HUMANITAS
CANCER CENTER

Phase II study of FFF-SBRT in 5 fractions for low and intermediate risk prostate cancer

Ciro Franzese, G D'Agostino, E Clerici, E Villa, A Tozzi, T Comito, C Iftode, AM Ascolese, F De Rose, S Pentimalli, P Navarria, G Reggiori, P Mancosu, S Tomatis, M Scorsetti

Department of Radiotherapy and Radiosurgery, Humanitas Clinical and Research Center, Rozzano (Mi)

Background

• Combination of IGRT and IMRT: delivery of an increased dose to the target while limiting toxicity to normal tissues.

• Several studies suggest that prostate cancer may have a low alpha/beta ratio. The slow proliferating prostate cancer cells have high sensitivity to dose per fraction.
Brenner et al., 2002; Dasu, 2007

• The linear/quadratic model suggests that SBRT is able to deliver the equivalent dose of a radical treatment in a few days schedule.

Background

Study	Treatment	# of patients	Risk group(s)	Median follow-up (months)	Late Grade 3 GU Toxicity	Late Grade 3 GI Toxicity	FFBF
GANTRY-BASED SYSTEMS							
Madsen et al.	33.5 Gy in 5 fx	40	low	41	None	None	90% 4-years actuarial
Boike et al.	45-50 Gy in 5 fx #	45	low & int	30, 18, 12	4%	2% plus 1 Grade 4	100%
Mantz et al.	40 Gy in 5 fx #	80	low	36	None	None	100%
CYBERKNIFE							
King et al.	36.25 Gy in 5 fx ‡	67	low	32	3.5%	None	97%
Friedland et al.	35 Gy in 5 fx	112	low, int, & high	24	< 1%	None	98%
Katz et al.	35 – 36.25 Gy in 5 fx	304	low, int & high	48	2%	None	97, 93, 75% 4-year actuarial
Freeman et al.	7-7.25 Gy in 5 fx	41	low	60	< 1%	None	93% 5-year actuarial
Bolzicco et al.	35 Gy in 5 fx	46	low, int	20	None	2%	100%
Jabbari et al.	38 Gy in 4 fx †	38	low & int	18	5%	None	100%
McBride et al.	36.25-37.5 Gy in 5 fx	45	low	44	< 1%	None	100%
Fuller et al.	38 Gy in 4 fx †	54	low & int	36	4%	None	98%
Kang et al.	32-36 Gy in 4 fx	44	low, int & high	40	None	None	100%, 100%, 90.9%

HUMANITAS

Objectives

Prospective phase II pilot feasibility study

Primary end-points

- Acute and late toxicity *(criteria CT-CAE v4.0 2010)*
- Survival free from biochemical failure *(Phoenix's definition 2005)*

Secondary end-points

- Quality of life *(EPIC questionnaire)*

ciro.franzese@humanitas.it

Materials and methods

Inclusion criteria

- Age ≤ 80 years
- WHO performance status ≤ 2.
- Histologically proven prostate adenocarcinoma →Any case where prophylactic lymph node irradiation is not required (risk of microscopic involvement ≤ 15%)
- PSA ≤ 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

Materials and methods

Radiotherapy schedule

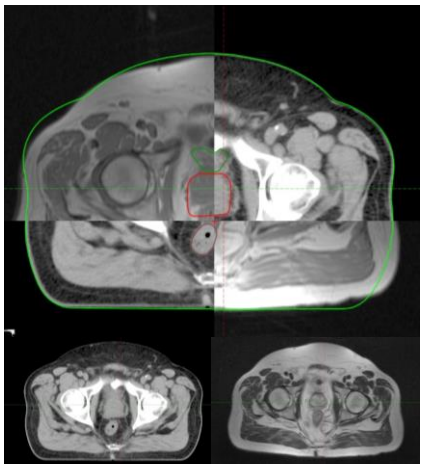
- Totale dose **35 Gy**
- 5 fractions of **7 Gy** on alternate days
- VMAT technique with FFF beams
- EQD2 = between 70 – 85 Gy for α/β between 3 -1.5 Gy**.**

Simulation and Target definition

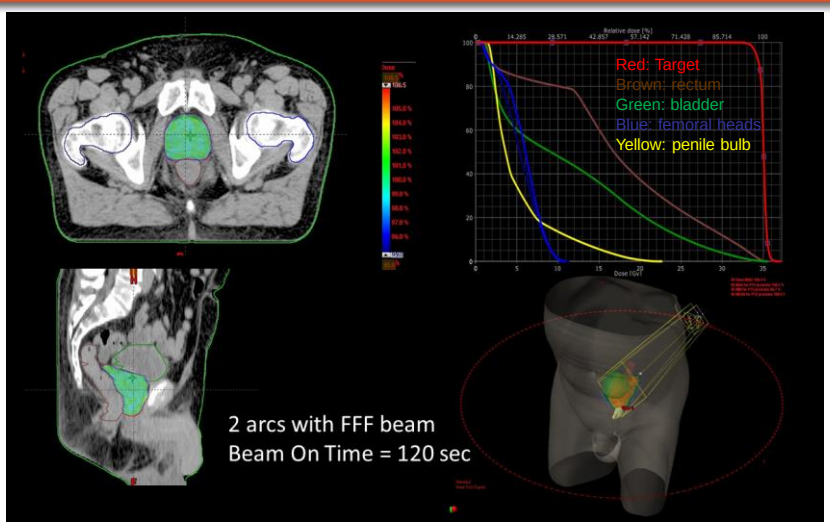
- Simulation CT
- Simulation MRI
- CT/MRI registration

CTV: prostate + SV, except for T1-T2 lesions with risk of SV involvement ≤ 15% in which case CTV is prostate only

PTV: CTV + 5 mm margin in each direction



Treatment planning



Prostate motion

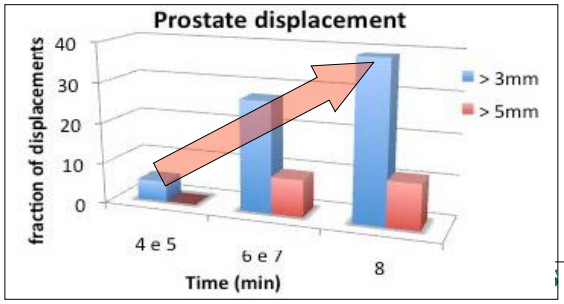
HUMANITAS CANCER CENTER

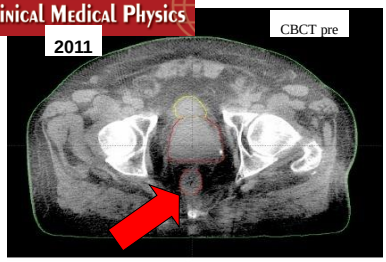
JOURNAL OF APPLIED CLINICAL MEDICAL PHYSICS, VOLUME 12, NUMBER 1, WINTER 2011

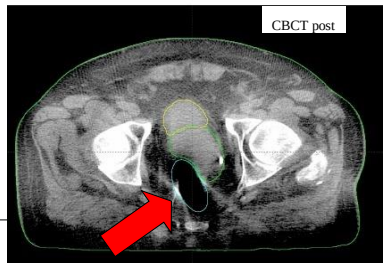
Cone beam CT pre- and post-daily treatment for assessing geometrical and dosimetric intrafraction variability during radiotherapy of prostate cancer

Giacomo Reggiori,[1] Pietro Mancosu,[1a] Angelo Tozzi,[1] Marie C Cantone,[2] Simona Castiglioni,[1] Paola Lattuada,[1] Francesca Lobefalo,[1] Luca Cozzi,[3] Antonella Fogliata,[3] Piera Navarria,[1] Marta Scorsetti[1]
Radiation Oncology Dept.,[1] IRCCS Istituto Clinico Humanitas, Milano (Rozzano), Italy; Physics Dept.,[2] Università degli studi di Milano, Milano, Italy; Medical Physics Unit,[3] Oncology Institute of Southern Switzerland, Bellinzona, Switzerland
pietro.mancosu@humanitas.it

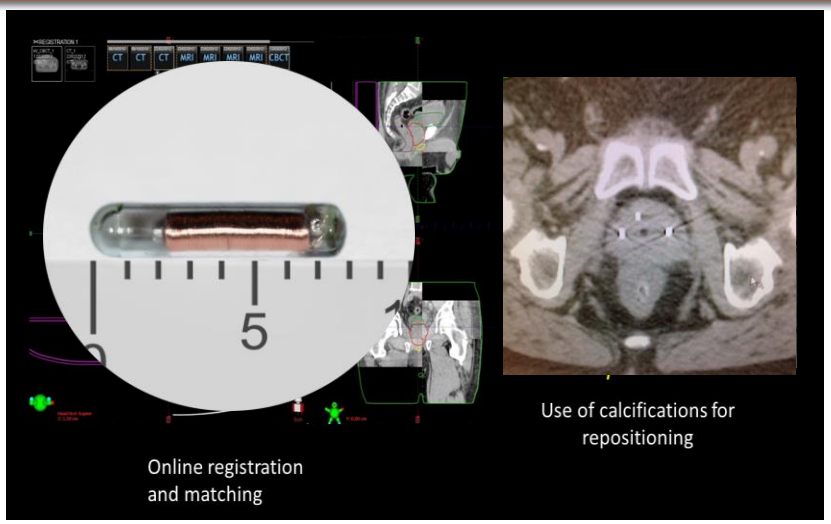
Journal of Applied Clinical Medical Physics
2011







Treatment verification



Results

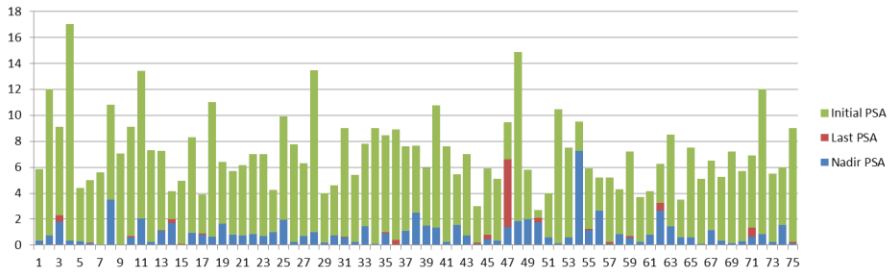
N. of patients	75 *
Recruitment	Dec 2011- Apr 2014
Median Age [year]	70 [48 - 80]
Median Gleason Score	6 [6-7]
Initial PSA [ng/mL]	Median: 7.17 [0.5-17]
NCCN Low Risk Class	47
NCCN Intermediate Risk Class	28
CTV [cm3]	Mean: 58.4 [25,1-110,2]
PTV [cm3]	Mean: 108.6 [52.8-182.2]

* First 40 pts: **Linac based SBRT for prostate cancer in 5 fractions with VMAT and flattening filter free beams: preliminary report of a phase II study.**
Alongi F, Cozzi L, Arcangeli S, Iftode C, Comito T, Villa E, Lobefalo F, Navarria P, Reggiori G, Mancosu P, Clerici E, Fogliata A, Tomatis S, Taverna G, Graziotti P, Scorsetti M.
Radiat Oncol. 2013 Jul 8;8:171

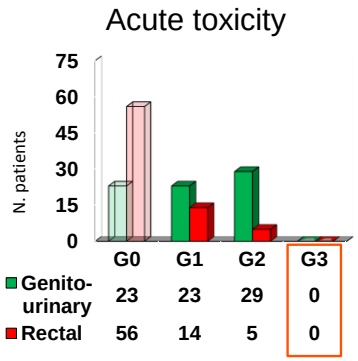
ciro.franzese@humanitas.it

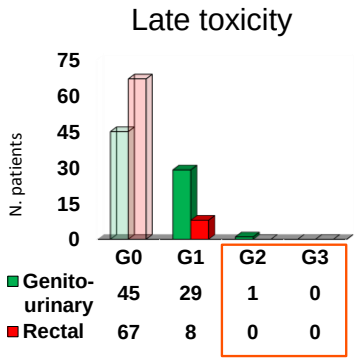
Results

Follow-up [months]	Mean: 17.1 Range: 6-29 Median: 17,8
Nadir PSA [ng/mL]	Mean: 0,97 Range: 0.02-7.25
Last PSA [ng/mL]	Mean: 1.10 Range: 0.02-7.25



Results





Conclusions

- SBRT with RapidArc and FFF beams in 5 fractions for prostate cancer is well tolerated in acute and late settings
- A longer follow-up is needed to assess definitive toxicity and outcome
- Randomized clinical trials could clarify the role of SBRT in prostate cancer.