Enhancing the ratio between tumor cell killing and normal tissue protection

Treatment outcome in patients treated with single-dose irradiation (SDRT) for oligometastatic disease

Carlo Greco

Champalimaud Foundation

Why is Single Dose IGRT (SDRT) in oligometastases?

Oligometastatic disease is an ideal model to assess the role of SDRT in tumor ablation.

SDRT is mature to challenge surgery and other emerging ablative modalities as the primary mode of tumor ablation because it is:

- highly effective
- non-invasive
- fast & convenient
- cost-effective

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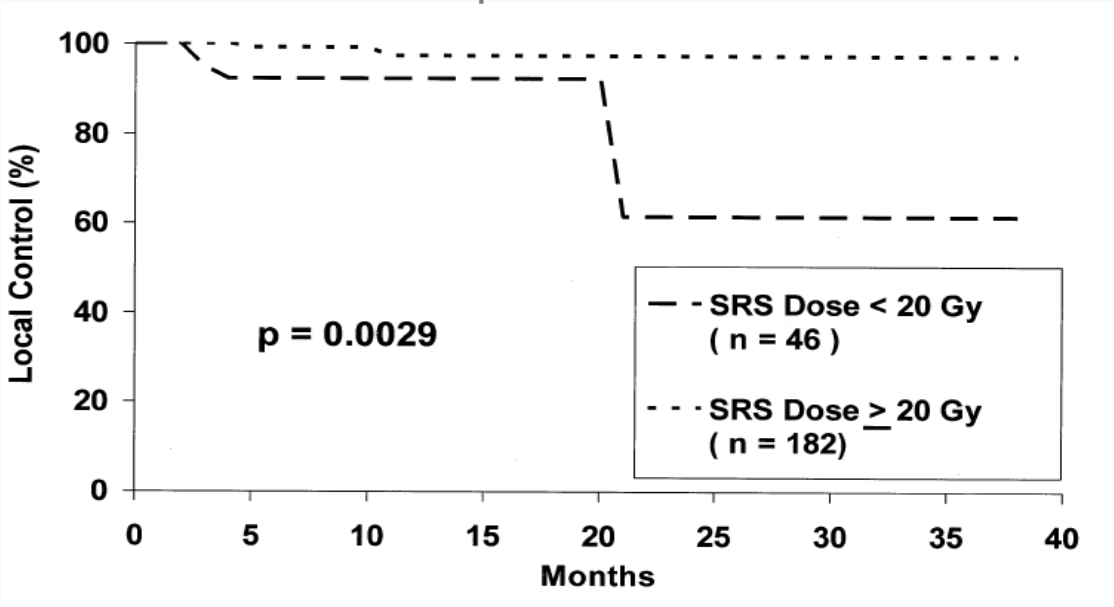
Brain metastases SRS dose response

468 pts with < 2cm lesions



Shehata, Int. J. Radiation Oncology Biol. Phys., Vol. 59, No. 1, pp. 87–93, 2004

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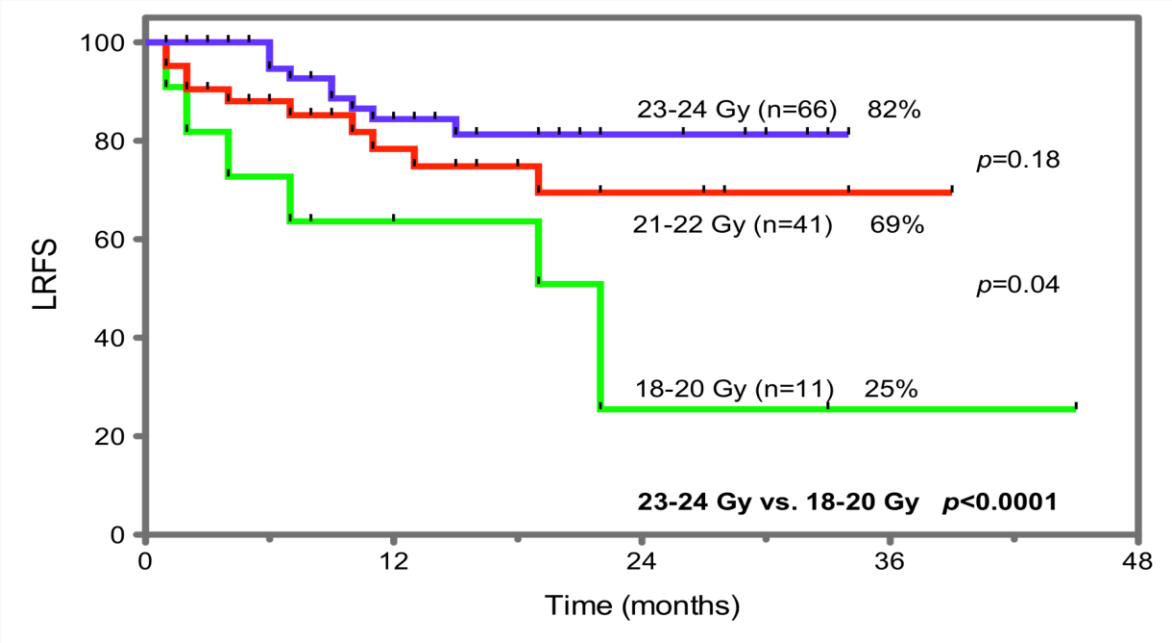
MSKCC SDRT Dose Escalation Study



High dose vs. Low dose
(82% vs. 25%) highly significant ($p < 0.0001$)

Greco C. *et al*. Int. J. Rad Oncol Biol. Phys, 2011

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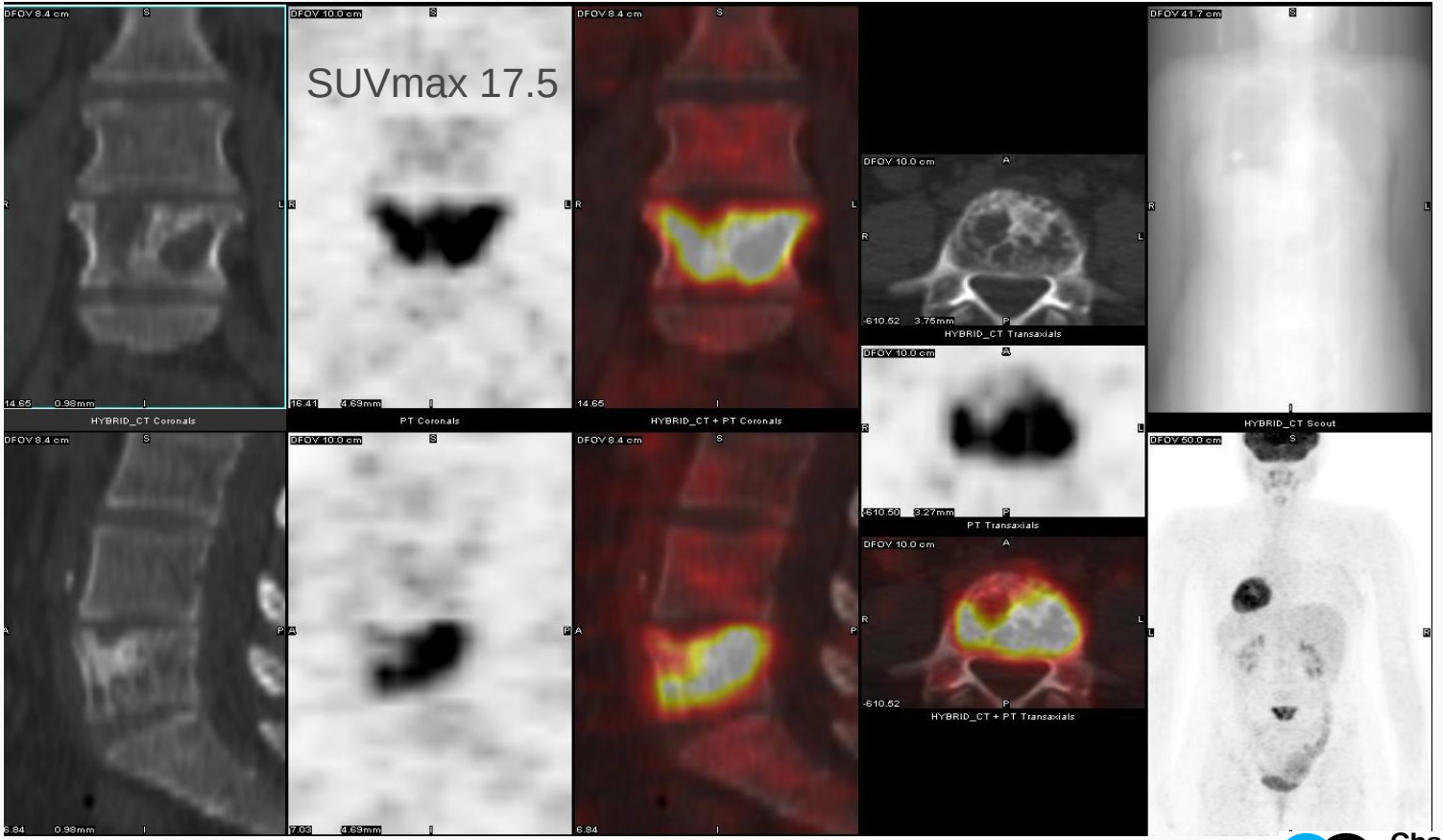
MSKCC study 10-154

Phase III randomized study to compare efficacy and toxicity of SD-IGRT *versus* Hypofractionation

24 Gy SD vs. 27 Gy (9 Gy x 3)

> 220 Patients accrued and over 500 lesions treated

Baseline PET/CT: solitary L5 lesion from Breast cancer



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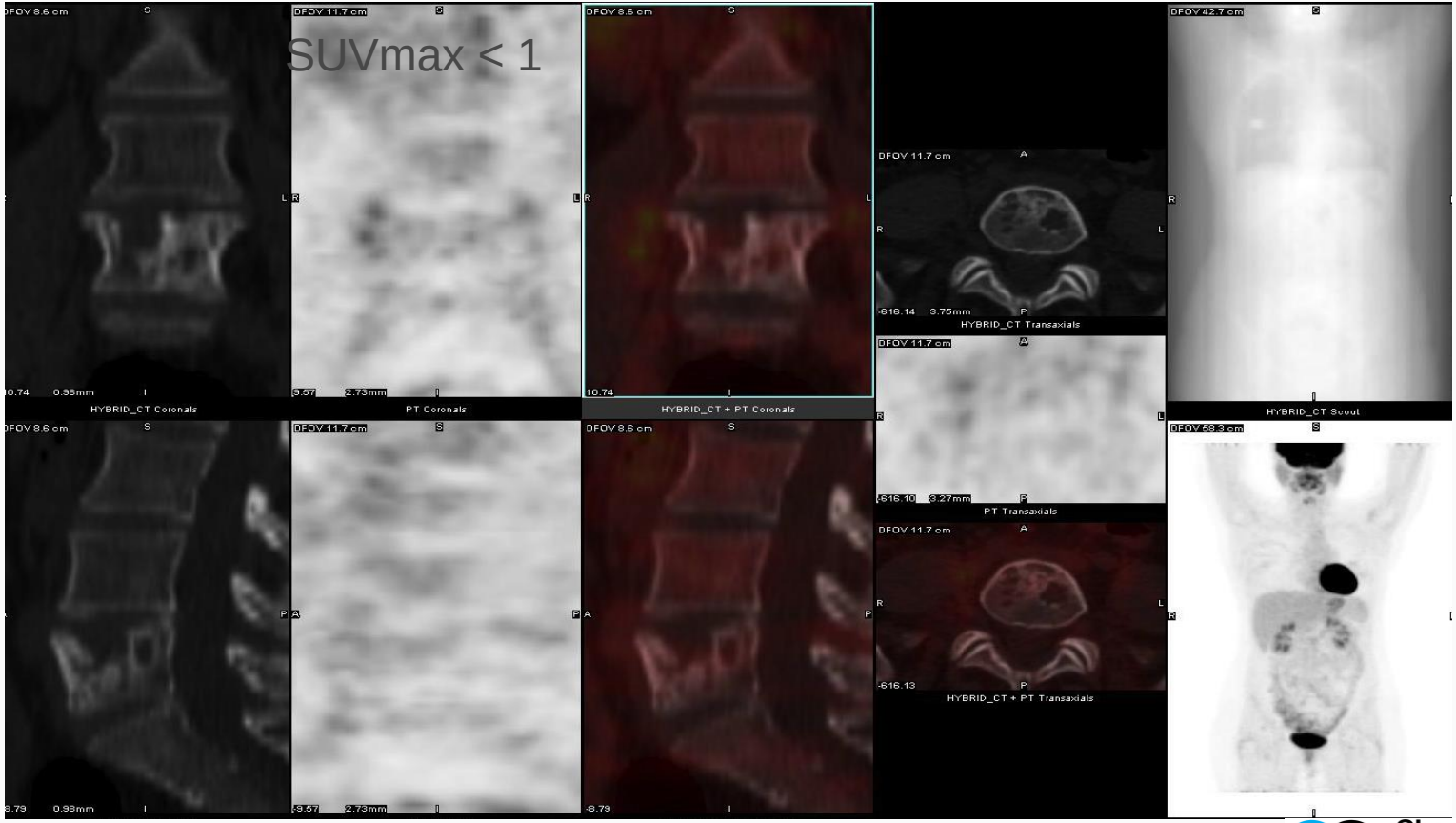
3 Months FU PET/CT: Complete metabolic response



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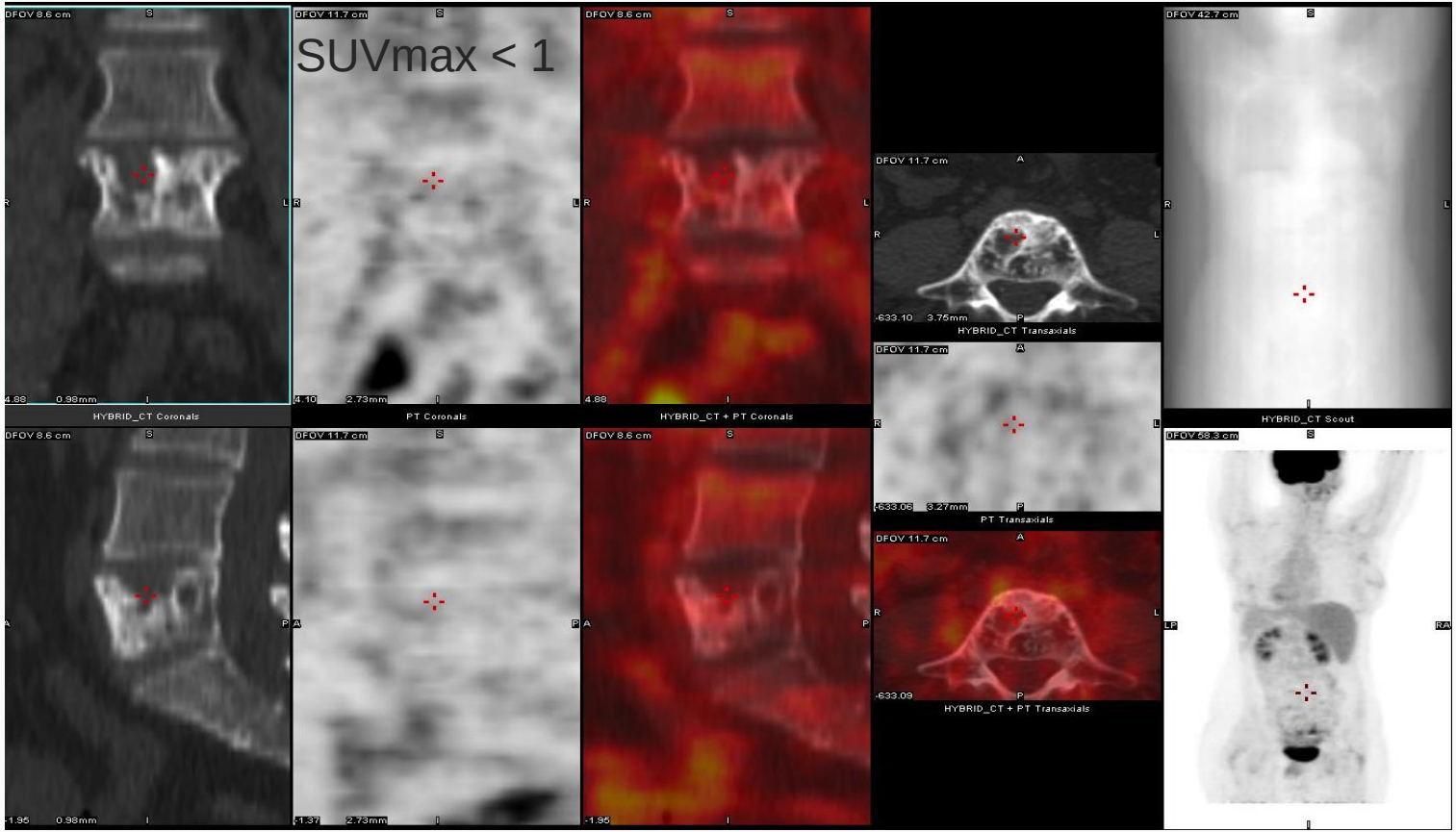
36 Months FU PET/CT: Complete metabolic response



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LRFS following SDRT (24 Gy) *vs.* Hypo (27 Gy in 3 Fx) CCU preliminary data

- 465 lesions in 202 patients (mean, 2.3 lesions per pt)
- Prescription based on ability to fulfill dose/volume constraints for SDRT
- 76% (355/465) of lesions treated with SDRT 24 Gy
- 24% (110/465) of lesions treated with 27 Gy in 3 fractions (9 Gy x 3)
- PET at baseline, 3 & 6 months and every 6 months post-treatment
- Response consistently assessed by metabolic (PERCIST) criteria

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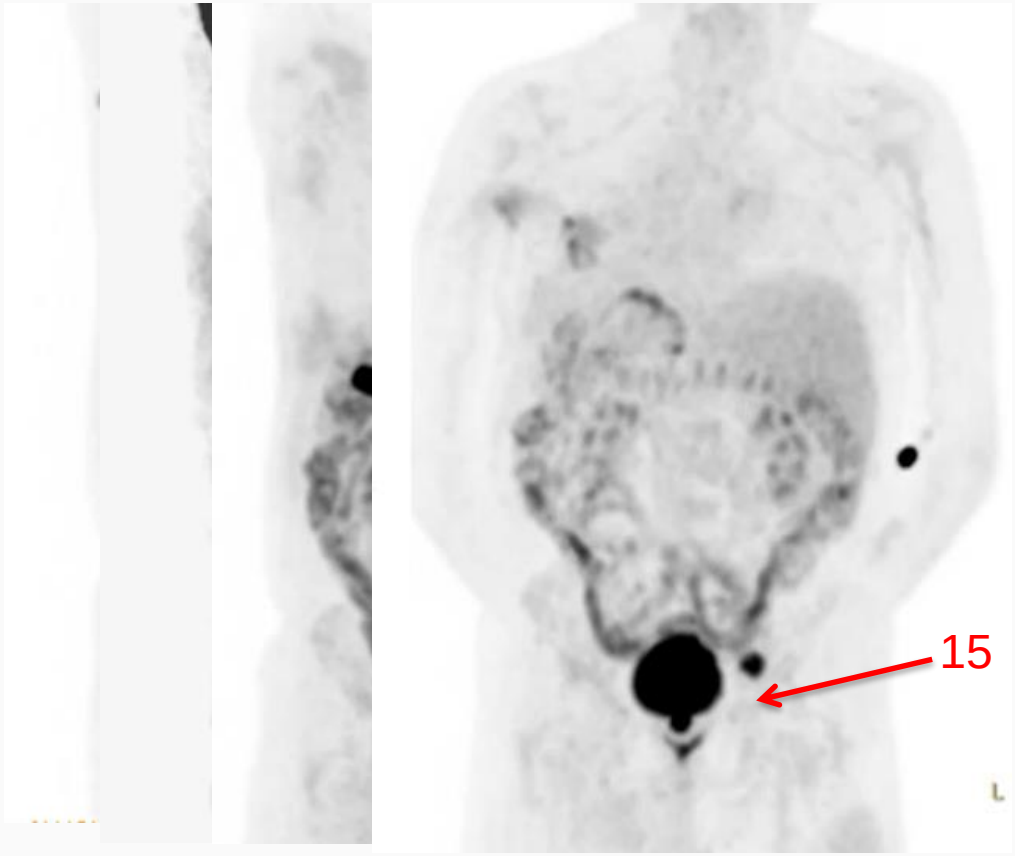
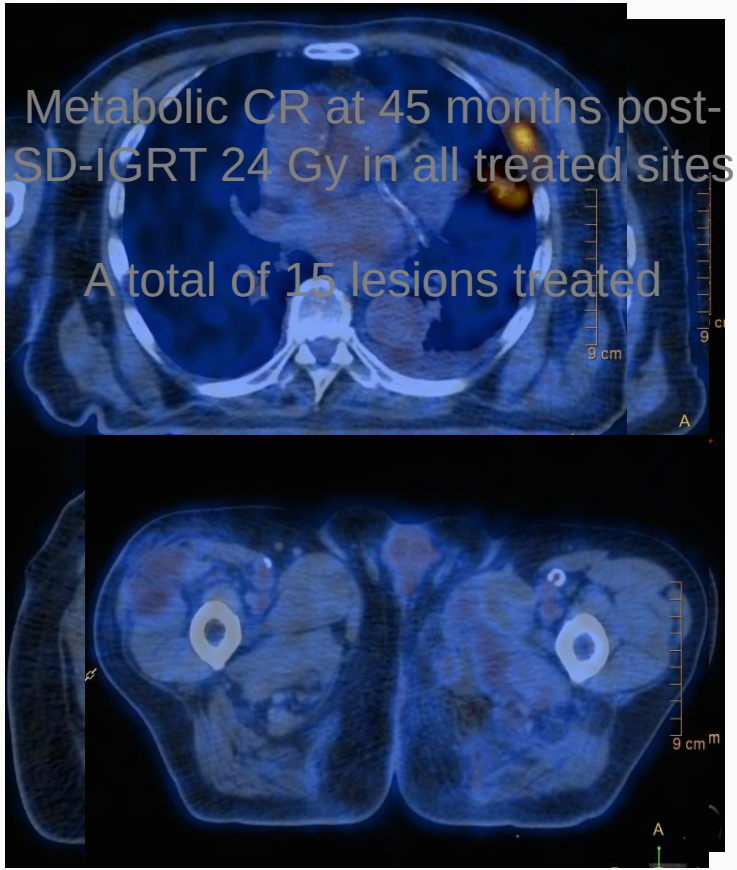
12/2013 03/2012 09/2013 03/2014



Metabolic CR at 45 months post-SD-IGRT 24 Gy in all treated sites

A total of 15 lesions treated



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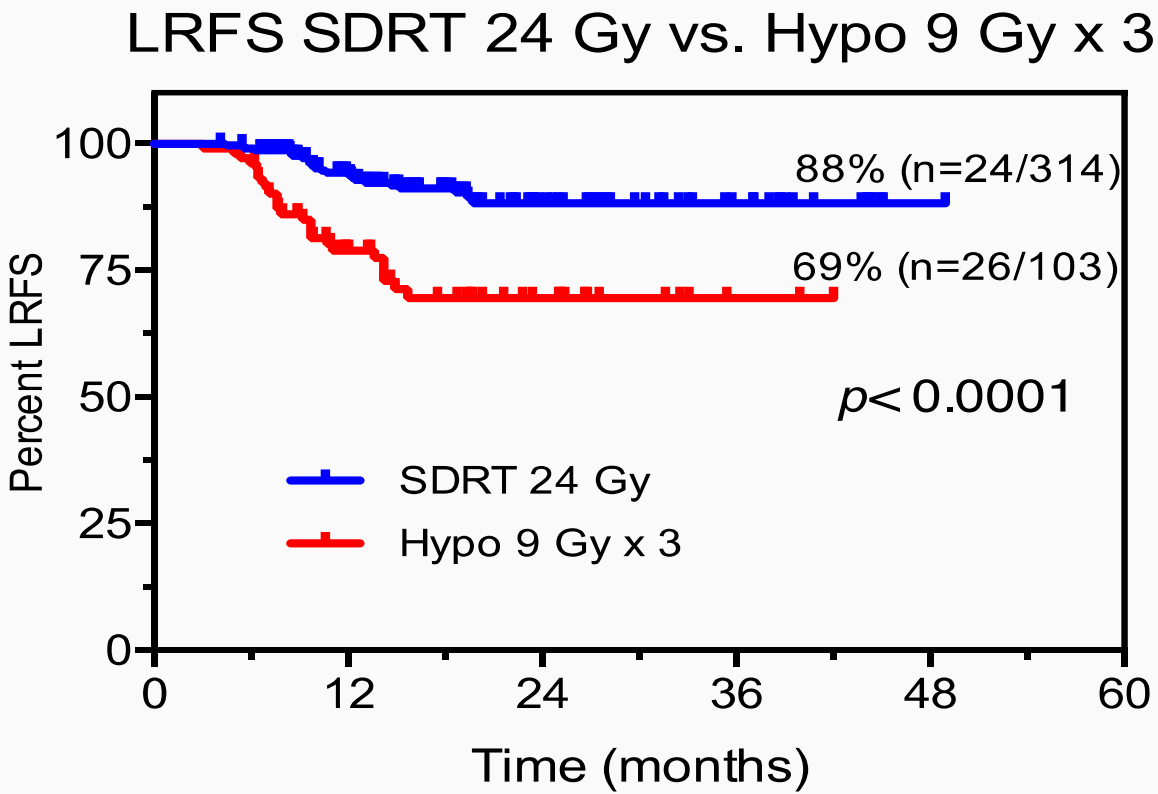

Greco C. *et al.* unpublished data

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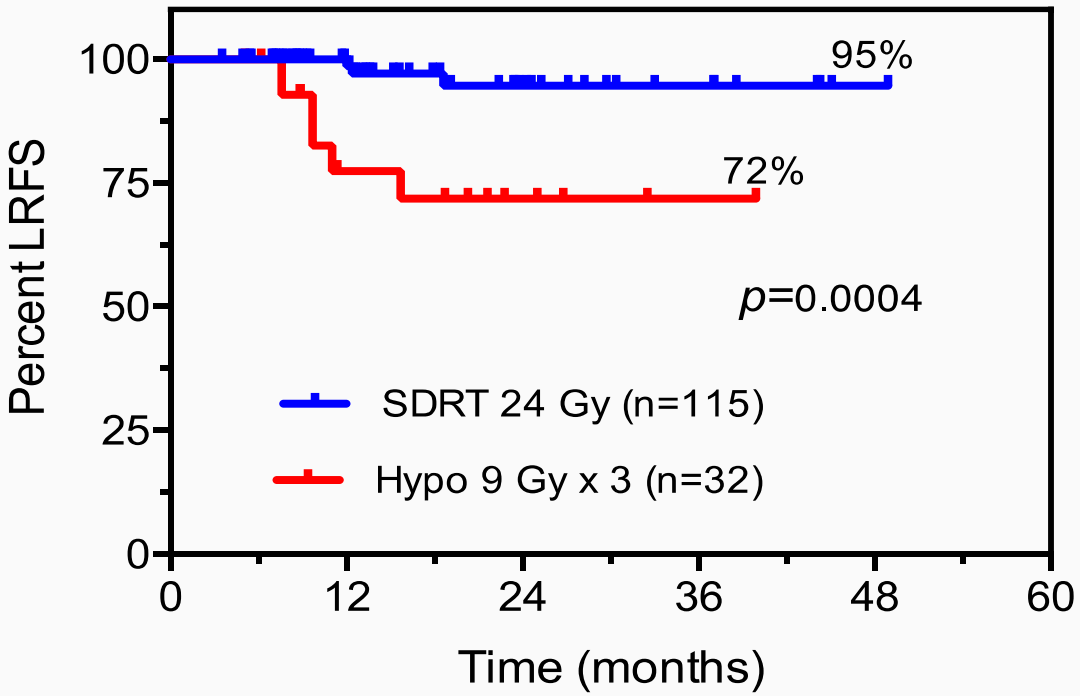
Bone only LRFS SDRT 24 Gy vs. Hypo 9 Gy x 3



Greco C. *et al.* unpublished data

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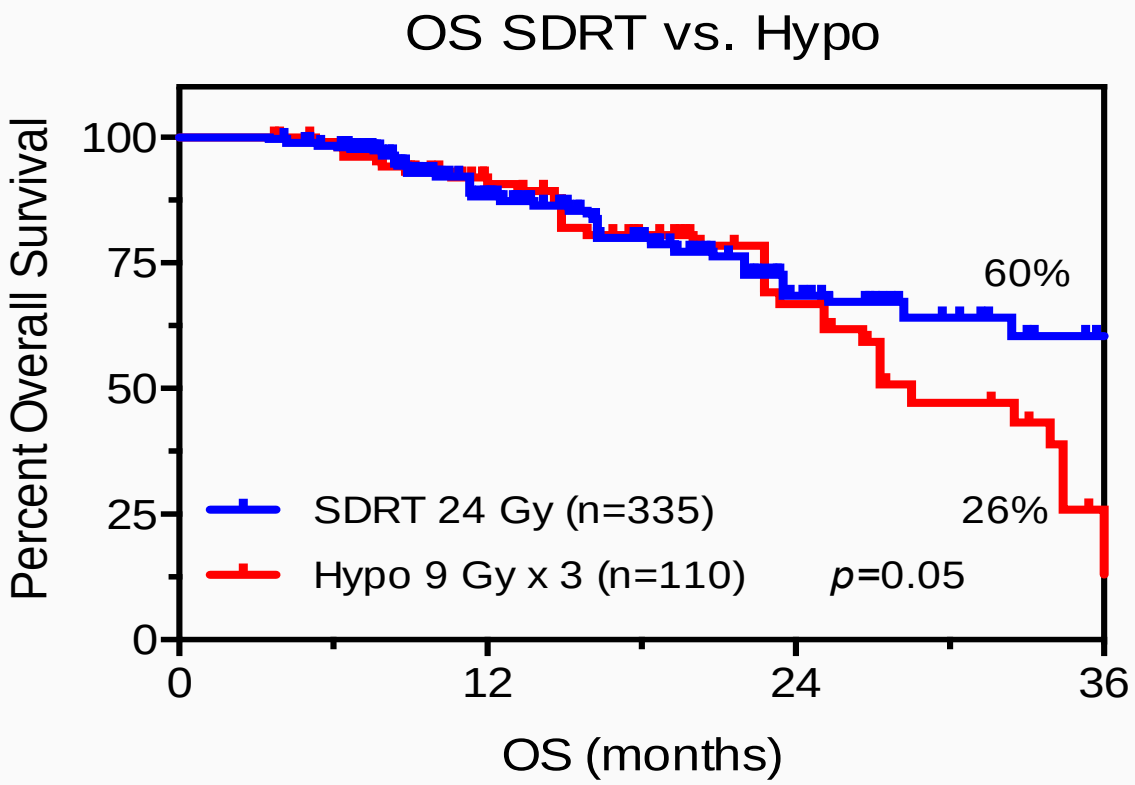

Greco C. *et al.* unpublished data

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The quest for an early predictor of local control post-SDRT
The role of molecular imaging

Post-treatment changes in FDG-PET SUV_{max} as a predictor of response

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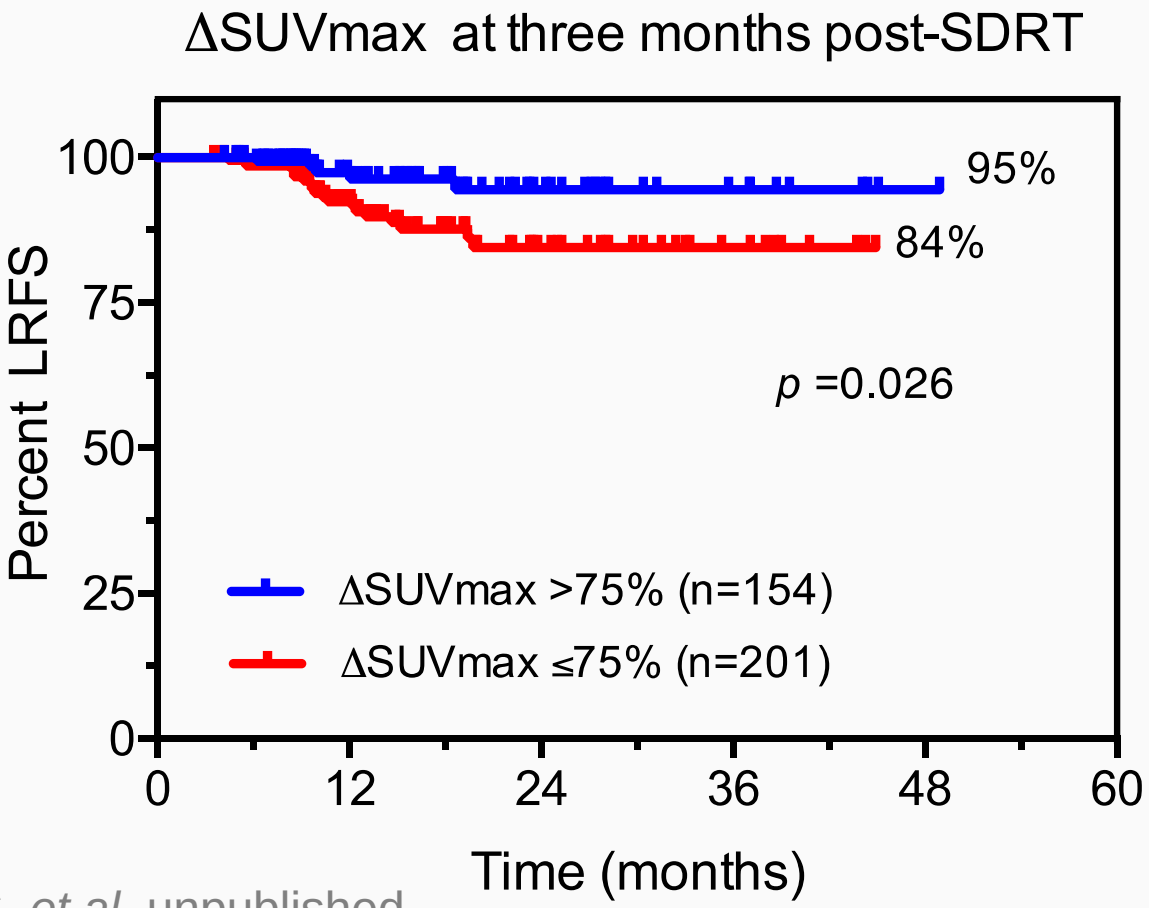

Greco C. *et al.* unpublished

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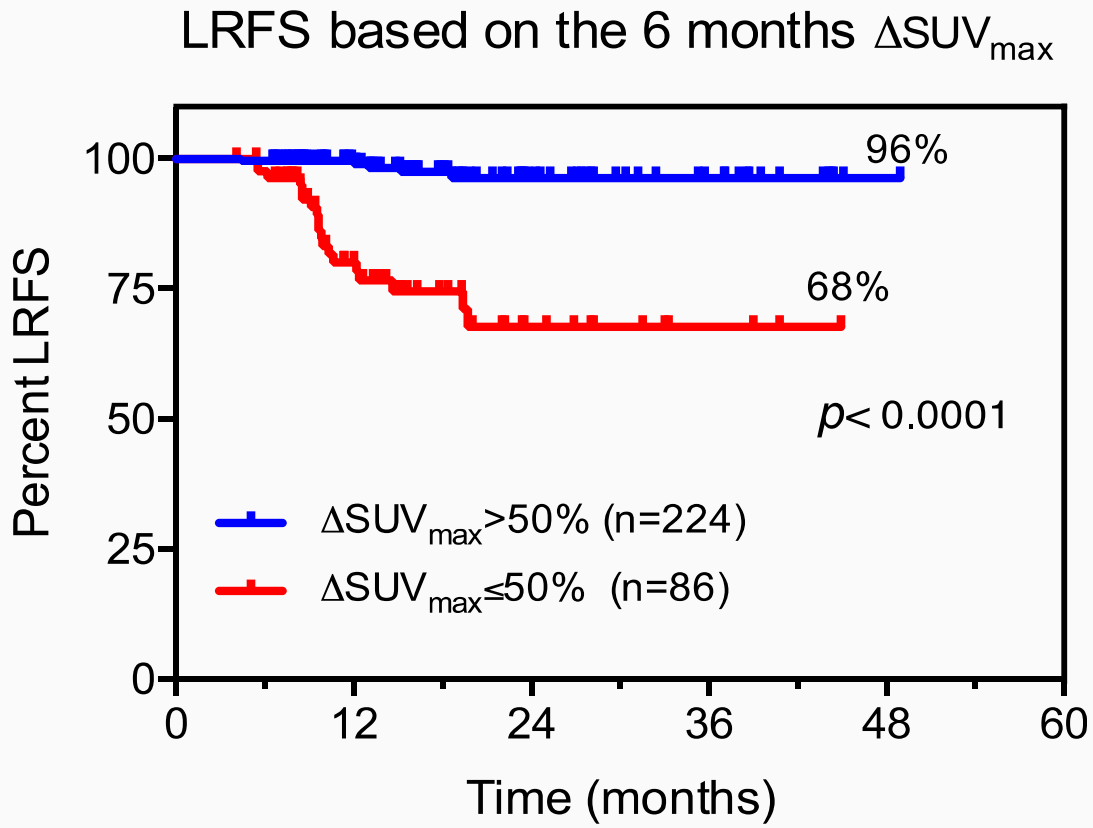

Greco C. *et al.* unpublished

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One size (dose) fits all?

- The exciting clinical outcomes achieved with 24 Gy prescribed to the PTV indicate a saturation of the vascular engagement and producing enhanced tumor stem cell kill even for the most radio-resistant phenotypes

- A quest for custom-tailored dose prescription based on tumor biological information is mandatory to expand the breadth of SD-IGRT applications

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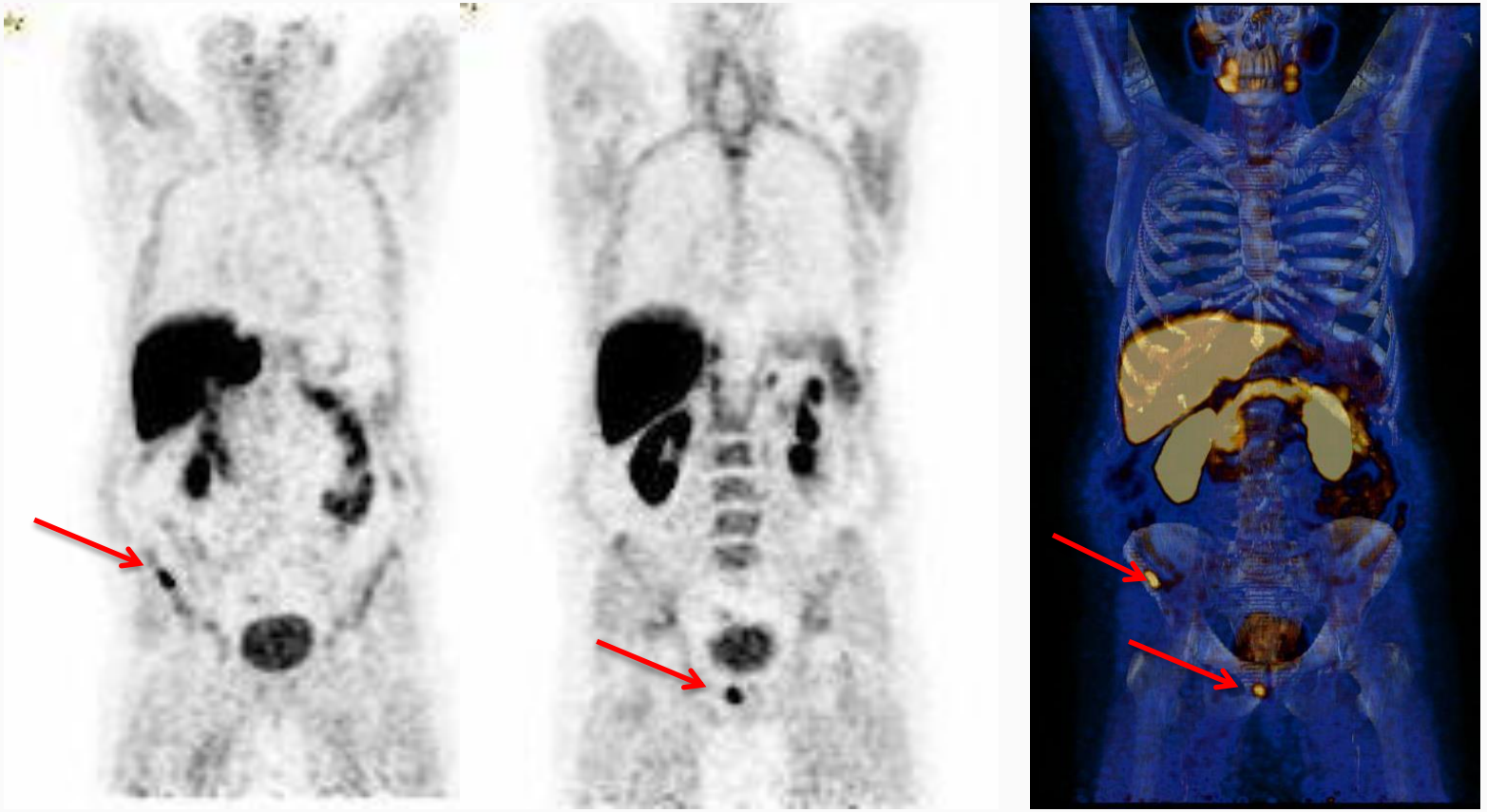
65 YO castration-resistant oligometastatic prostate cancer

T3 posterior R lobe lesion – initial diagnosis in 2010
Solitary bone M+ at presentation
GPS 8 (4+4) iPSA >30 ng/mL
3 Years of MAB
PSA rise to 11 ng/mL in 10/2013



Only 2 active foci of disease: 1 bone
and a persistent local treatment-naïve prostate lesion

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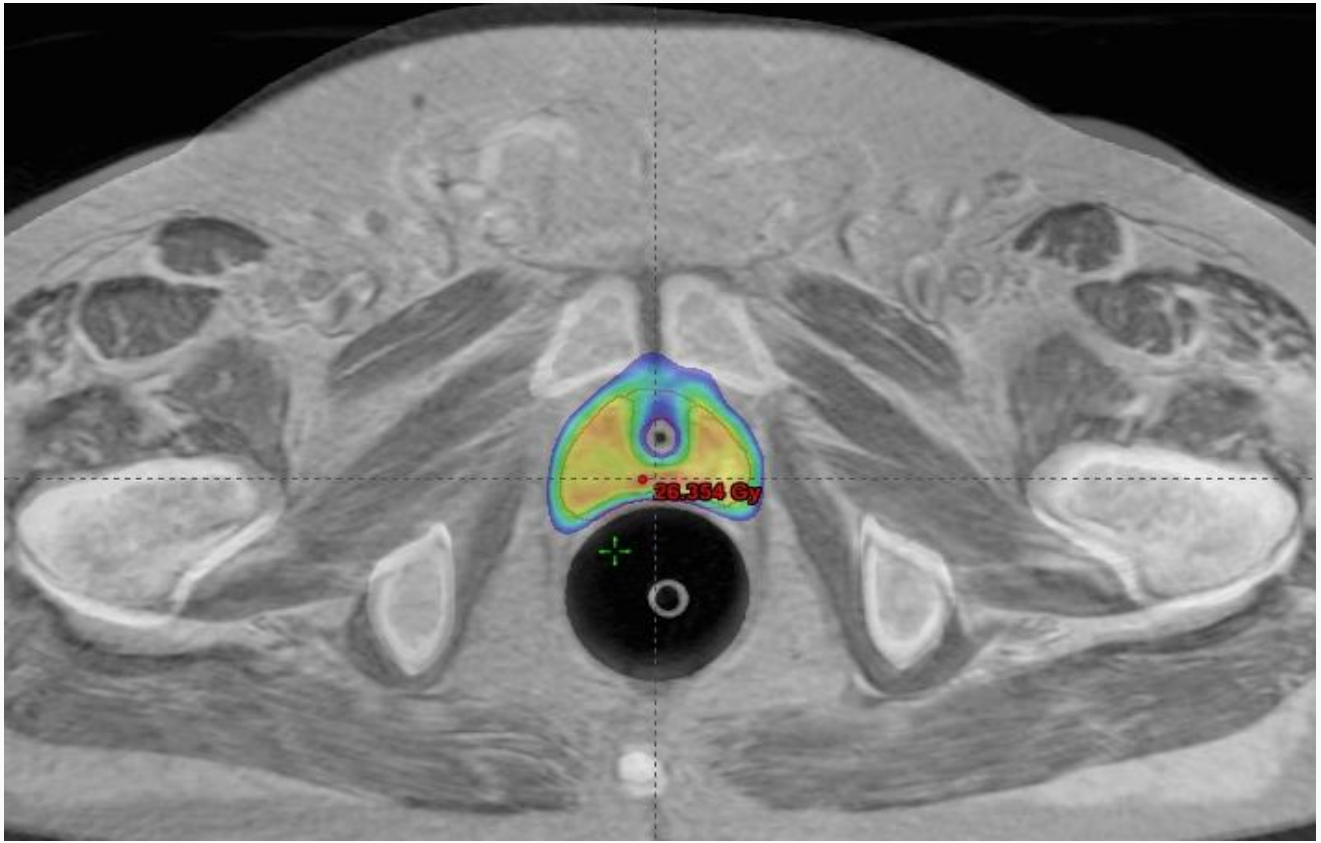
Single dose IGRT to the primary prostate tumor in a Stage IV patient receiving concurrent SD-IGRT to a metastatic bone lesion



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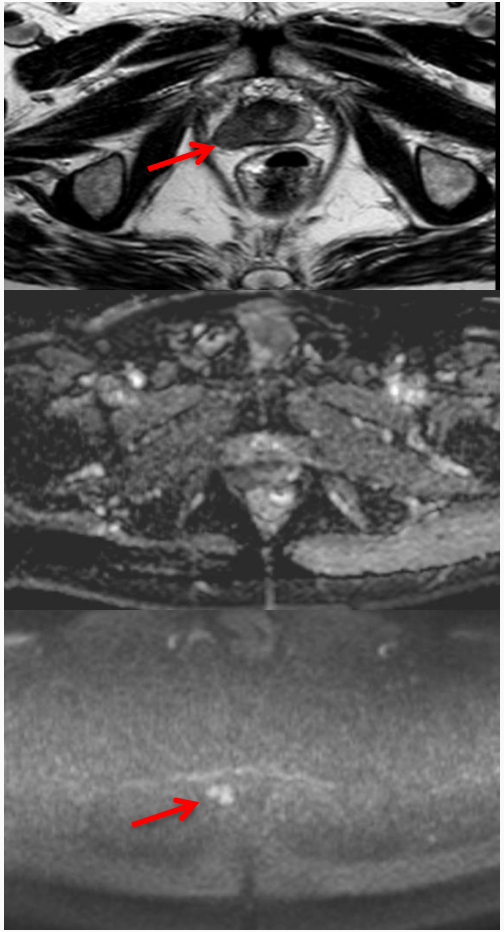
Baseline (iPSA 11)

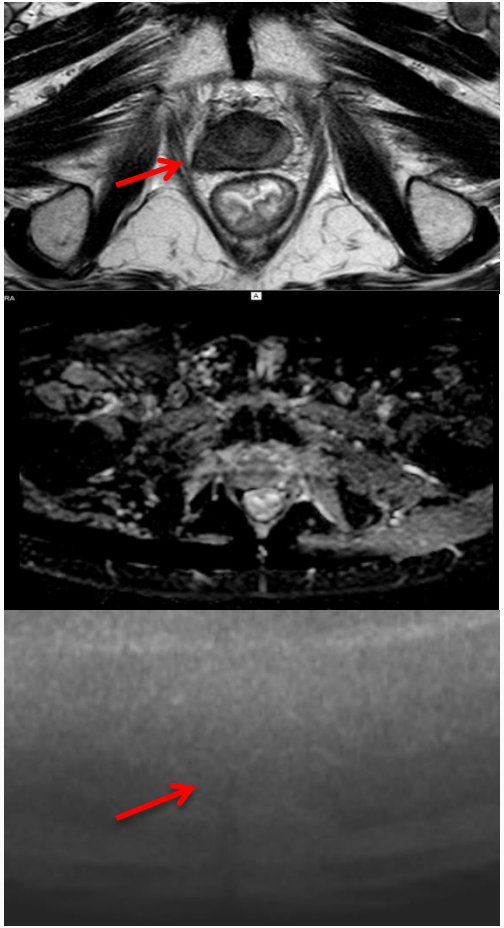
3 Mo post treatment (PSA 0.47)



T2

ADC

DWI



Posterior R lobe
lobe
dominant lesion

GPS 8 (4+4)

Solitary bone M+ at presentation

Complete loss of hyperintense DWI signal at 3 months

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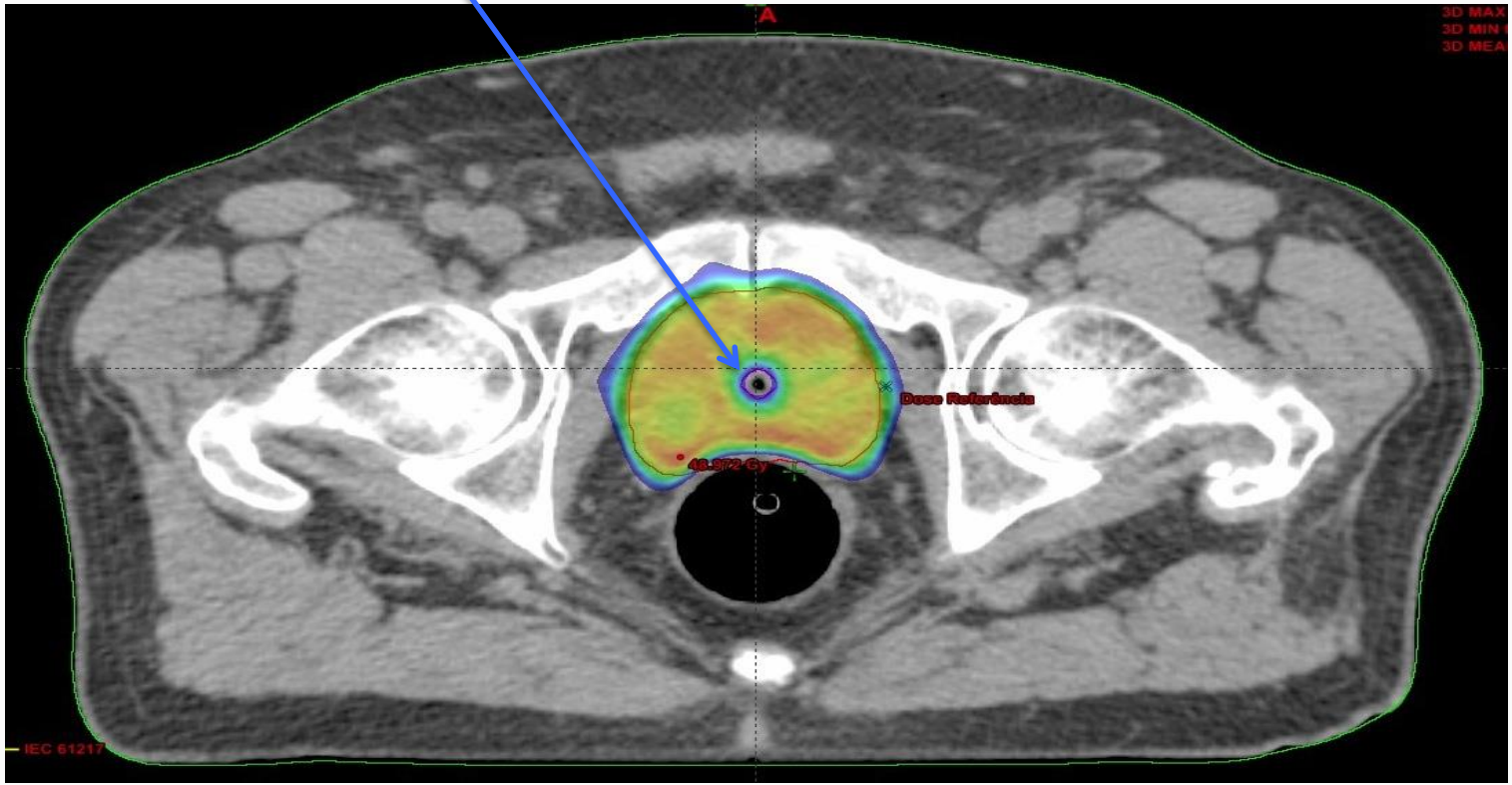
Urethral-sparing in ultra-high dose IGRT



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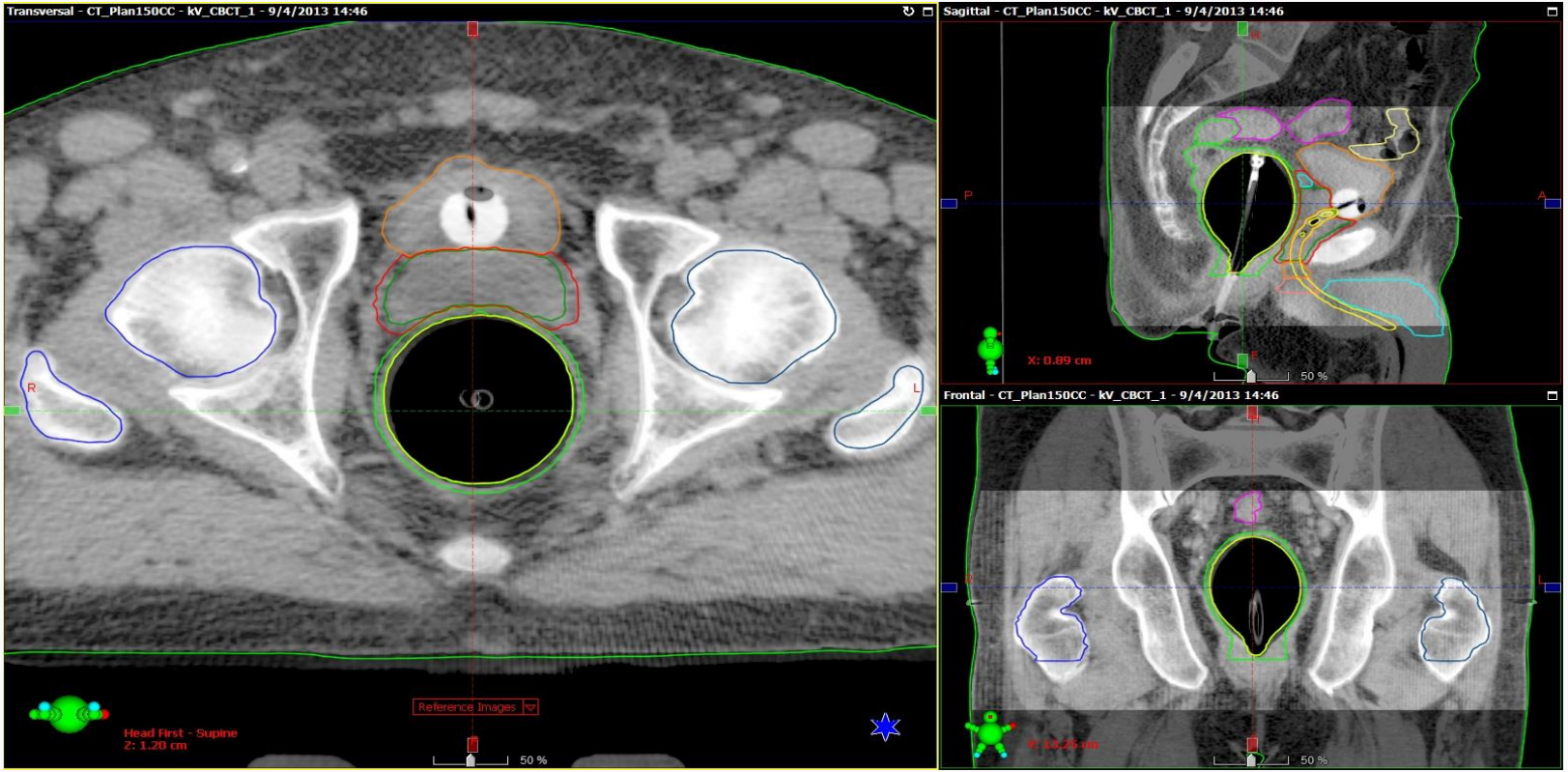

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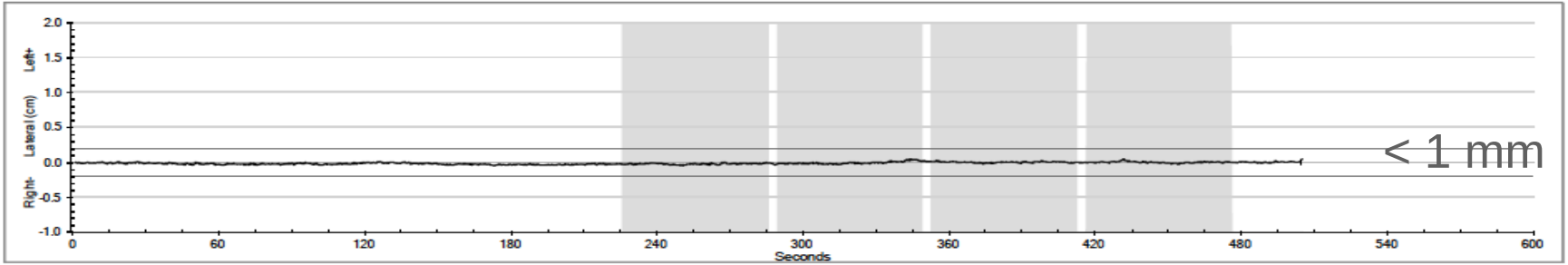

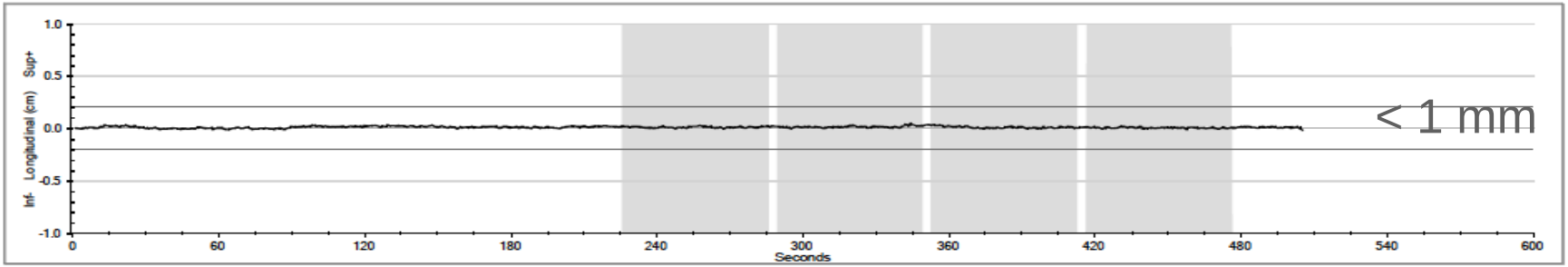

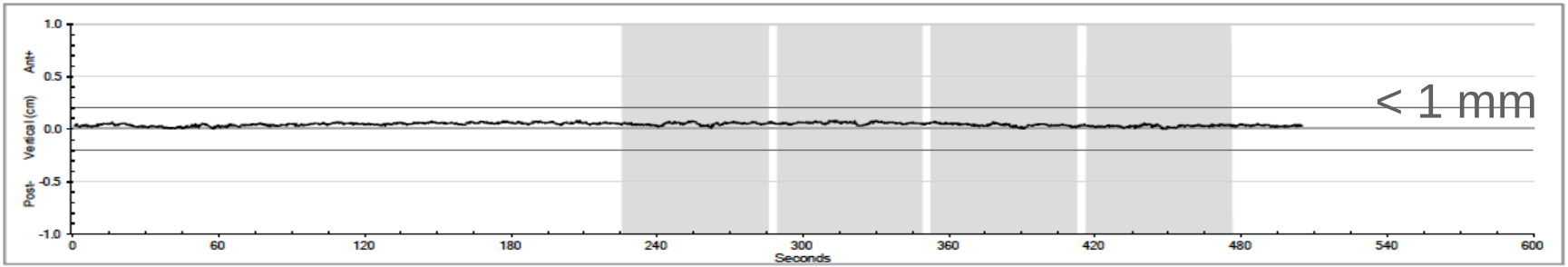

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Radiation Detected

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24 Gy SDRT for oligometastatic, local treatment-naïve prostate cancer

CCU initial experience

22 patients treated since July 2013
Median follow-up 21 months (range, 3-31)

Acute GU ≥G2 5% - No G3
Acute GI ≥G2 0%

Late GU ≥G2 5% No G3
Late GI ≥G2 0%

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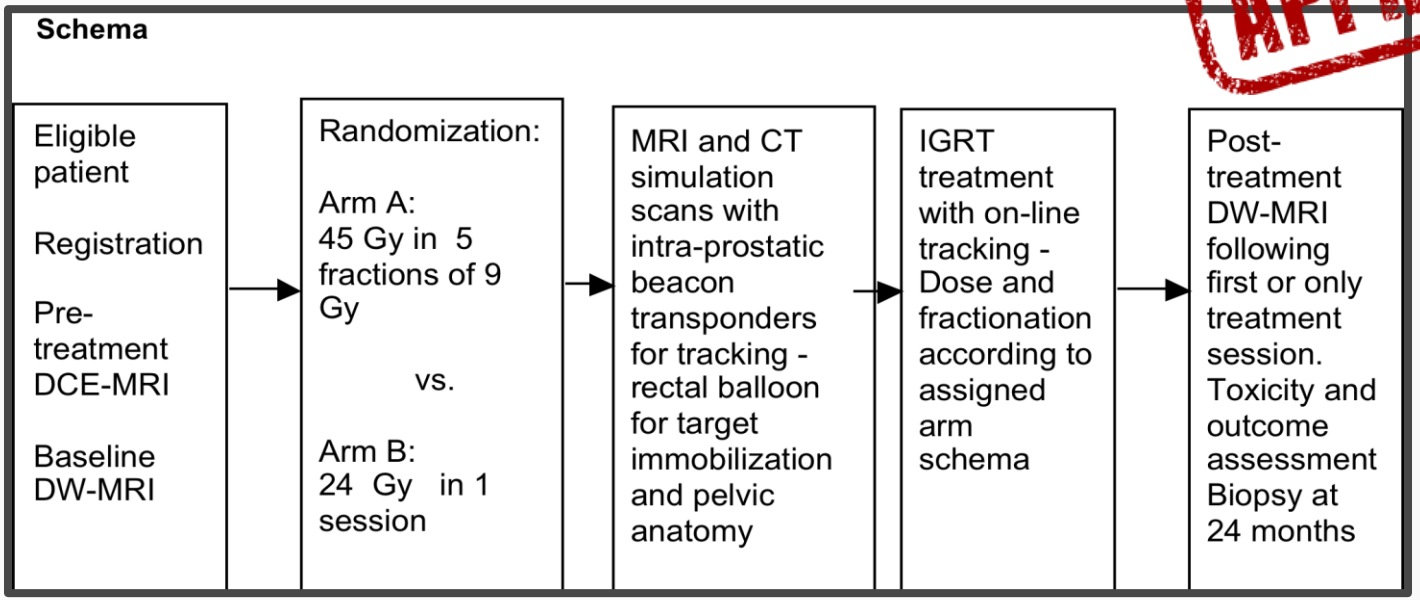
PROSINT

Phase II Randomized Study Comparing Ultra-High-Dose Hypofractionated vs. Single-Dose Image-Guided Radiotherapy (IGRT) with Urethral Sparing for Intermediate Risk Prostate Cancer

NCT02570919

APPROVED

Schema



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