

# “Linac Based SBRT for Low–intermediate Risk Prostate Cancer in 5 Fractions: Preliminary Report of a Phase II Study with FFF Delivery”

FILIPPO ALONGI MD

Radiation Oncology & Radiosurgery

Istituto Clinico Humanitas

Rozzano–Milan



UNIVERSITÀ  
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DI MILANO

INTERNATIONAL  
MEDICAL SCHOOL

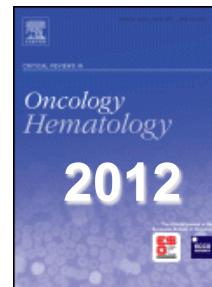
ISTITUTO CLINICO  
HUMANITAS  
Istituto di Ricovero e Cura  
a Carattere Scientifico



## SBRT and (Extreme) Hypofractionation



ELSEVIER



Critical Reviews in Oncology/Hematology xxx (2012) xxx–xxx

CRITICAL REVIEWS IN

*Oncology  
Hematology*

*Incorporating Geriatric Oncology*

[www.elsevier.com/locate/critrevonc](http://www.elsevier.com/locate/critrevonc)

Will SBRT replace conventional radiotherapy in patients with  
low-intermediate risk prostate cancer? A review

Stefano Arcangeli\*, Marta Scorsetti, Filippo Alongi

*Radiotherapy and Radiosurgery department, Istituto Clinico Humanitas, Humanitas Cancer Center, Rozzano, Milano, Italy*

Accepted 23 November 2011

## Humanitas Protocol: FEATURES

**SBRT**  
7Gy x5  
(alternative days)

**FFF beams**  
(RapidArc Technique  
on TrueBeam)

**SpaceOAR**  
(optionally)

## Is $\alpha/\beta$ ratio really low in prostate cancer?

### CLINICAL INVESTIGATION

### Genitourinary Cancer



#### DOSE-FRACTIONATION SENSITIVITY OF PROSTATE CANCER DEDUCED FROM RADIOTHERAPY OUTCOMES OF **5,969 PATIENTS** IN SEVEN INTERNATIONAL INSTITUTIONAL DATASETS: $\alpha/\beta = 1.4$ (0.9–2.2) GY

RAYMOND MIRALBELL, M.D.,\*<sup>†</sup> STEPHEN A. ROBERTS, PH.D.,<sup>‡</sup> EDUARDO ZUBIZARRETA, M.D.,<sup>§</sup>  
AND JOLYON H. HENDRY, PH.D.<sup>||</sup>

### CLINICAL INVESTIGATION

### Prostate



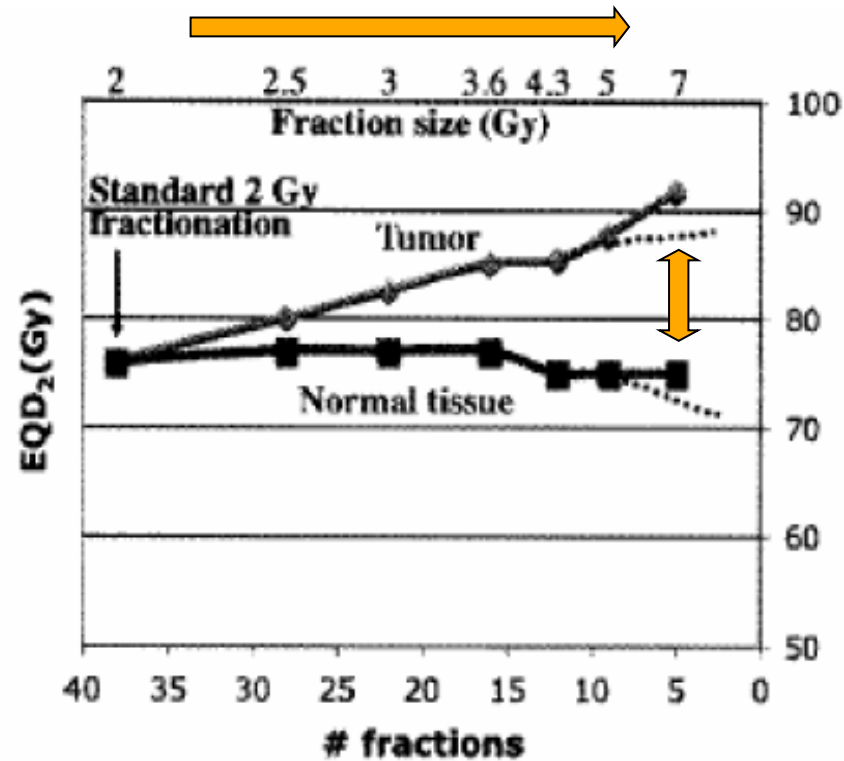
#### CONFIRMATION OF A LOW $\alpha/\beta$ RATIO FOR PROSTATE CANCER TREATED BY EXTERNAL BEAM RADIATION THERAPY ALONE USING A POST-TREATMENT REPEATED-MEASURES MODEL FOR PSA DYNAMICS

CÉCILE PROUST-LIMA, PH.D.,\*<sup>†</sup> JEREMY M. G. TAYLOR, PH.D.,<sup>‡§</sup> SOLÈNE SÉCHER, PH.D.,\*<sup>†</sup>  
HOWARD SANDLER, M.D.,<sup>||</sup> LARRY KESTIN, M.D.,<sup>¶</sup> TOM PICKLES, M.D.,<sup>#</sup> KYOUNGWHA BAE, PH.D.,\*\*  
ROGER ALLISON, F.R.A.N.Z.C.R.,<sup>††</sup> AND SCOTT WILLIAMS, M.D., F.R.A.N.Z.C.R.<sup>‡‡</sup>

..in **5,069pts**



## BACKGROUND: Hypofractionation and therapeutic Ratio



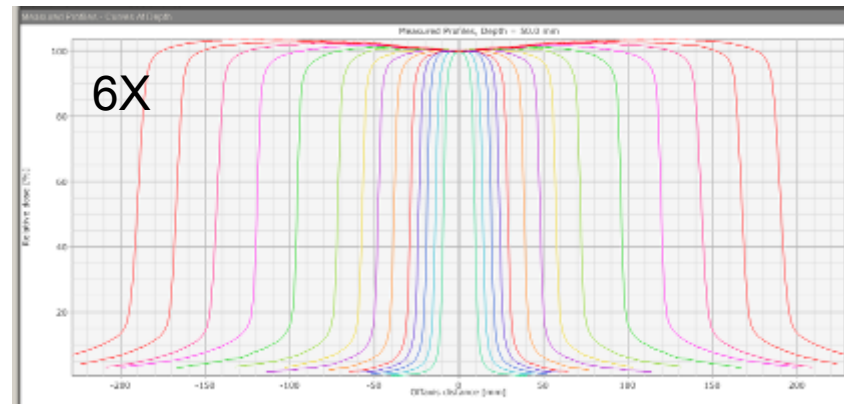
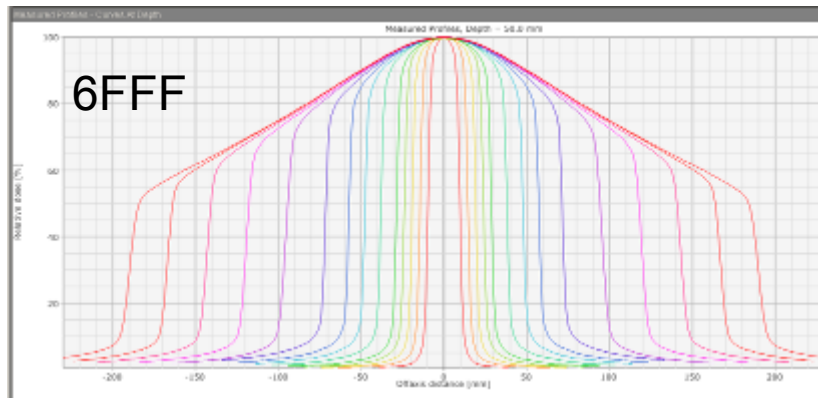
Ritter et al Cancer J 2009

## Humanitas Protocol :Treatment Schedule

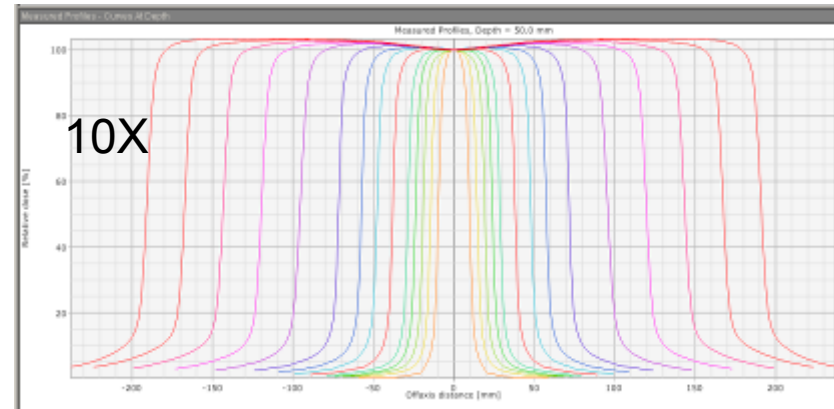
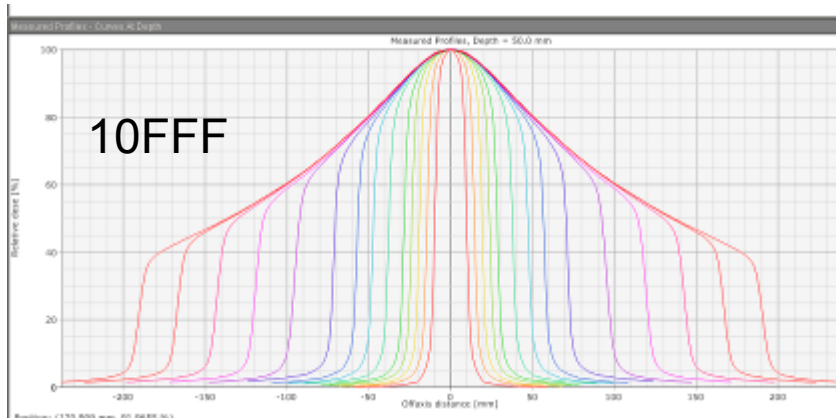
n. of fractions	fraction size (Gy)	Total dose (Gy)	weeks of treatment	NTD <sub>2</sub> for an $\alpha/\beta$ (Gy) value of			OK BED <sub>10</sub> (Gy)
				1,5	3	10	
5	7	35,0	1,5	85,0	70,0	49,6	56,7

NTD<sub>2</sub> OK for controlling low and intermediate risk disease and late tox

## Unflattened Beam and SBRT



### TRUE BEAM: Beams profiles



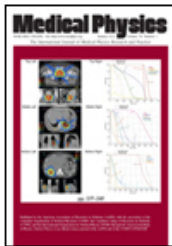
## Unflattened Beam and SBRT: our experience



2012

### Stereotactic body radiation therapy for liver tumours using flattening filter free beam: dosimetric and technical considerations.

Pietro Mancosu, Simona Castiglioni, Giacomo Reggiori, Maddalena Catalano, Filippo Alongi, Chiara Pellegrini, Stefano Arcangeli, Angelo Tozzi, Francesca Lobefalo, Antonella Fogliata, Piera Navarria, Luca Cozzi and Marta Scorsetti



2012

### Can volumetric modulated arc therapy with flattening filter free beams play a role in stereotactic body radiotherapy for liver lesions? A volume-based analysis

Giacomo Reggiori, Pietro Mancosu,<sup>a)</sup> Simona Castiglioni, Filippo Alongi, Chiara Pellegrini, Francesca Lobefalo, and Maddalena Catalano  
*IRCCS Istituto Clinico Humanitas, 20089 Rozzano (Milano), Italy*

Antonella Fogliata  
*Oncology Institute of Southern Switzerland, Bellinzona, Switzerland*

Stefano Arcangeli and Piera Navarria  
*IRCCS Istituto Clinico Humanitas, 20089 Rozzano (Milano), Italy*

Luca Cozzi  
*Oncology Institute of Southern Switzerland, Bellinzona, Switzerland*

Marta Scorsetti  
*IRCCS Istituto Clinico Humanitas, 20089 Rozzano (Milano), Italy*

*....SBRT delivered High dose per fractions (25 Gy) by means of FFF resulted to be feasible with shorter treatment time*

## Humanitas Protocol: end points

**PRIMARY:**

Technical feasibility

Acute toxicity

**SECONDARY**

Late toxicity

Outcome

## MATERIAL AND METHODS

Between January 2012 and January 2013 :*40* patients for low and intermediate risk were recruited in the phase II study.

In all 40 patients:

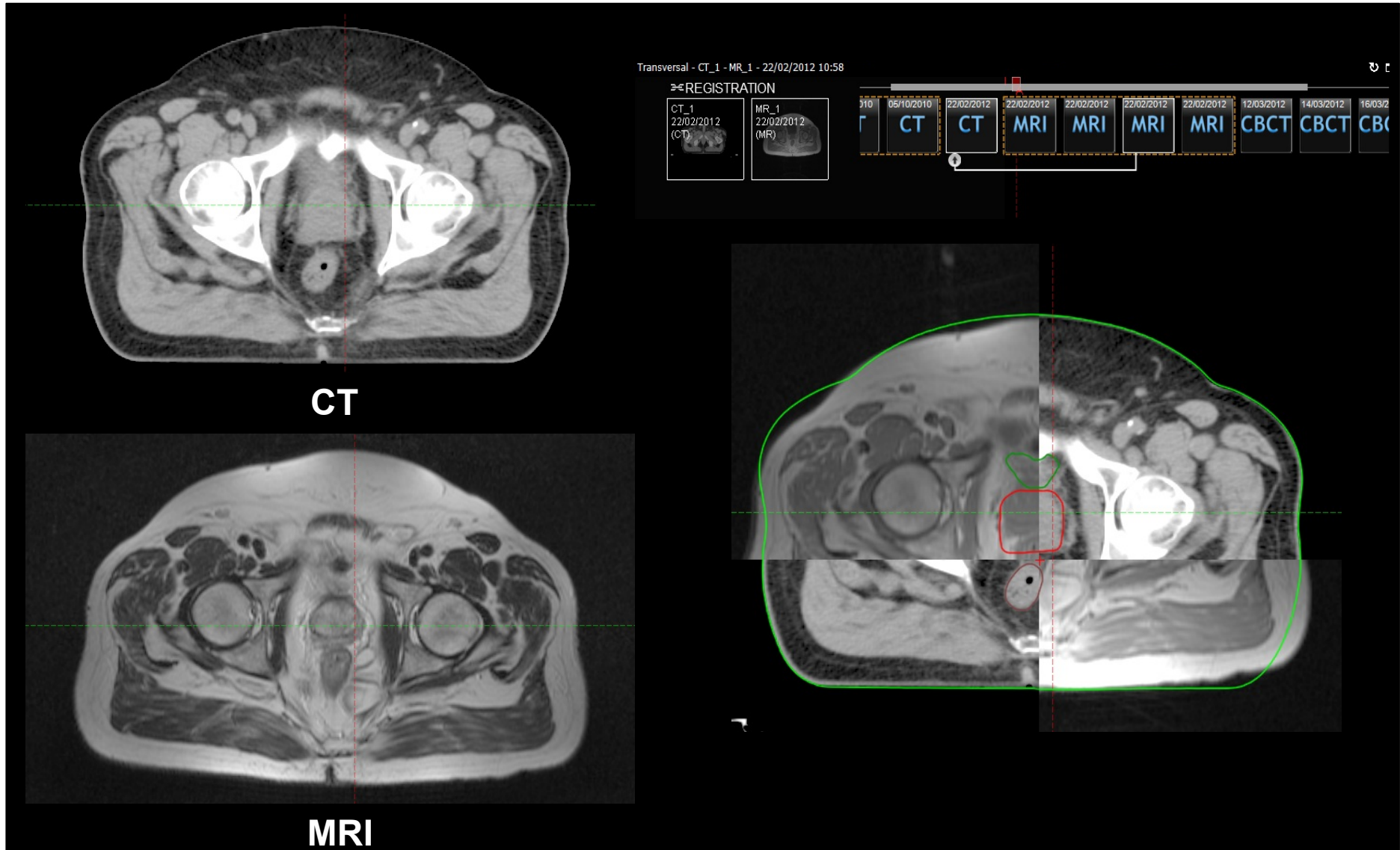
- CT/MRI was utilized for simulation procedure
- Dose prescription was: *35 Gy in 5 fractions* on prostate +/-seminal vesicles (based on Roach Formula risk for seminal vesicles)
- CTV→PTV margin was in 5 all direction and 3 posteriorly
- Delivery was performed by *TrueBeam with FFF beams* (RapidArc Technique)
- Daily CBCT was performed.



## Humanitas Protocol: Inclusion Criteria

- Age  $\leq$  80 years
- WHO performance status  $\leq$  2.
- Histologically proven prostate adenocarcinoma  $\rightarrow$  Any case where prophylactic lymph node irradiation is not required (risk of microscopic involvement  $\leq$  15%)
- PSA  $\leq$  20 ng/ml.
- T1–T2 (localized)–stage
- No pathologic lymph nodes at CT/ MR and NO distant metastases
- No previous prostate surgery other than TURP
- No malignant tumors in the previous 5 years
- IPSS 0–7
- Combined HT according to risk factors.
- Informed consent

## IMAGING and TARGET DEFINITION

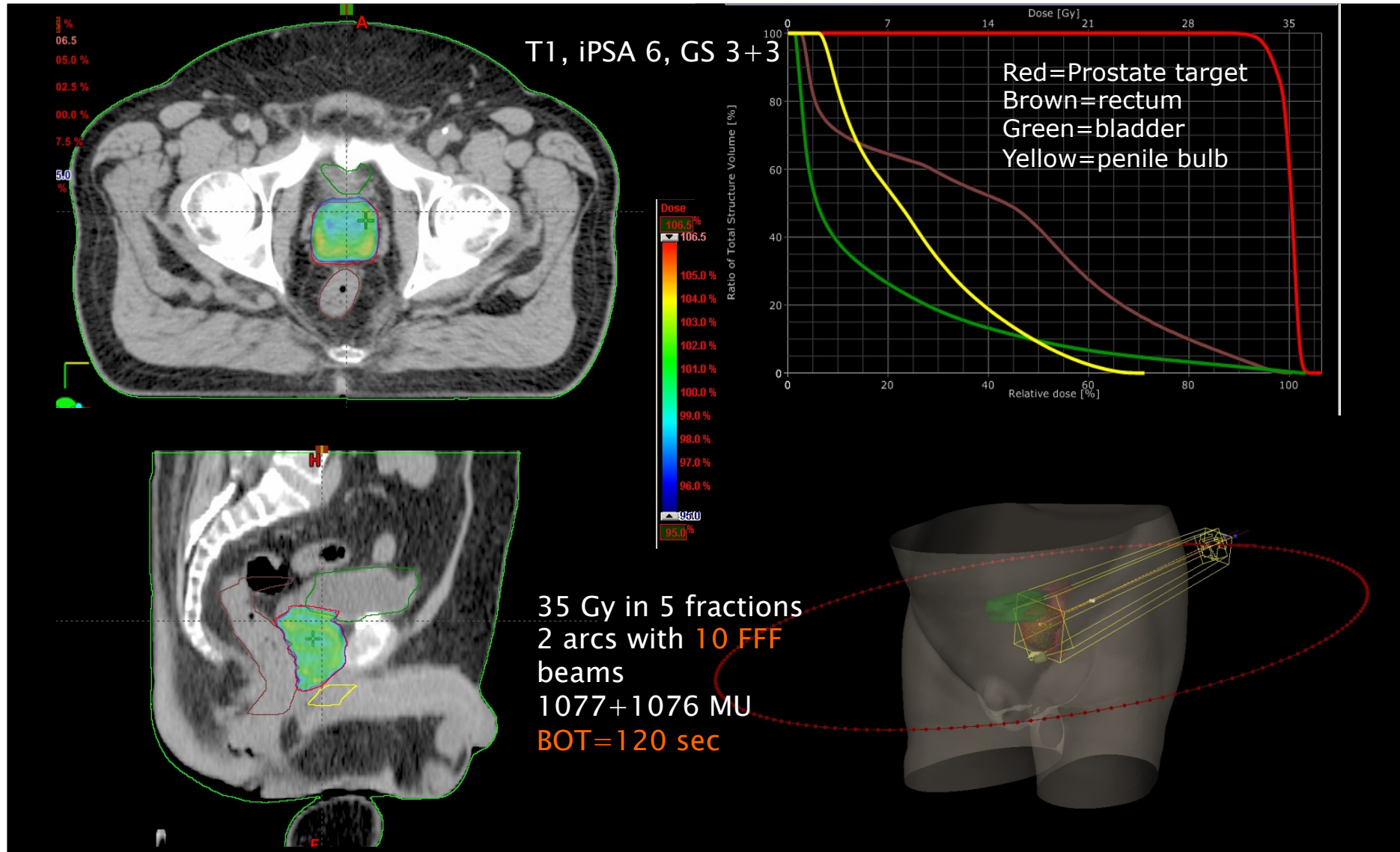


## PLANNING-CONSTRAINTS

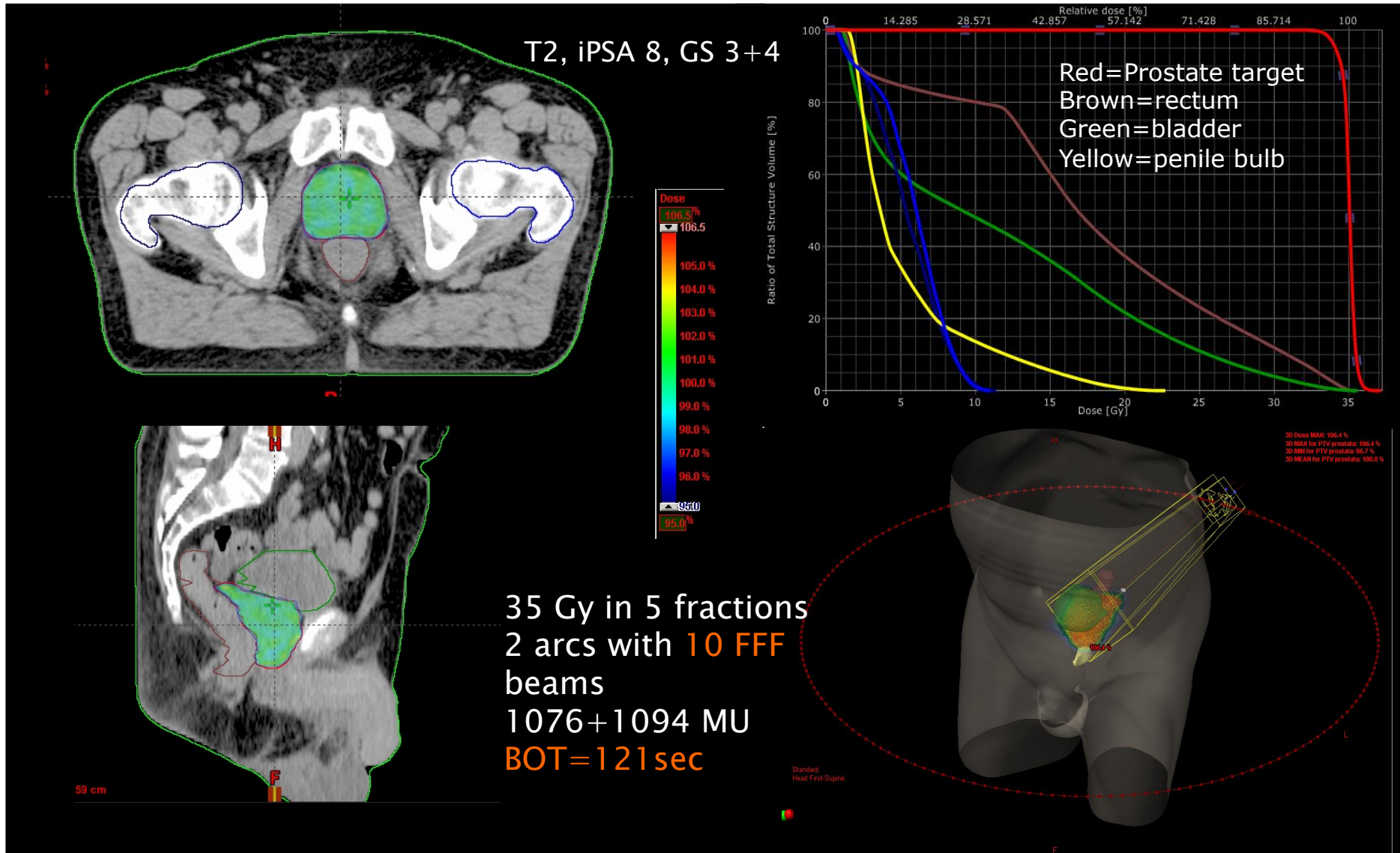
RECTUM	$V_{18 \text{ Gy}} \leq 35\%$ $V_{28 \text{ Gy}} \leq 10\%$ $V_{32 \text{ Gy}} \leq 5\%$ $V_{35 \text{ Gy}} \leq 5\%$ $D_{1\%} \leq 35 \text{ Gy}$
BLADDER	$D_{1\%} \leq 35 \text{ Gy}$

\*Target coverage was required to be:  **$V_{95\%} > 99\%$  on CTV ( $95\%$  on PTV)**

## PLANNING – LOW RISK



PLANNING – INTERMEDIATE RISK





## PROSTATE ON TRUE BEAM STx NOVALIS EXAC TRAC MATCHING

**Define DRR Settings**      Define Implanted Markers

Select Isocenter  
Isocenter Number - "External Name"  
Isocenter 1 - "CBCT,Field 1,Field 2"

Axial CT Slice: 64

View  
 Crosshair  
 Contours

Options  
 DRR VOI

Select Contours  
"cTV prostata" - Isocenter 1  
"HT1" - <not assigned>  
"Bulbo" - <not assigned>  
"Vescica" - <not assigned>

DRR Preview

Modify DRR Rendering ...

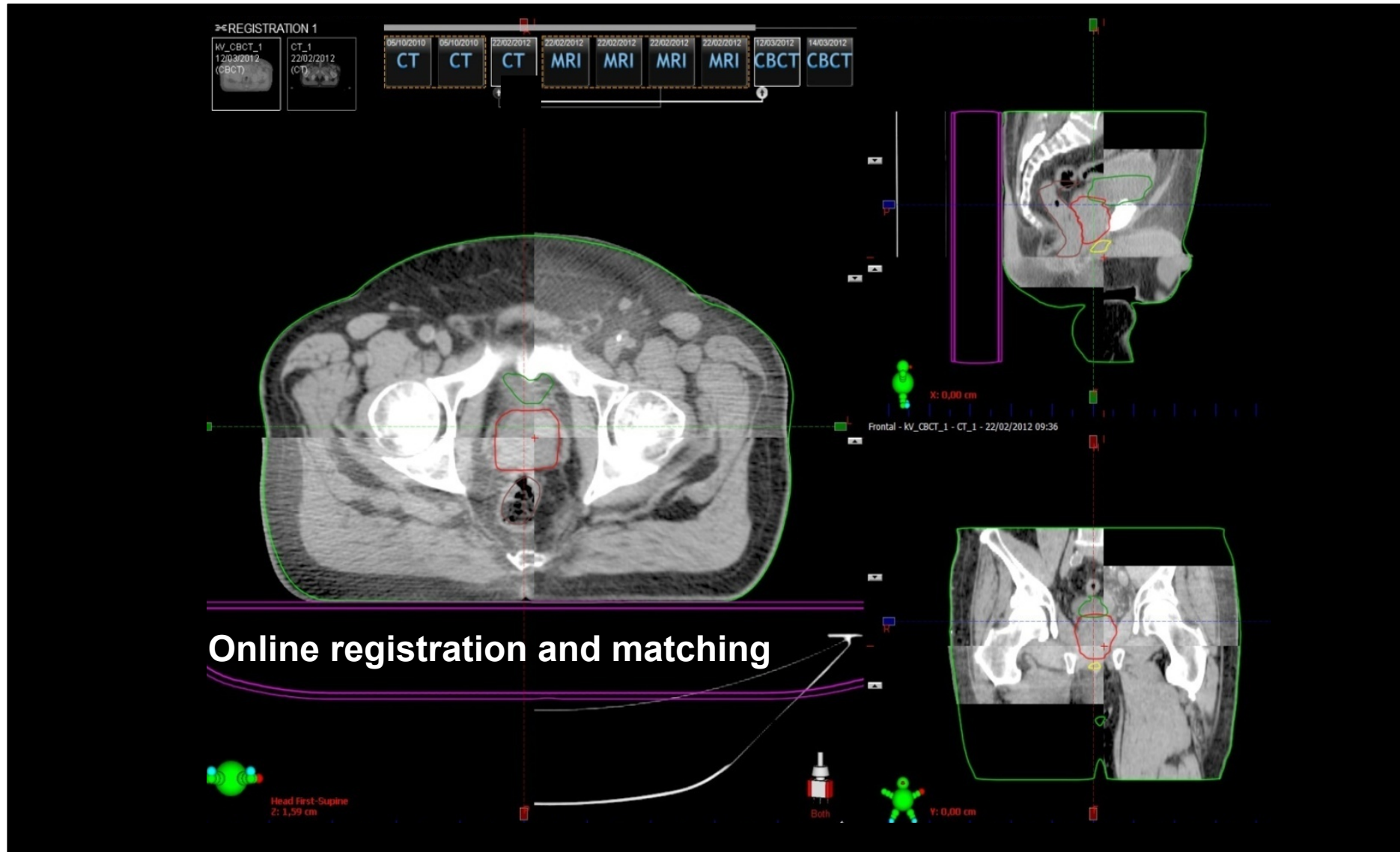
Coronal

Sagittal

Axial Slices



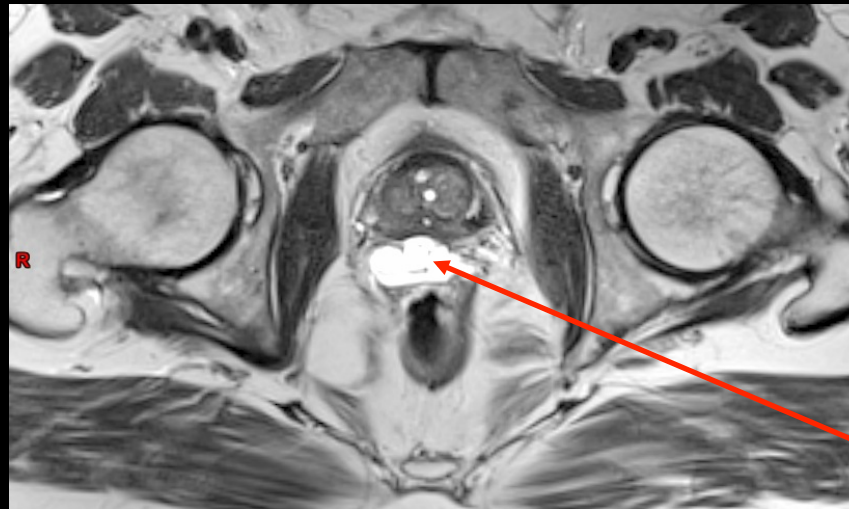
## DAILY TREATMENT VERIFICATION



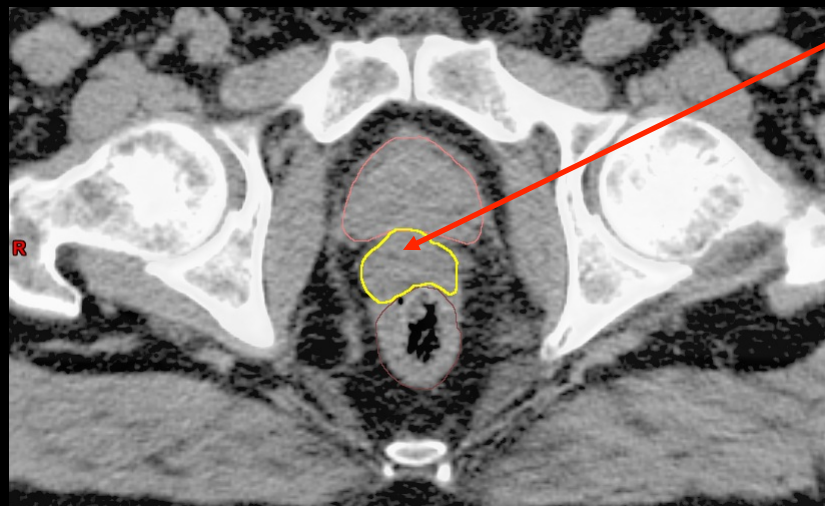
## SPACEOAR IN HUMANITAS SBRT PROTOCOL

CASE 1

MRI T2 Image

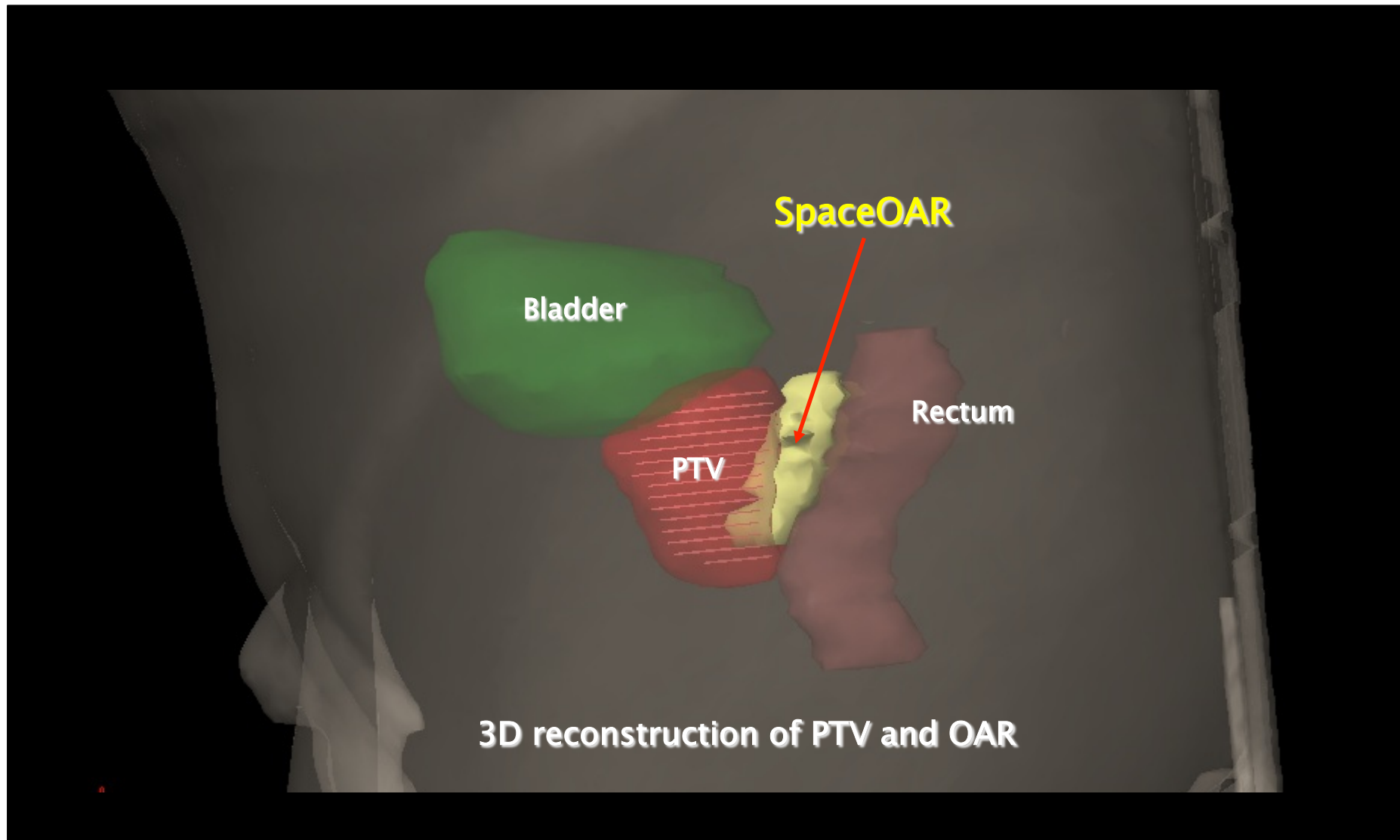


CT Image



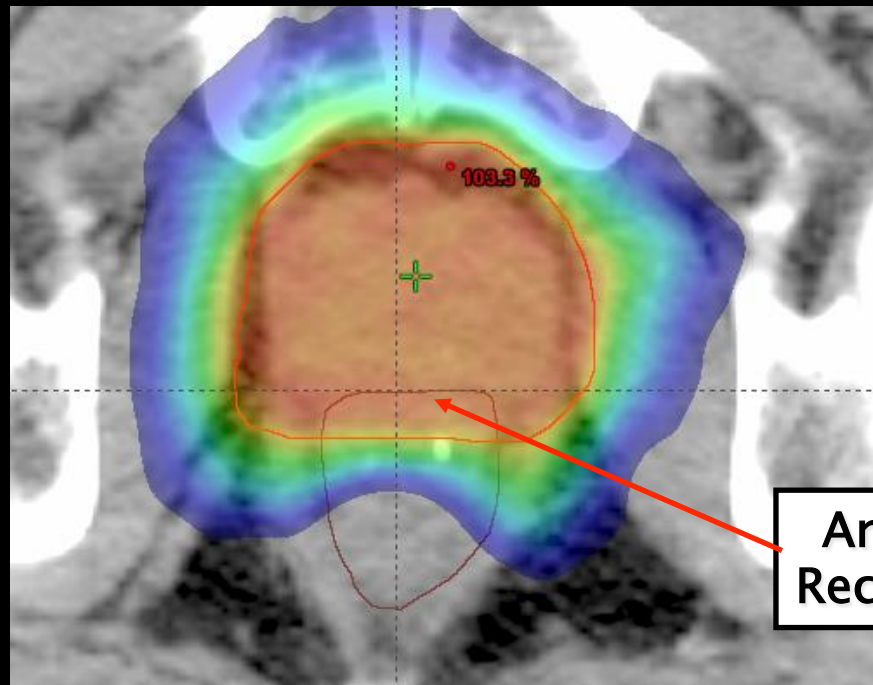
SpaceOAR

## SPACEOAR IN SBRT PROTOCOL

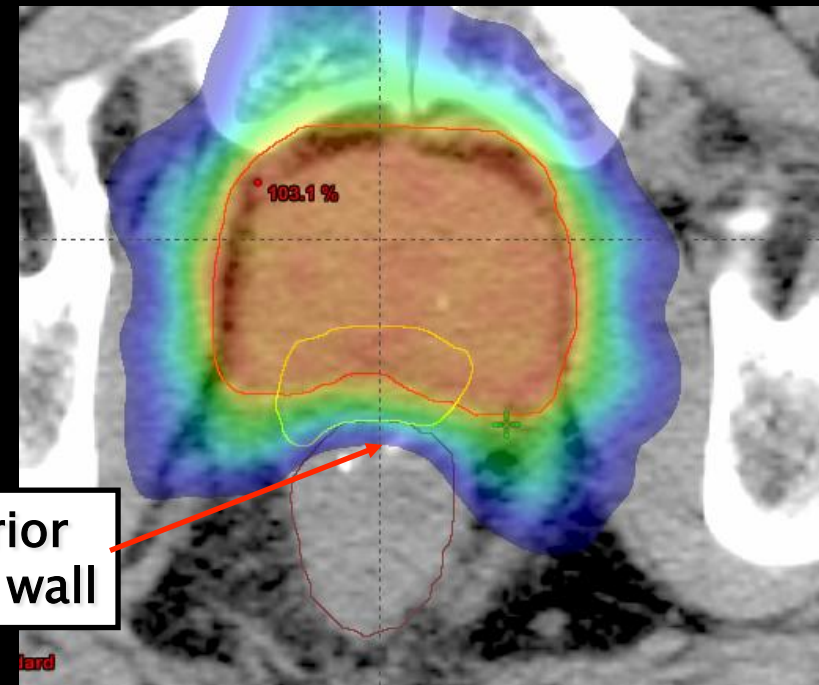


## SPACEOAR IN HUMANITAS SBRT PROTOCOL

### CASE 5



Dose Distribution  
Isodose 50%



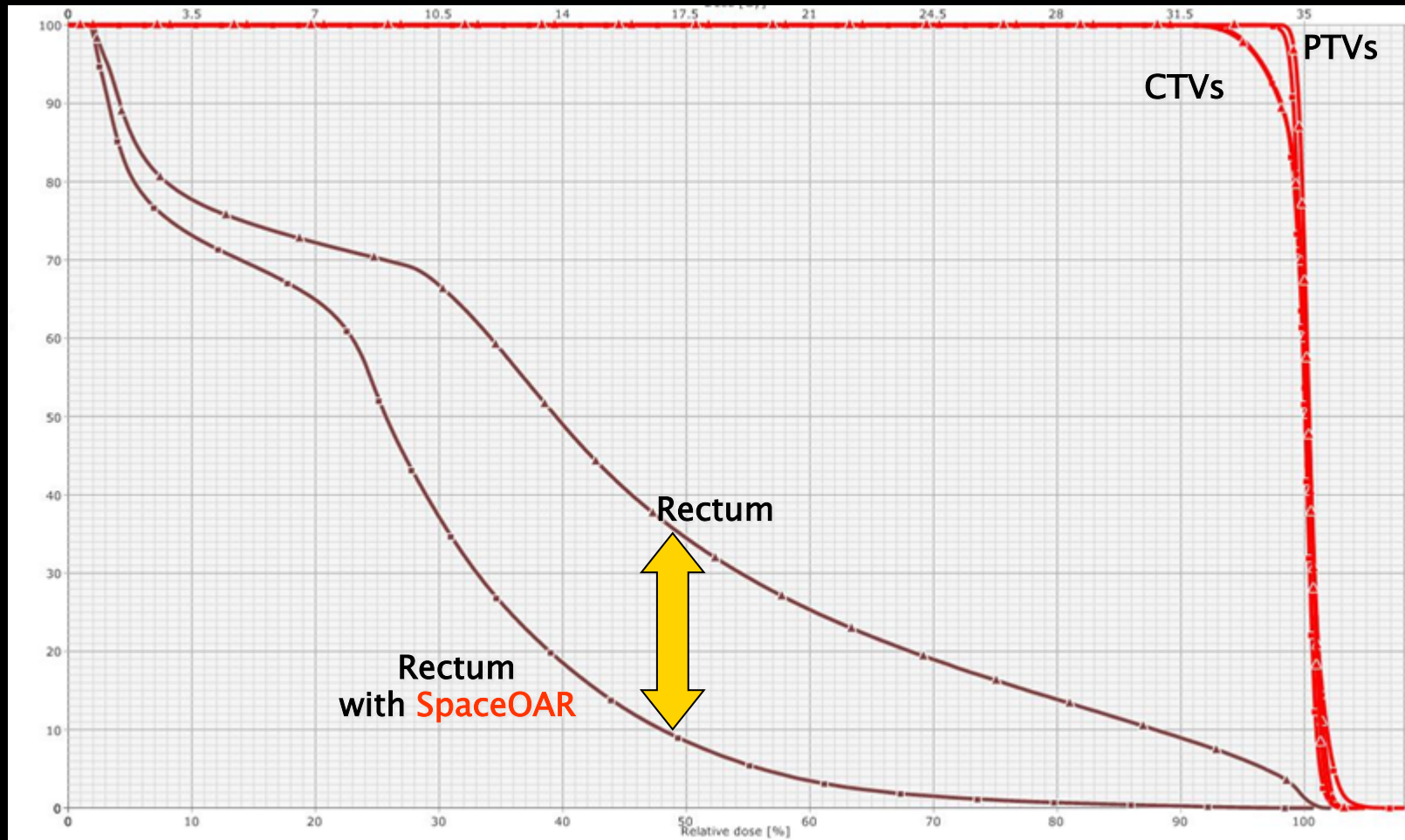
Dose distribution  
Isodose 50%  
with **SpaceOAR**

Anterior  
Rectal wall



## SPACEOAR IN SBRT PROTOCOL

CASE 5



DVH COMPARISON

## Humanitas Protocol: PRELIMINARY RESULTS

Alongi et al. *Radiation Oncology* 2013, **8**:171  
<http://www.ro-journal.com/content/8/1/171>



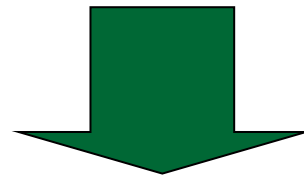
Published on June 2013

RESEARCH

Open Access

### Linac based SBRT for prostate cancer in 5 fractions with VMAT and flattening filter free beams: preliminary report of a phase II study

Filippo Alongi<sup>1,4\*</sup>, Luca Cozzi<sup>2</sup>, Stefano Arcangeli<sup>1</sup>, Cristina Iftode<sup>1</sup>, Tiziana Comito<sup>1</sup>, Elisa Villa<sup>1</sup>, Francesca Lobefalo<sup>1</sup>, Pierina Navarria<sup>1</sup>, Giacomo Reggiori<sup>1</sup>, Pietro Mancosu<sup>1</sup>, Elena Clerici<sup>1</sup>, Antonella Fogliata<sup>2</sup>, Stefano Tomatis<sup>1</sup>, Gianluigi Taverna<sup>3</sup>, Pierpaolo Graziotti<sup>3</sup> and Marta Scorsetti<sup>1</sup>



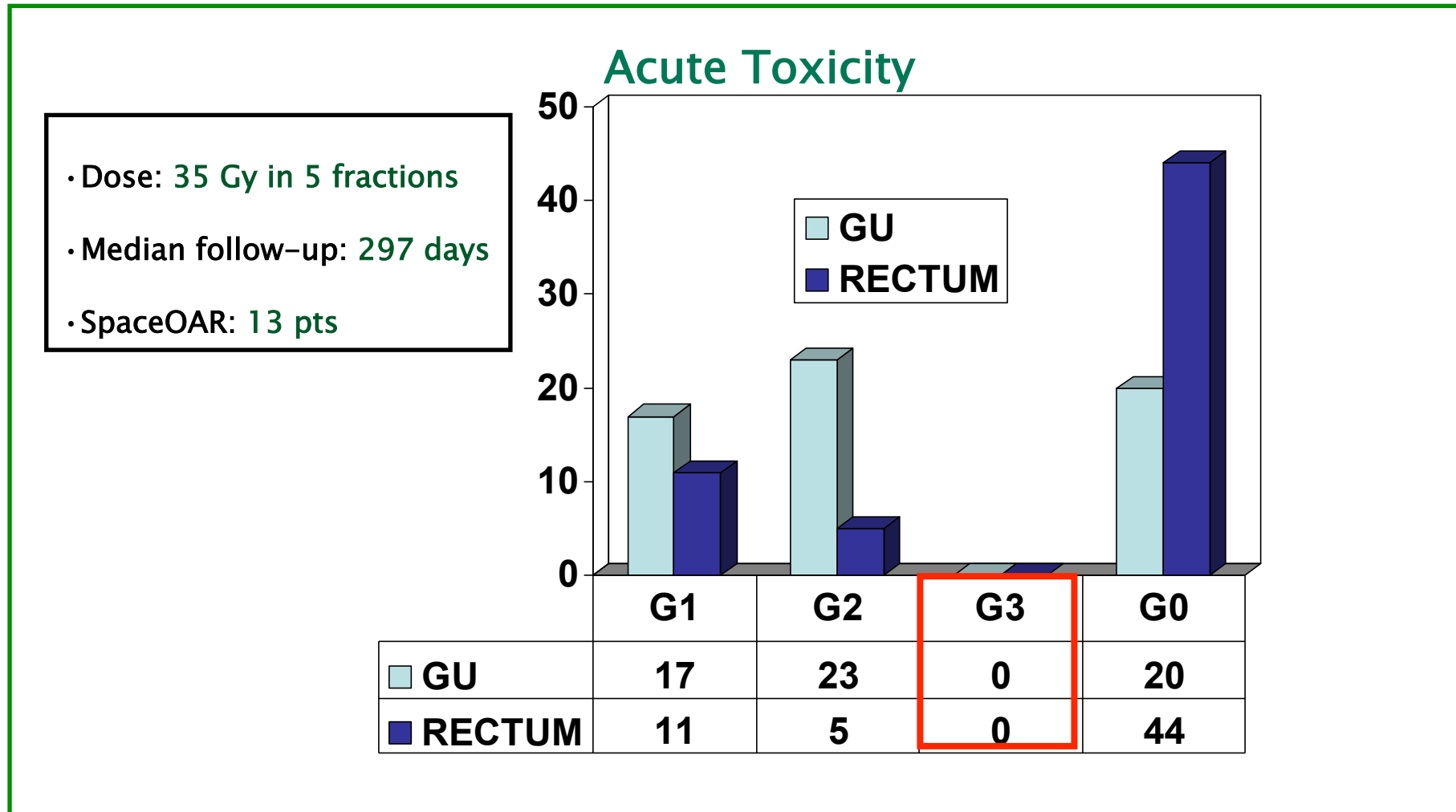
The first **40** patients analysis



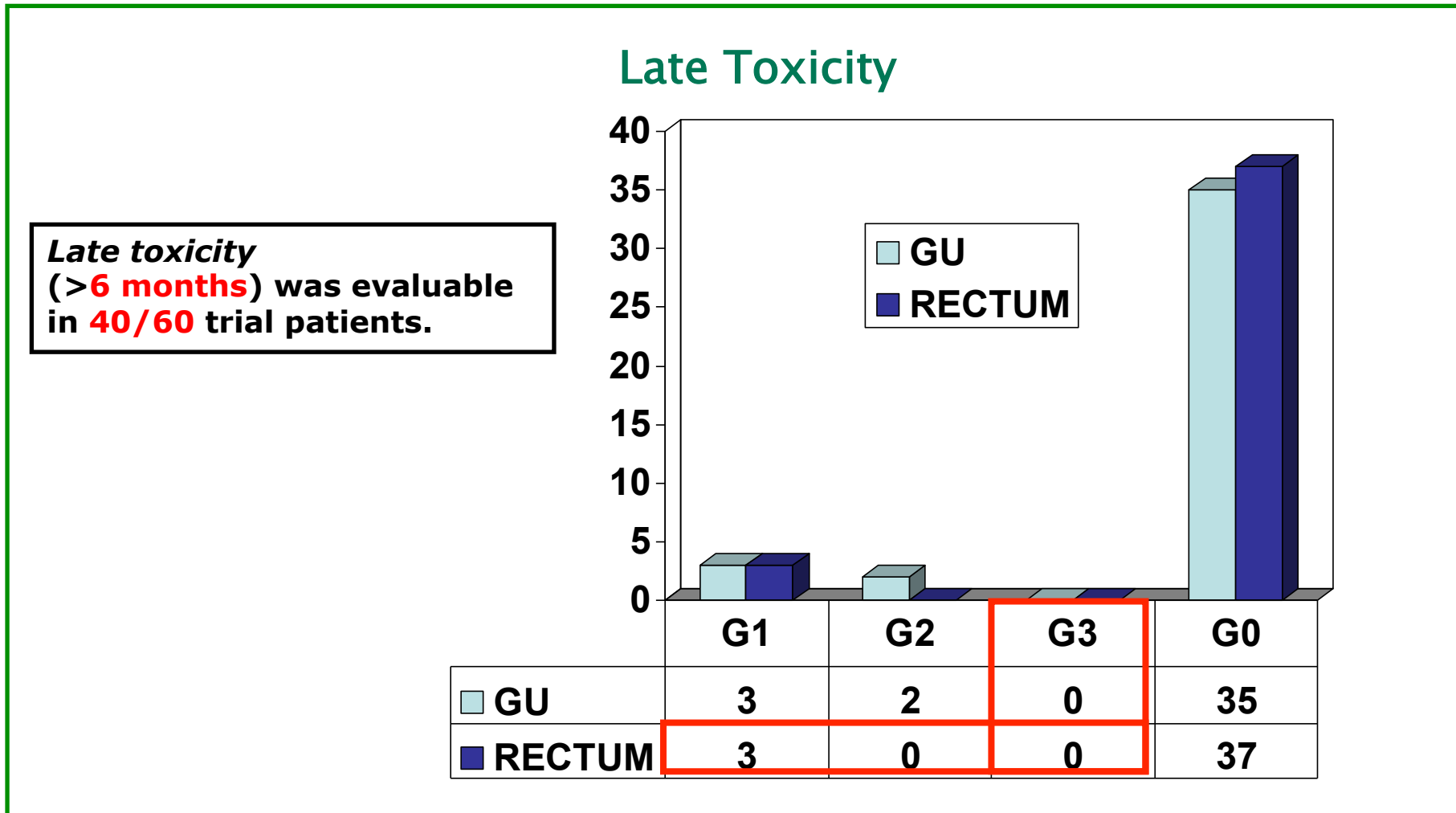
PATIENTS CHARACTERISTICS (60 pts):

N. of patients	60
Recruitment	Feb 2012–August 2013
Median Age [year]	70 [56, 80]
Median Initial PSA [ng/mL]	6.45 [0.50, 17]
Median Gleason Score	6 [6, 7]
NCCN Low Risk Class	35
NCCN Intermediate Risk Class	25
Median F–UP [days]	297 [30–532]
N. of patients with SpaceOAR™	13

PRELIMINARY RESULTS (60 pts):



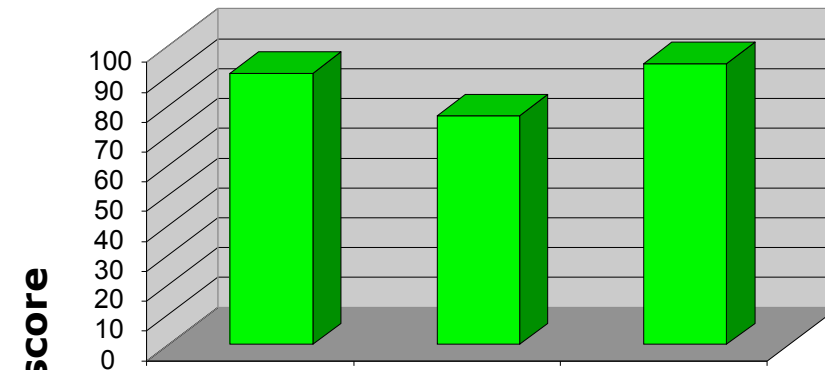
PRELIMINARY RESULTS



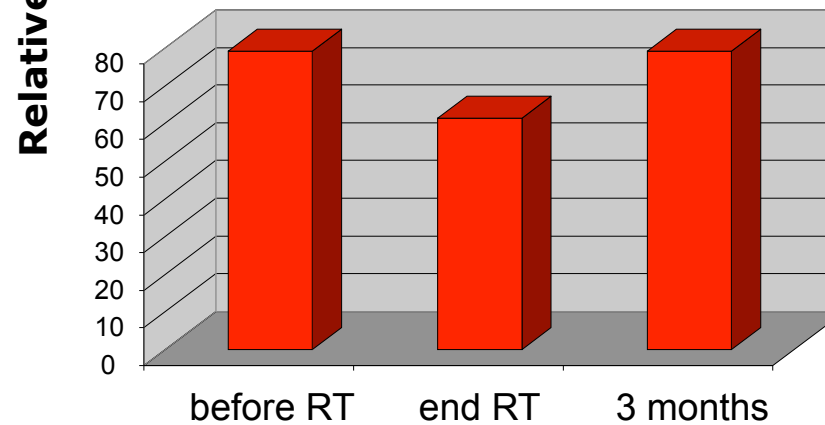
## PRELIMINARY RESULTS

### QoL: EPIC QUESTIONNAIRE

**Bowel**



**Urinary**



## CONCLUSIONS

- In summary, our early findings suggest that LINAC based *SBRT FFF treatment for prostate cancer in 5 fractions is feasible, fast and well tolerated* in acute setting.

- *No cases of biochemical recurrence were found.*  
However, longer follow-up is needed for definitive assessment of late toxicity and clinical outcome

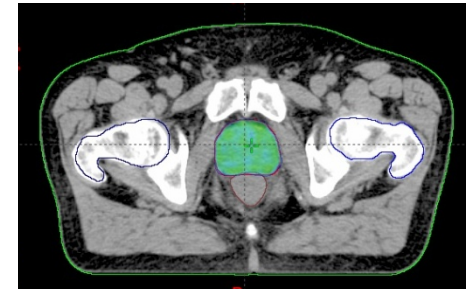
## SBRT: A NEW EFFECTIVE AND NON INVASIVE OPTION FOR LOCALIZED CANCER?



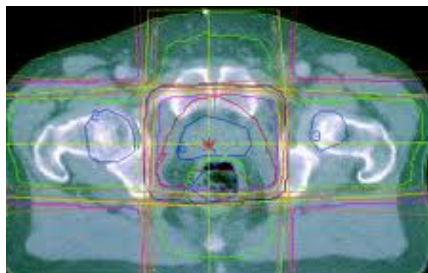
Robotic and traditional  
SURGERY



LOCALIZED PROSTATE CANCER



SBRT



Conventional EBRT



Brachytherapy