benefit?
- Who should you treat?
- How should you treat them?
- Toxicity and adverse impact on QoL
- May still develop metastases



Food for thought

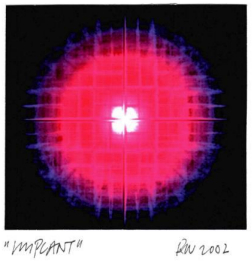


Median life expectancy of man aged 63 = 19yrs

Median life expectancy with local failure post LDR = 12yrs

Identifying suitable salvage candidates

- Low and intermediate risk men
- MRI
- Bone Scan
- Choline PET-CT
- Targeted Template Biopsy

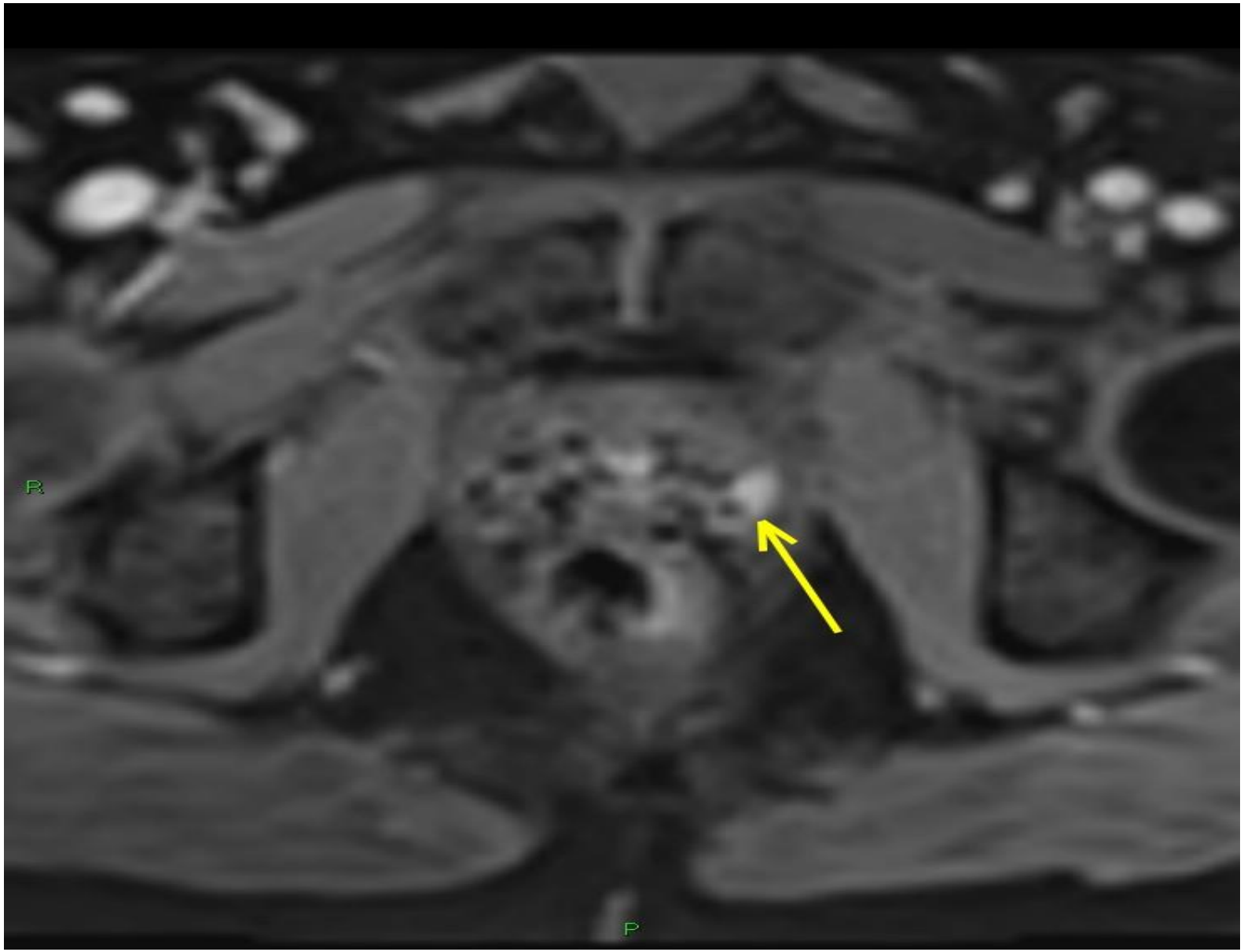


Case study

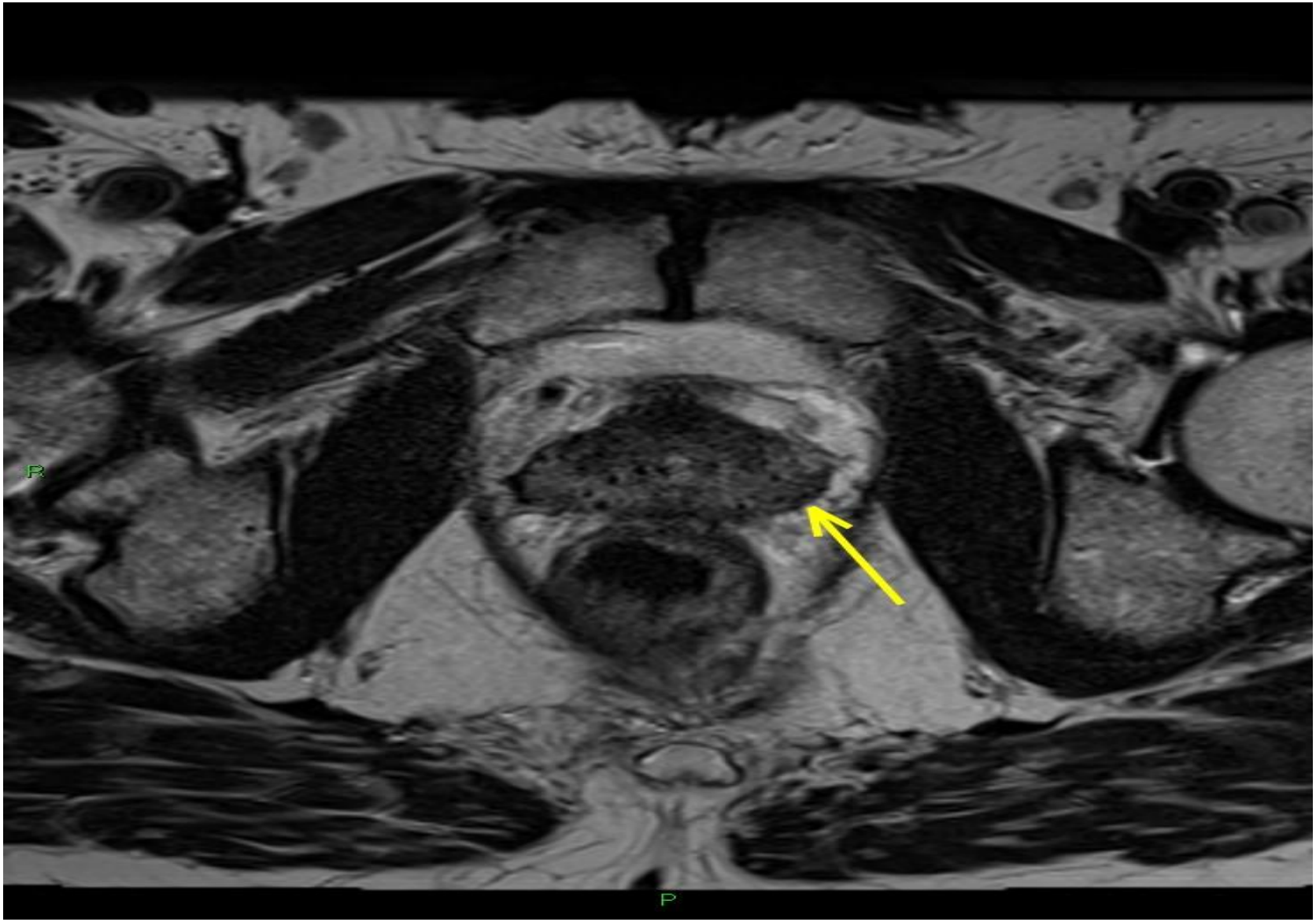
- 56 year with T1c Gleason bilateral 3+3=6 and PSA 5
- Hx of prostatitis, IPSS 3, Q-max 17cc/sec no residual
- 30cc prostate
- Implanted July 2005
- PSA bounce in year 2 from 1.6 to 1.9 and down to nadir of 1.4ng/ml 30 months post implant
- PSA then steadily rose to 5.1ng/ml

- Restaging scans done Jan 2014 possible enhancement left side of prostate on multi-parametric MRI

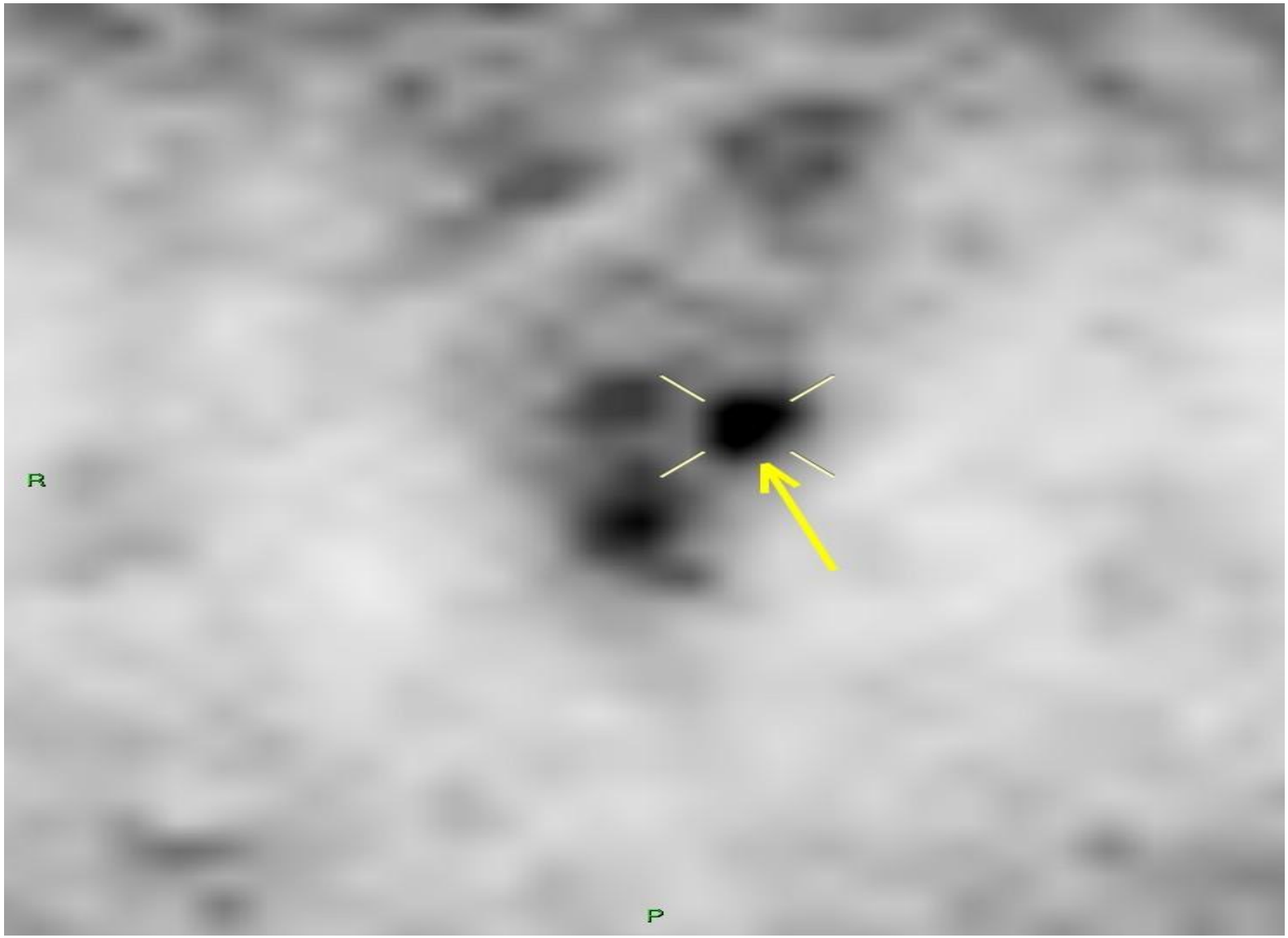
DCE MRI



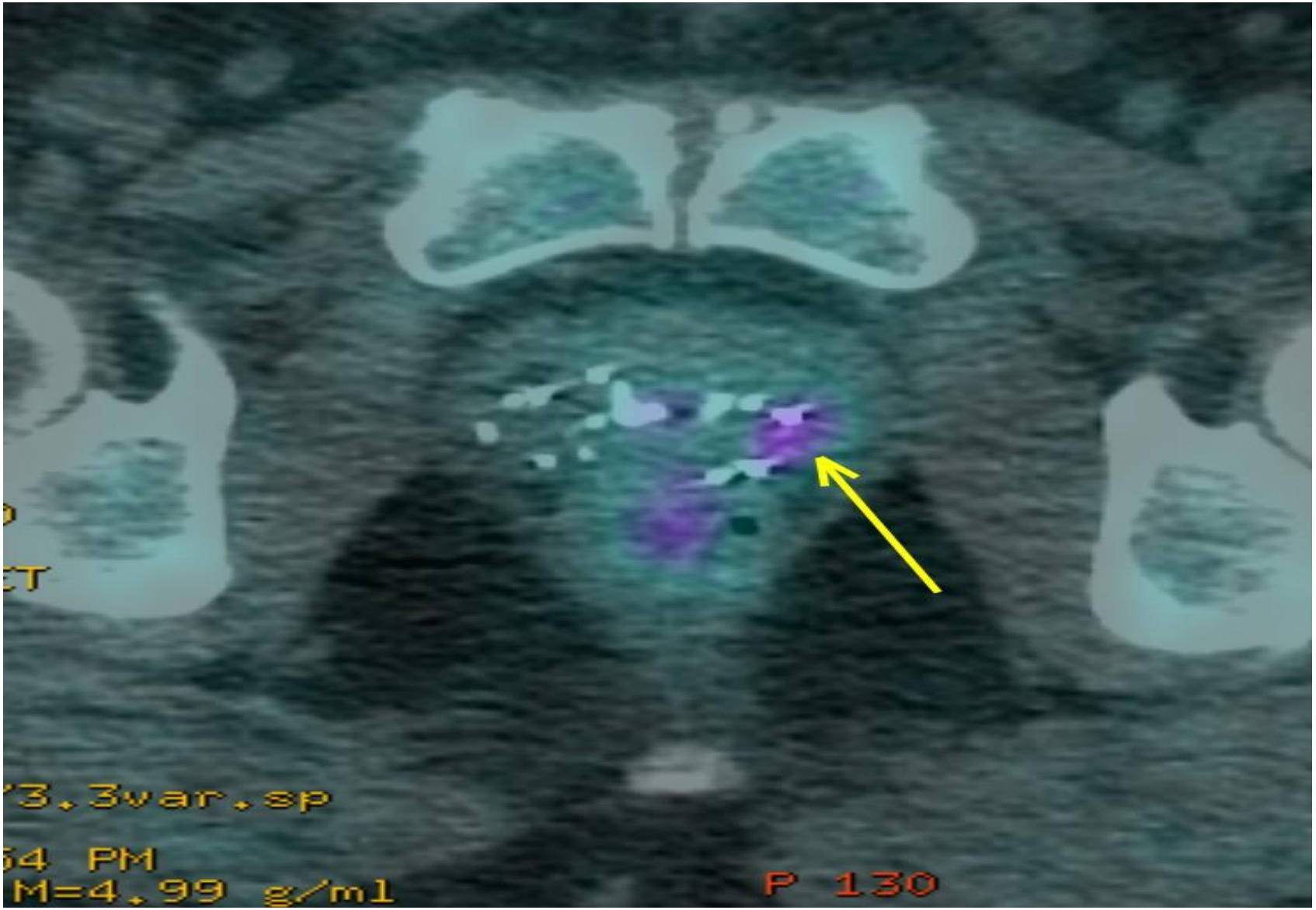
T2 MRI

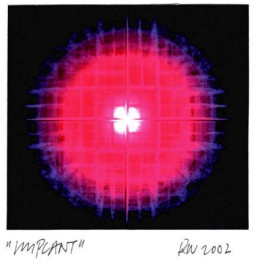


Choline PET scan



Choline PET-CT

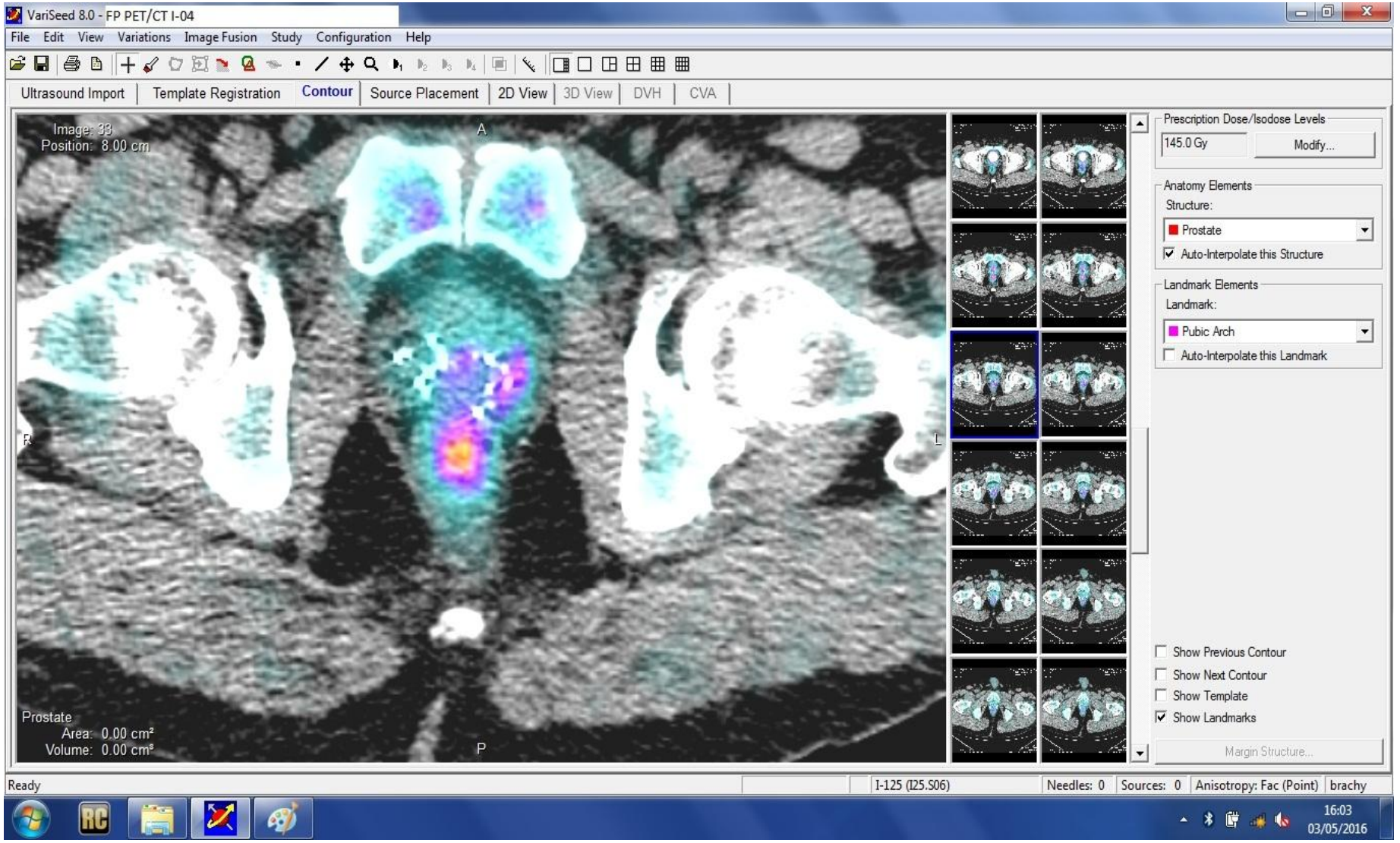




Case study cont

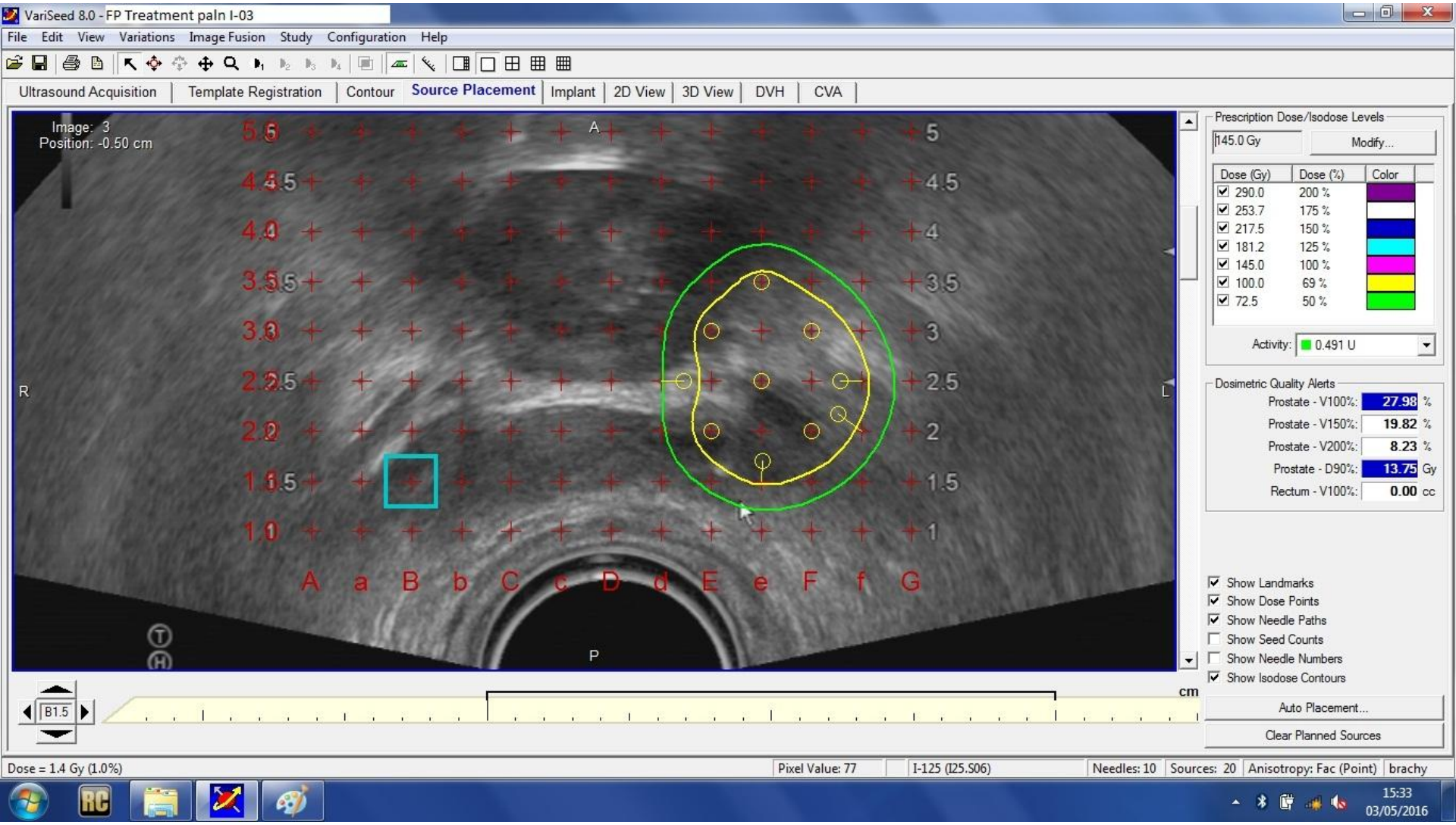
- Template targeted biopsy arranged with volume study and tumour mapping performed
- PSA 9.2ng/ml
- Biopsies Gleason 3+4=7 left mid zone and apex, Rt clear
- Review of Day 28 post implant dosimetry scan suggested relatively poor peripheral dose coverage at recurrence
- Fusion of Choline PET-CT with post implant CT
- Focal implant planned

Choline PET-CT Scan



Treatment Plan

23 seeds, 12 needles, 145Gy prescription dose



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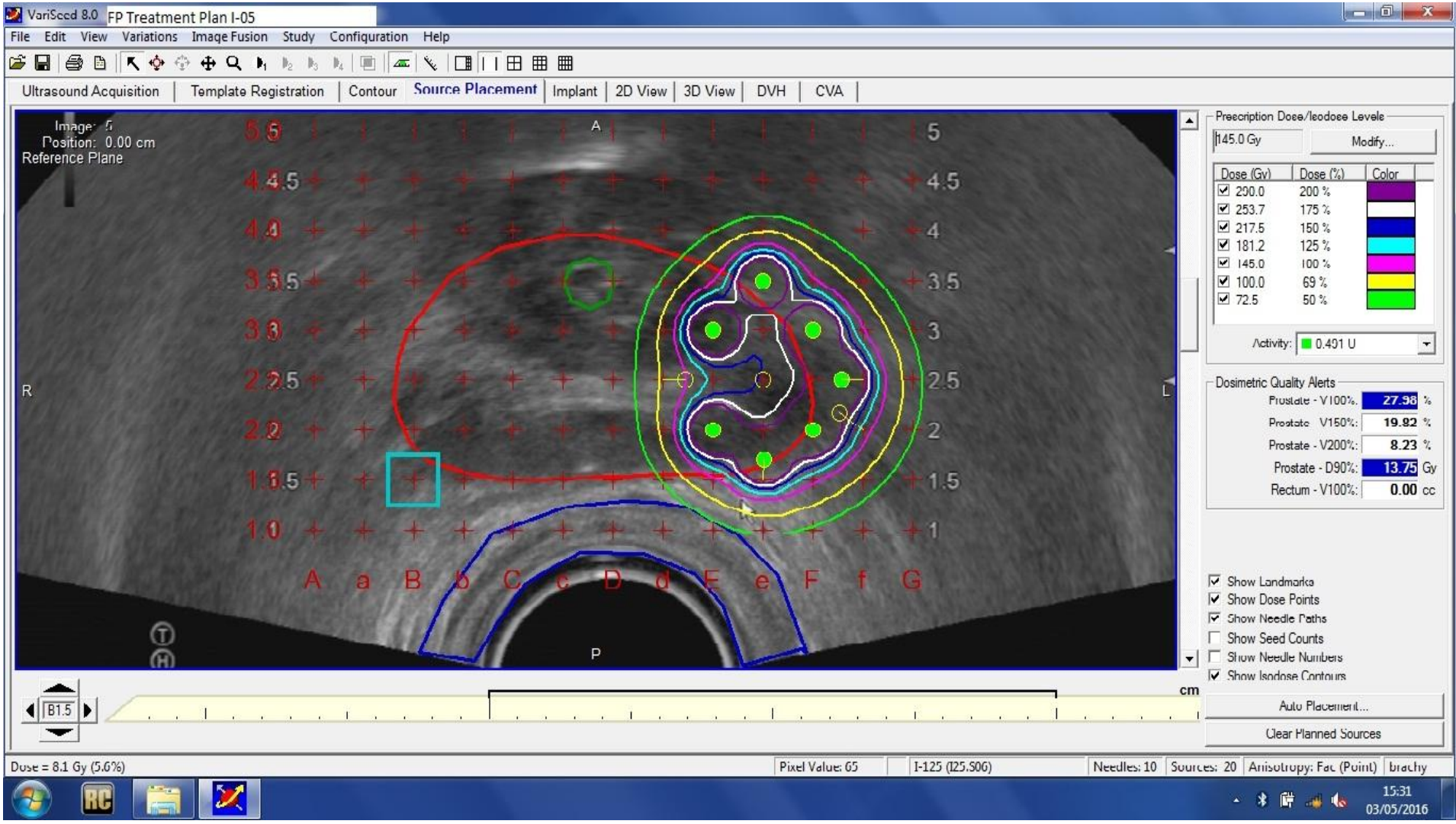

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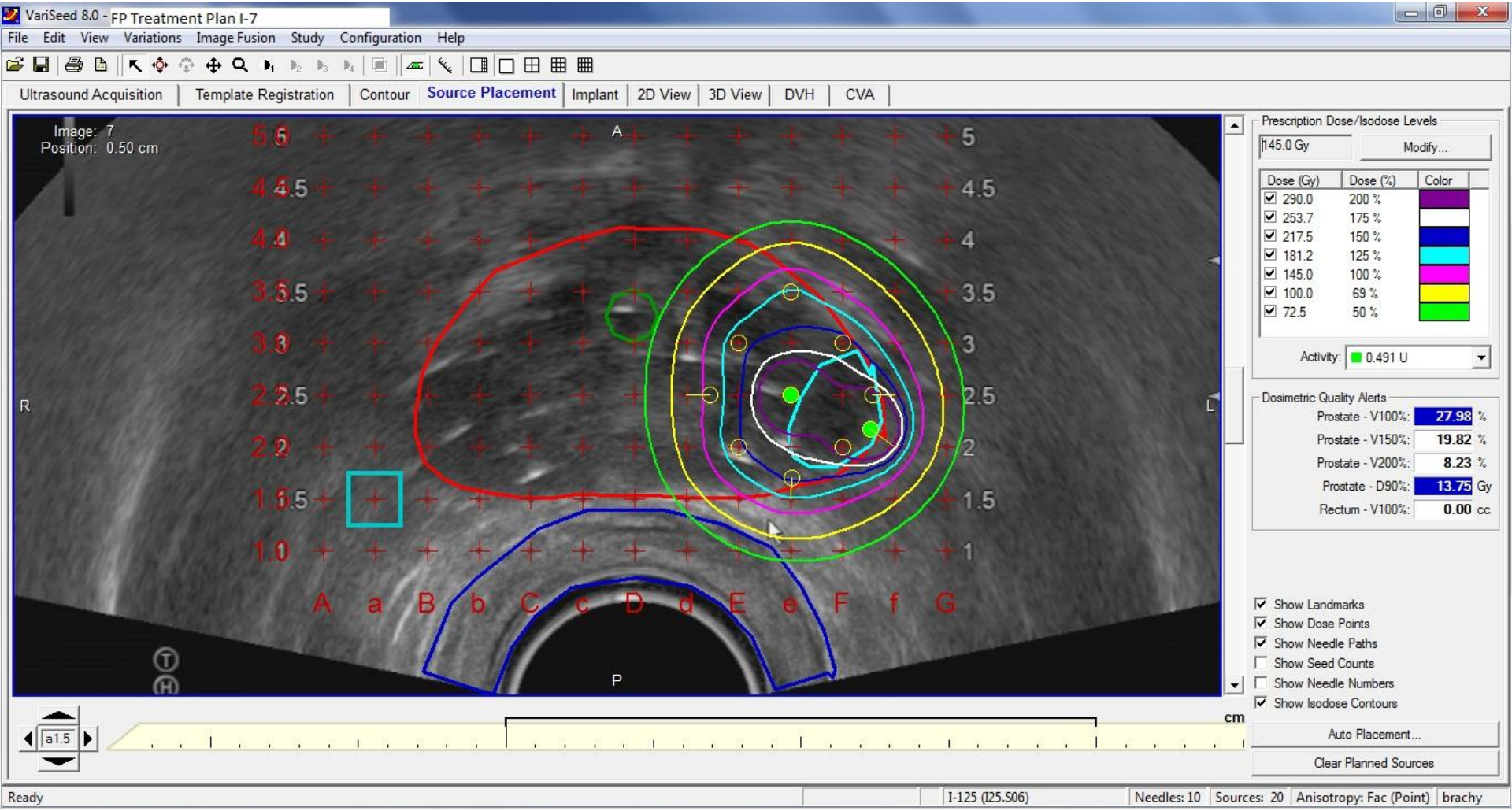

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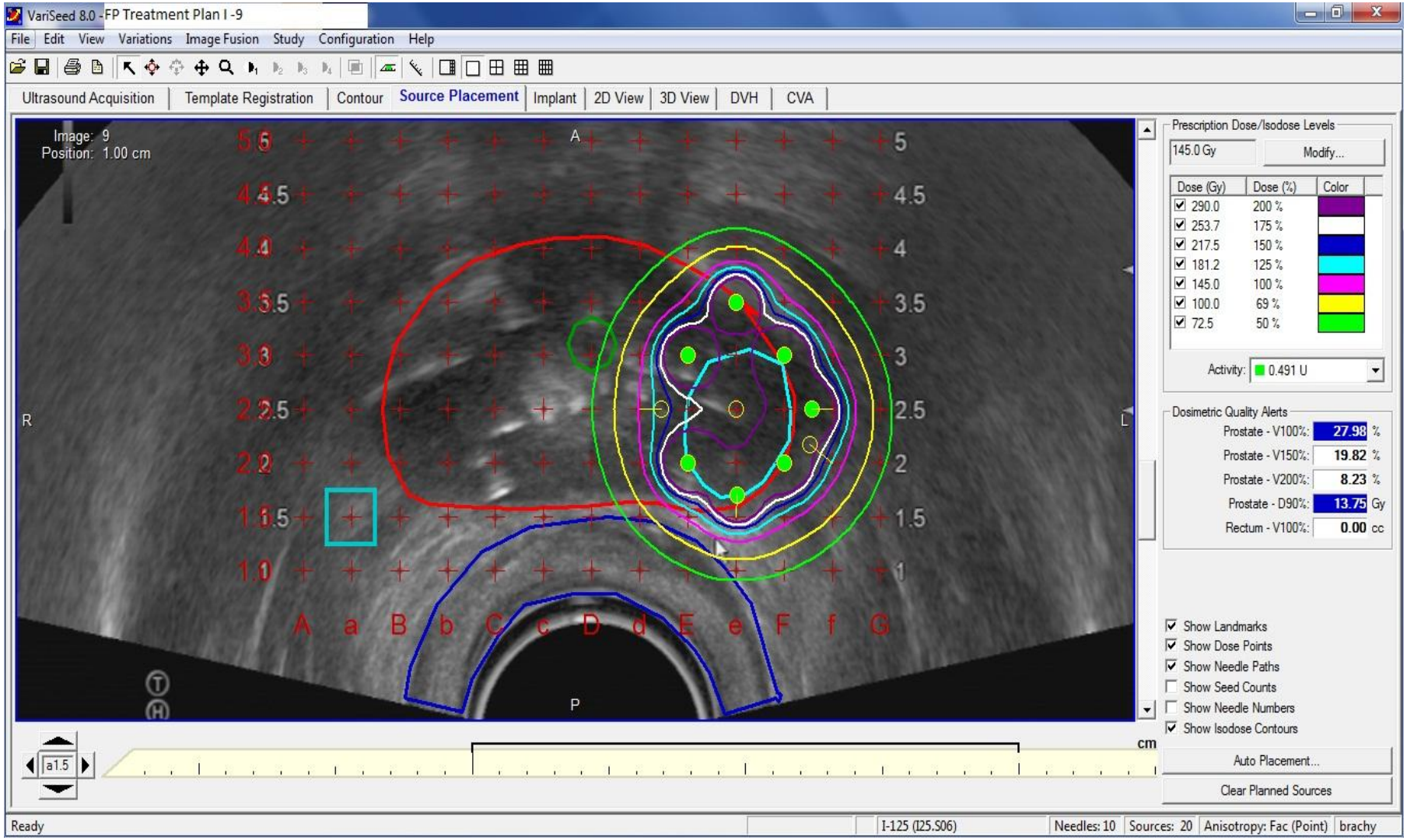

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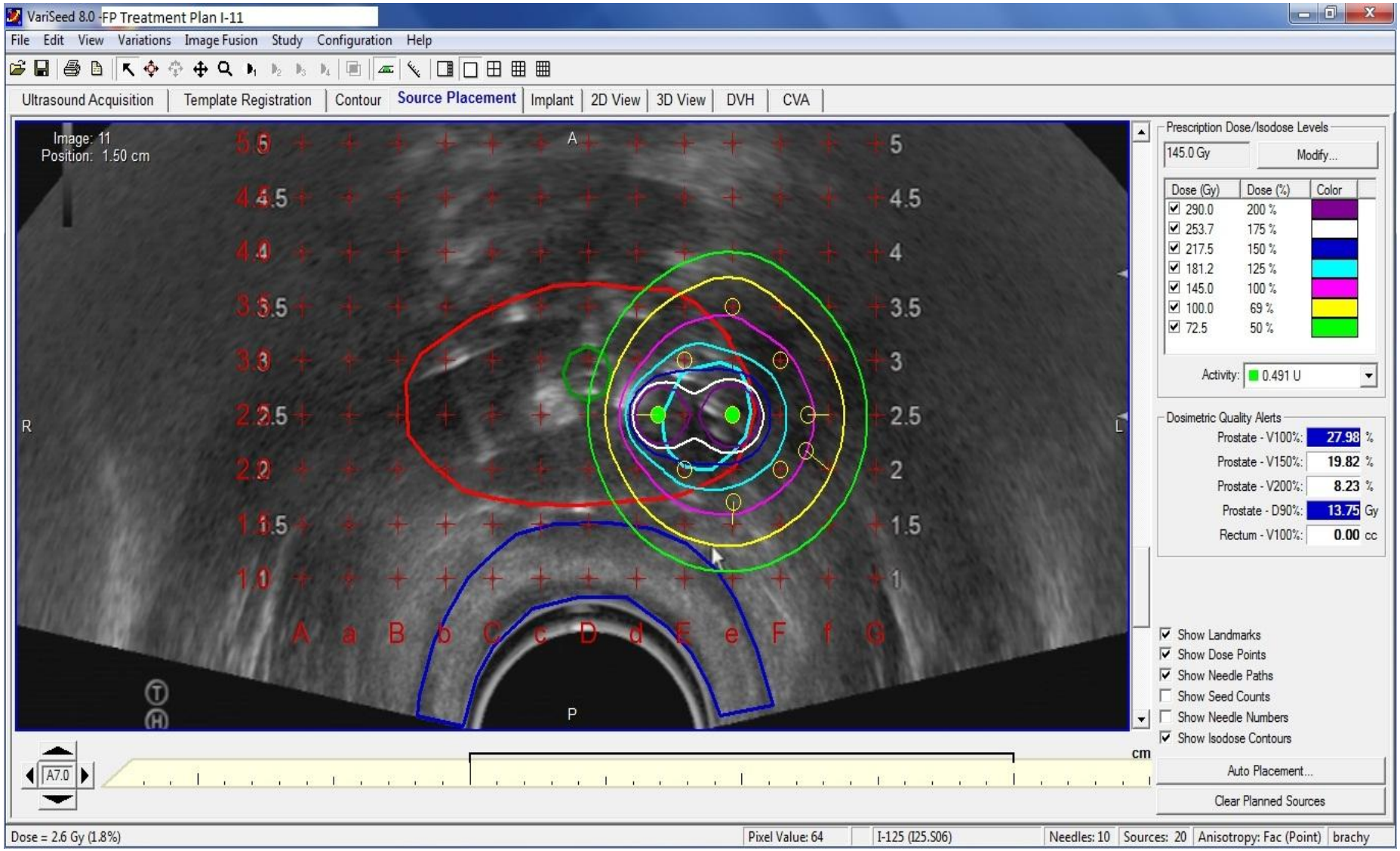

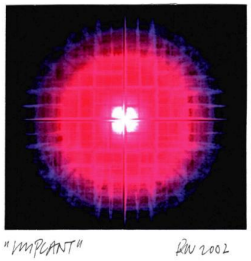

Case study cont

- Implant performed 16/1/15
- Follow up 3 months PSA 7.6ng/ml, IPSS 3 and patient really well
- 6 Months 4.1ng/ml IPSS 4, remains well
- 12 Months PSA 0.8ng/ml IPSS 2.0ng/ml
- 15 Months PSA 0.3ng/ml IPSS 2.0- lowest level ever achieved
- Patient delighted and no adverse toxicity

- So far so good!!

Can we do a randomised patient preference study?

- 2000 implants per annum in UK & Ireland
- 20,000 implants over 10 years
- Low risk 10% failure @10yrs
- Intermediate risk 20% failure @10yrs

- Assume 40:60 split
- 800 low risk
- 2400 intermediate risk
- 3200 failures over 10yrs

- Local relapse in 90% low risk =720
- Local relapse in 60% intermediate risk =1440
- Total 2160 patients

Registration of brachytherapy case

Randomised to nadir +2.0 v nadir +0.4ng based on initial risk grouping

Local Relapse confirmed by PSA after year 3
Choline PET-CT performed

Template targeted biopsy

Clinician and patient choice re subsequent management

Focal LDR implant | Prostatectomy | Focal HDR implant | Cryotherapy | HIFU | AS | WW

Primary Endpoint – OS

Secondary endpoints-
QoL, Time to metastatic disease progression
Cost benefit analysis

Can this group do such a study?