

XXXII CONGRESSO NAZIONALE AIRO
XXXIII CONGRESSO NAZIONALE AIRB
XII CONGRESSO NAZIONALE AIRO GIOVANI

AIRO2022

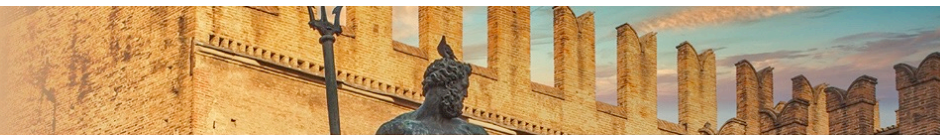
Radioterapia di precisione per un'oncologia innovativa e sostenibile

BOLOGNA, 25-27 NOVEMBRE
PALAZZO DEI CONGRESSI

RADIOTERAPIA STEREOTASSICA IPOFRAZIONATA LINAC-BASED NEI PAZIENTI ANZIANI CON CARCINOMA PROSTATICO: RISULTATI PRELIMINARI DI UNO STUDIO DI FASE II

M.P. CILIBERTI

U.O.C. RADIOTERAPIA ONCOLOGICA – OSPEDALE GENERALE REGIONALE F.MIULLI - ACQUAVIVA DELLE FONTI (BA)

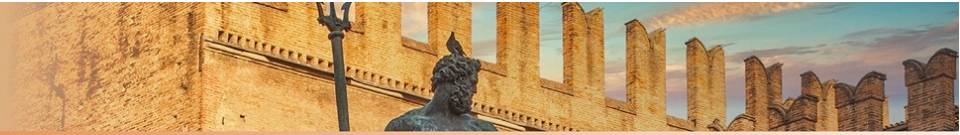


DICHIARAZIONE

Relatore: **NOME COGNOME**

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario (**NIENTE DA DICHIARARE**)
- Consulenza ad aziende con interessi commerciali in campo sanitario (**NIENTE DA DICHIARARE**)
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario (**NIENTE DA DICHIARARE**)
- Partecipazione ad Advisory Board (**NIENTE DA DICHIARARE**)
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario (**NIENTE DA DICHIARARE**)
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario (**NIENTE DA DICHIARARE**)
- Altro



INTRODUCTION

- Elderly patients are under-represented in clinical trials with a lack of strong evidence for this subgroup of patients
- Conventional fractionation RT (70-80 Gy)
- Hypofractionated RT (60-68 Gy /20-28 fr) → low alpha/beta ratio
- Ultra-HF

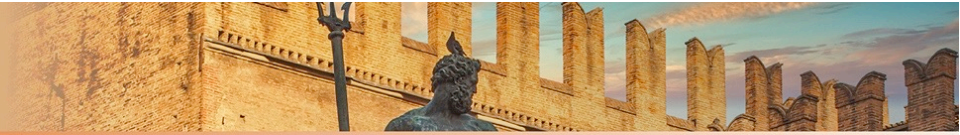


INTRODUCTION: SBRT

- Stereotactic body radiotherapy (SBRT) with extreme hypofractionation was tested for localized prostate cancer
- PROs
 - Good outcomes
 - Few toxicities
 - Reduced OTT
 - Better QOL
 - Costs

Meduri B, 2020

Voong KR, 2017



ARTICLES | VOLUME 22, ISSUE 2, P235-245, FEBRUARY 01, 2021

Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer (HYPO-RT-PC): patient-reported quality-of-life outcomes of a randomised, controlled, non-inferiority, phase 3 trial

Per Fransson, PhD • Per Nilsson, PhD • Adalsteinn Gunnlaugsson, MD • Lars Beckman, MD • Björn Tavelin, BSc
David Norman, BSc • et al. [Show all authors](#)

Published: January 11, 2021 • DOI: [https://doi.org/10.1016/S1470-2045\(20\)30581-7](https://doi.org/10.1016/S1470-2045(20)30581-7) • Check for updates

Worse acute GI toxicity

No differences in acute GU toxicity and in late toxicity

42.7 Gy in seven fractions, 3 days per week for 2.5 weeks

No differences in acute and late toxicity

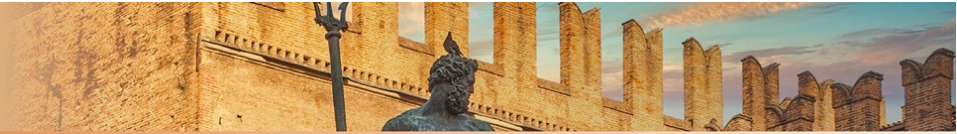
36.25 Gy in five fractions over 1–2 weeks

ARTICLES | VOLUME 23, ISSUE 10, P1308-1320, OCTOBER 01, 2022

Intensity-modulated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): 2-year toxicity results from an open-label, randomised, phase 3, non-inferiority trial

Alison C Tree, MDRes • Peter Ostler, FRCR • Hans van der Voet, MD • William Chu, MD • Andrew Loblaw, MD • Daniel Ford, FRCR • et al. [Show all authors](#) • [Show footnotes](#)

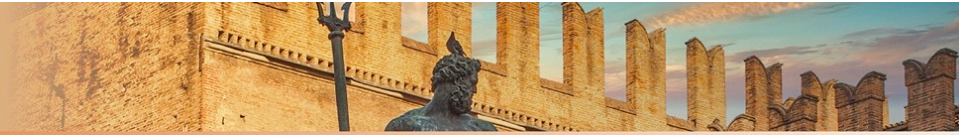
Published: September 13, 2022 • DOI: [https://doi.org/10.1016/S1470-2045\(22\)00517-4](https://doi.org/10.1016/S1470-2045(22)00517-4) • Check for updates



THE PROSPECTIC PHASE II TRIAL: METHODS

Inclusion criteria

- Age \geq 70 years
- histologically confirmed prostate cancer
- good PS - life expectancy $>$ 3 months
- T1-T3 stage
- no pathologic lymph nodes (N0) on CT and/or MRI
- no distant metastases
- no previous pelvic RT
- no previous surgery (except TURP)
- absence of active inflammatory bowel disease or collagen vascular disease
- ability to understand and sign the written informed consent
- *combined androgen deprivation therapy (ADT) according to risk category was permitted*



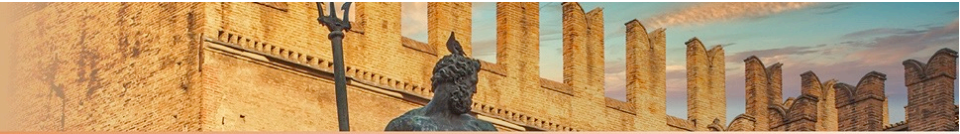
THE PROSPECTIC PHASE II TRIAL: METHODS

SIMULATION

- 1 mm slice thickness CT
- supine position - flexed legs immobilized in knee
- Vac-Lock devices
- patients were educated at the use of fleet enemas 2 hours before the CT scan and treatment for rectal emptying, and they were required to drink 500 ml of water 30 minutes before the procedures for bladder filling

TARGET VOLUME

- CTV = the prostate gland only for low risk patients, the prostate + seminal vesicles for intermediate and high risk
- PTV = CTV +3 mm margin in all direction (posteriorly 2 mm).



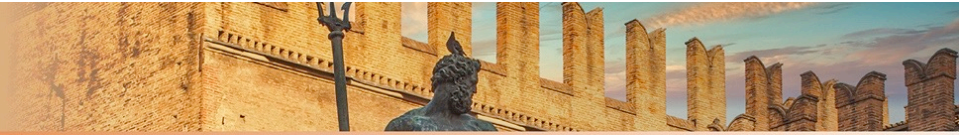
THE PROSPECTIC PHASE II TRIAL: METHODS

SCHEDULE AND PLANNING

- 35 Gy in 5 fractions administered in 1 or 2 weeks (target volume ≥ 150 cc and IPSS score ≥ 8)
- At least 95% of the PTV (minus overlap with rectum, bladder, urethra) receive at least 95% of 35 Gy
- $< 2\%$ of the PTV receives 107%

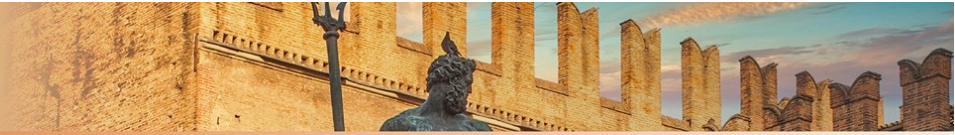
DELIVERY

- IGRT (daily CBCT)

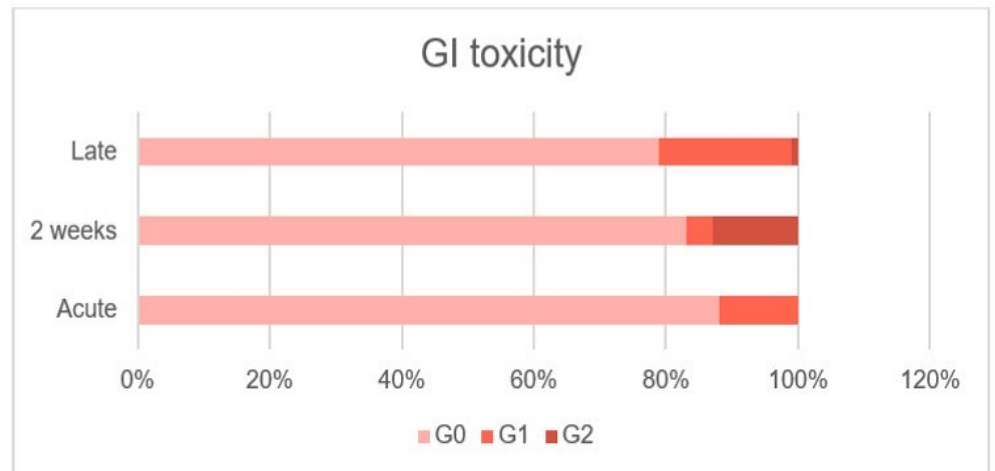
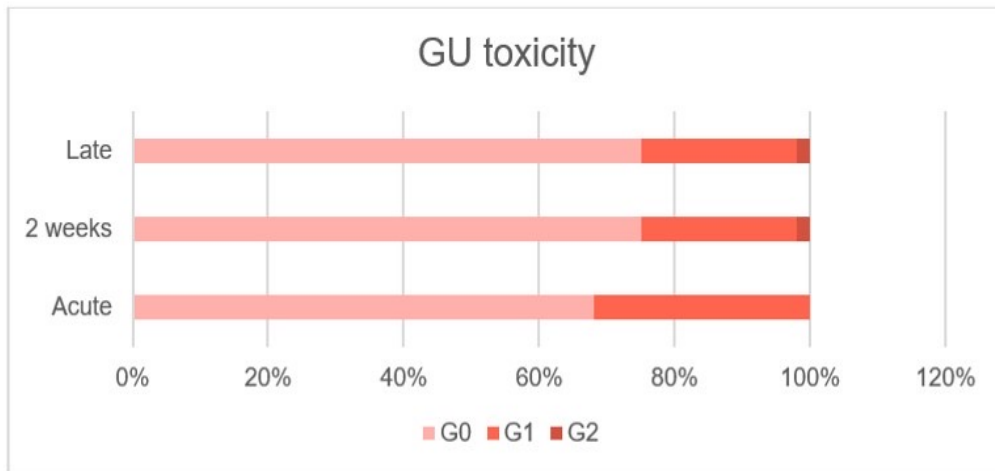


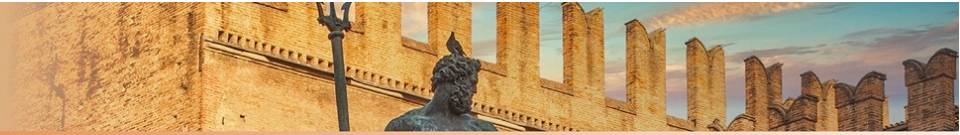
THE PROSPECTIC PHASE II TRIAL: RESULTS

- July 2019 - September 2021 → **111 patients**
- MEDIAN FOLLOWUP = **23 months**
- Median age = 77 years (range 70-86)
- **33% low-risk disease**
- **48% favorable/unfavorable intermediate-risk disease**
- **19% high-risk disease**
- Median pre-treatment PSA value = 6.61 ng/ml (range 0.2-40 ng/ml)
- ADT in 58 patients (52%)
- Median baseline IPSS = 6 (range 0-19)
- 65% five consecutive fractions
- Median PTV = 99.5 cc (range 51-192.2)
- Median Dmax to PTV = 38.9 Gy (range 35.4-43.8)



THE PROSPECTIC PHASE II TRIAL: RESULTS





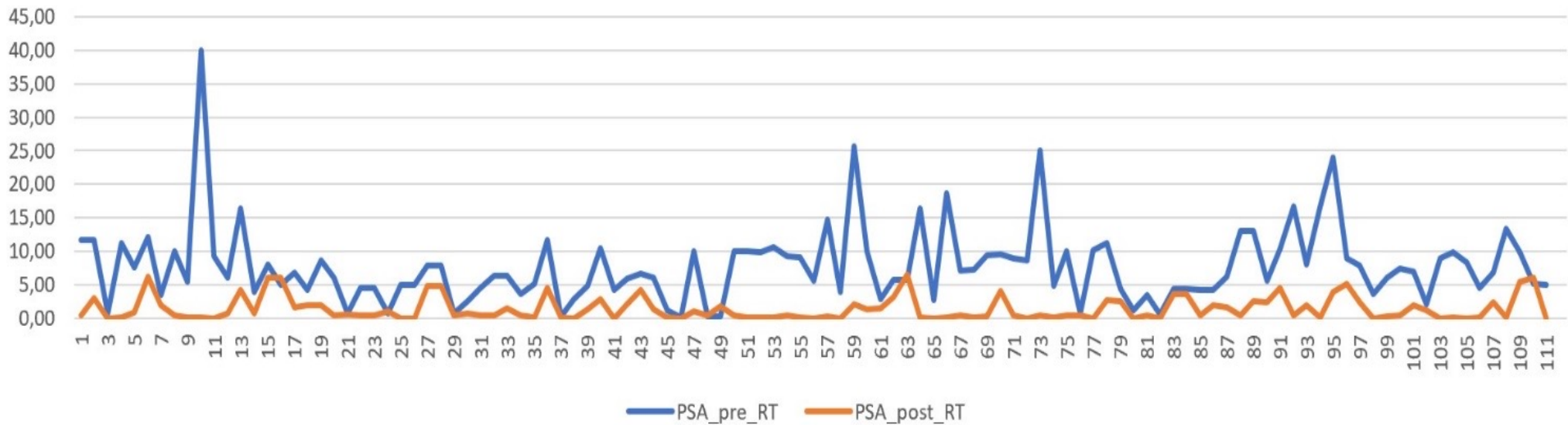
VARIABLE	GU TOXICITY				GI TOXICITY			
	UNIVARIATE		MULTIVARIATE		UNIVARIATE		MULTIVARIATE	
	X SQUARE	P	OR (95%CI)	P	X SQUARE	P	OR (95%CI)	P
Age (>77 years)	0.09	0.75	-	-	0.02	0.86	-	-
ADT (Yes)	2.31	0.12	-	-	0.22	0.63	-	-
Gleason Score (>7)	0.04	0.83	-	-	0.04	0.82	-	-
MR_pre_RT (Yes)	1.12	0.27	-	-	0.24	0.61	-	-
IPSS (>6)	4.67	0.03	1.93 [0.8-4.6]	0.14	9.38	0.002	0.32 [0.1-1.5]	0.1
Day_RT (Consecutive)	1.33	0.24	1.47 [0.6-3.5]	0.41	6.07	0.02	1.17 [0.2-4.6]	0.8
PTV_volume (>99.5cc)	2.78	0.05	0.58 [0.2-1.4]	0.23	1.73	0.18	2.27 [0.6-8.4]	0.2
Isodose (>90)	0.58	0.44	-	-	0.23	0.62	-	-
D_max_PTV (>38.9Gy)	5.88	0.01	1.95 [0.7-5.1]	0.16	0.07	0.78	2.01 [0.4-8.2]	0.3
D_max_rectum (>36.5Gy)	2.17	0.14	-	-	1.69	0.19	0.23 [0.05-1]	0.05
D_max_bladder (>37.6Gy)	0.01	0.91	0.53 [0.1-1.7]	0.3	0.09	0.76	-	-
Urethra_sparing (Yes)	0.037	0.03	0.39 [0.013-1]	0.05	1.07	0.29	-	-
Late_toxicity_GI (Yes)	4.59	0.03	2.44 [6.3-9.4]	0.04	-	-	-	-
Late_toxicity_GU (Yes)	-	-	-	-	43.26	<0.001	43.2 [10-182]	<0.001

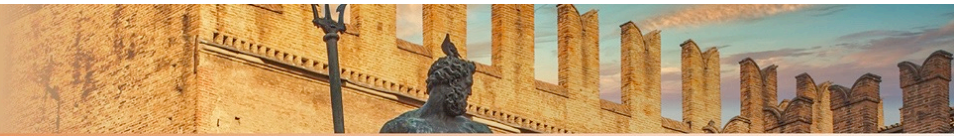


THE PROSPECTIC PHASE II TRIAL: RESULTS

PSA biochemical response

P=0.01



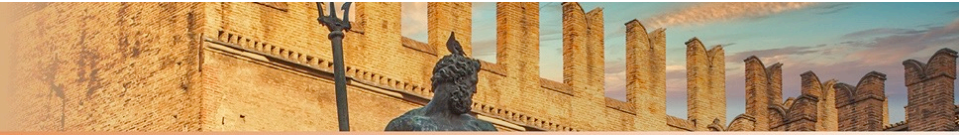


THE PROSPECTIC PHASE II TRIAL: RESULTS

Variables	Mann-Whitney U test	
	Median PSA_post RT [IQR] (ng/ml)	P
Age (>77 years)	0.5 [0.0-2.43]	0.18
Age (≤77 years)	0.5 [0.0-2.0]	
ADT (Not)	1.5 [0.5-3.0]	< 0.001
ADT (Yes)	0.18 [0.0-0.6]	
PSA_pre_RT (>6.61 ng/ml)	0.5 [0.1-2.7]	0.15
PSA_pre_RT (≤6.61 ng/ml)	0.5 [0.1-1.9]	
Gleason_Score (>7)	0.3 [0.0-1.7]	0.03
Gleason_Score (≤7)	0.9 [0.4-2.1]	
Risk group (low)	1.29 [0.5-2.6]	0.04
Risk group (intermediate+high)	0.5 [0.0-1.9]	
IPSS (>6)	0.5 [0.0-2.03]	0.11
IPSS (≤6)	0.5 [0.2-2.1]	

Variables	Mann-Whitney U test	
	Median PSA_post RT [IQR] (ng/ml)	P
Day_RT (consecutive)	0.5 [0.1-1.8]	0.4
Day_RT (every other day)	0.5 [0.1-2.5]	
PTV_volume (>99.5cc)	0.8 [0.5-2.5]	0.01
PTV_volume (≤99.5cc)	0.3 [0.0-1.7]	
Isodose (>90Gy)	0.5 [0.0-1.0]	0.11
Isodose (≤90Gy)	0.5 [0.0-2.1]	
D_max_PTV (>38.9Gy)	0.5 [0.0-1.9]	0.05
D_max_PTV (≤38.9Gy)	0.9 [0.2-2.2]	
Urethra_sparing (Not)	0.5 [0.1-2.16]	0.4
Urethra_sparing (Yes)	0.5 [0.1-2.0]	

No biochemical failure or death
 PFS and OS of 100% at 1 year



THE PROSPECTIC PHASE II TRIAL: CONCLUSION

- SBRT attractive for elderly (logistic issue)
- Emerging aspects:
 - increasing age not correlated with toxicity
 - GU toxicity related to urethra sparing, PTV volume, D max PTV and IPSS
 - GI toxicity related to day RT (non-consecutive), D max rectum and IPSS
 - both toxicities are correlated each other
- Hypothesis for the best SBRT planning approach = **SBRT with urethra sparing, an each other day RT scheduling, a Dmax for rectum < 36.5 Gy and for PTV > 38.9 Gy**



THE PROSPECTIC PHASE II TRIAL: CONCLUSION

- In the setting of elderly patients affected by localized PC, despite the absence of definitive data, the choice of “no or palliative treatment” should be avoided.
- The **new technologies and radiobiological knowledge** have been demonstrated the safety and efficacy of extreme hypofractionation, regardless age.
- Despite the **limitation** of the present analysis in terms of sample size and short follow-up, the present preliminary report in elderly patients affected by PC, highlighted the **feasibility, safety, effectiveness and attractiveness** of SBRT in 5 fraction.