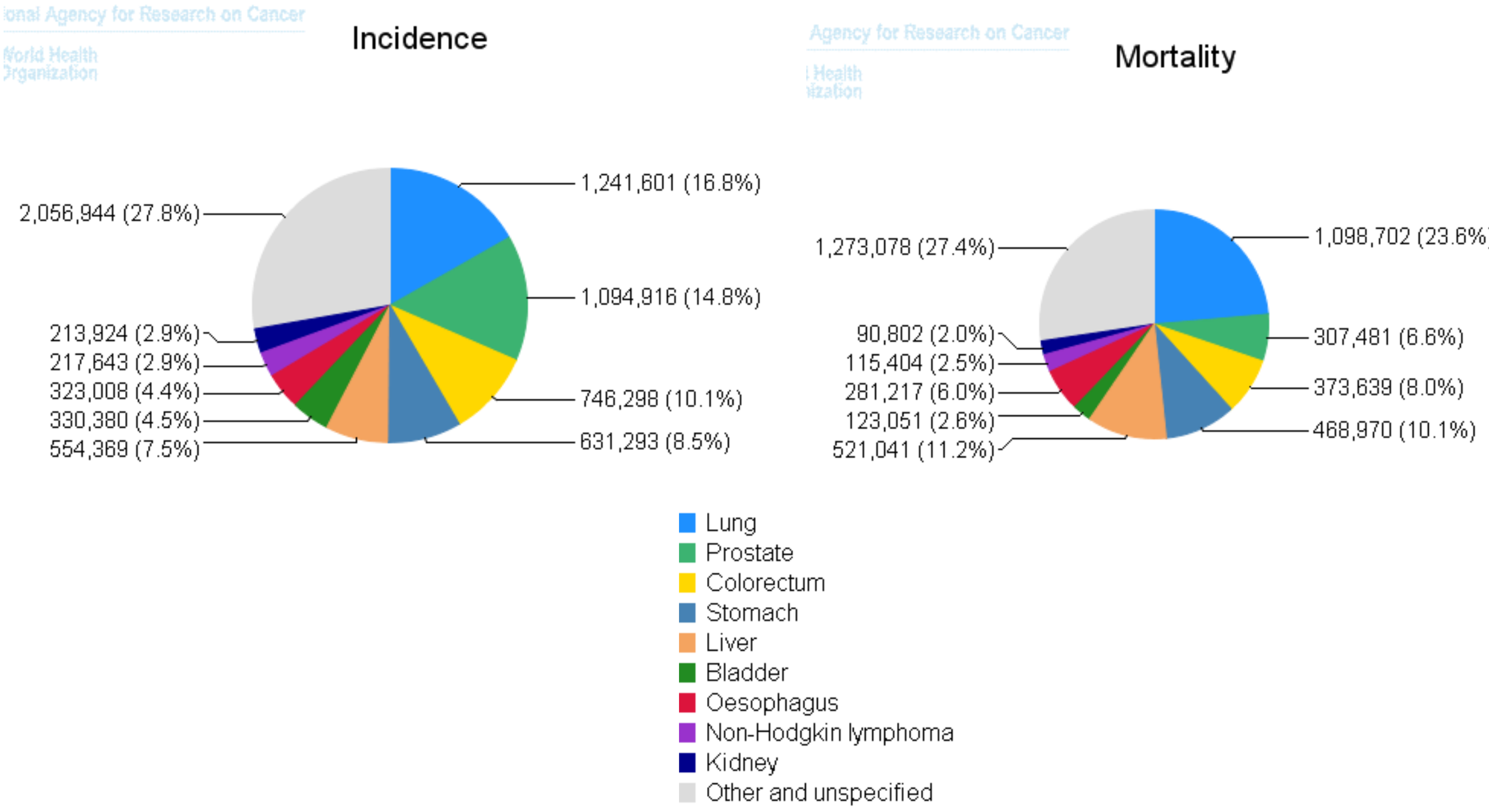
Hypo-fractionation in Carcinoma Prostate

Dr Haresh KP
Associate Professor
Department of Radiation Oncology
DRBRAIRCH, AIIMS, New Delhi

Ca Prostate; World Males



India, Males

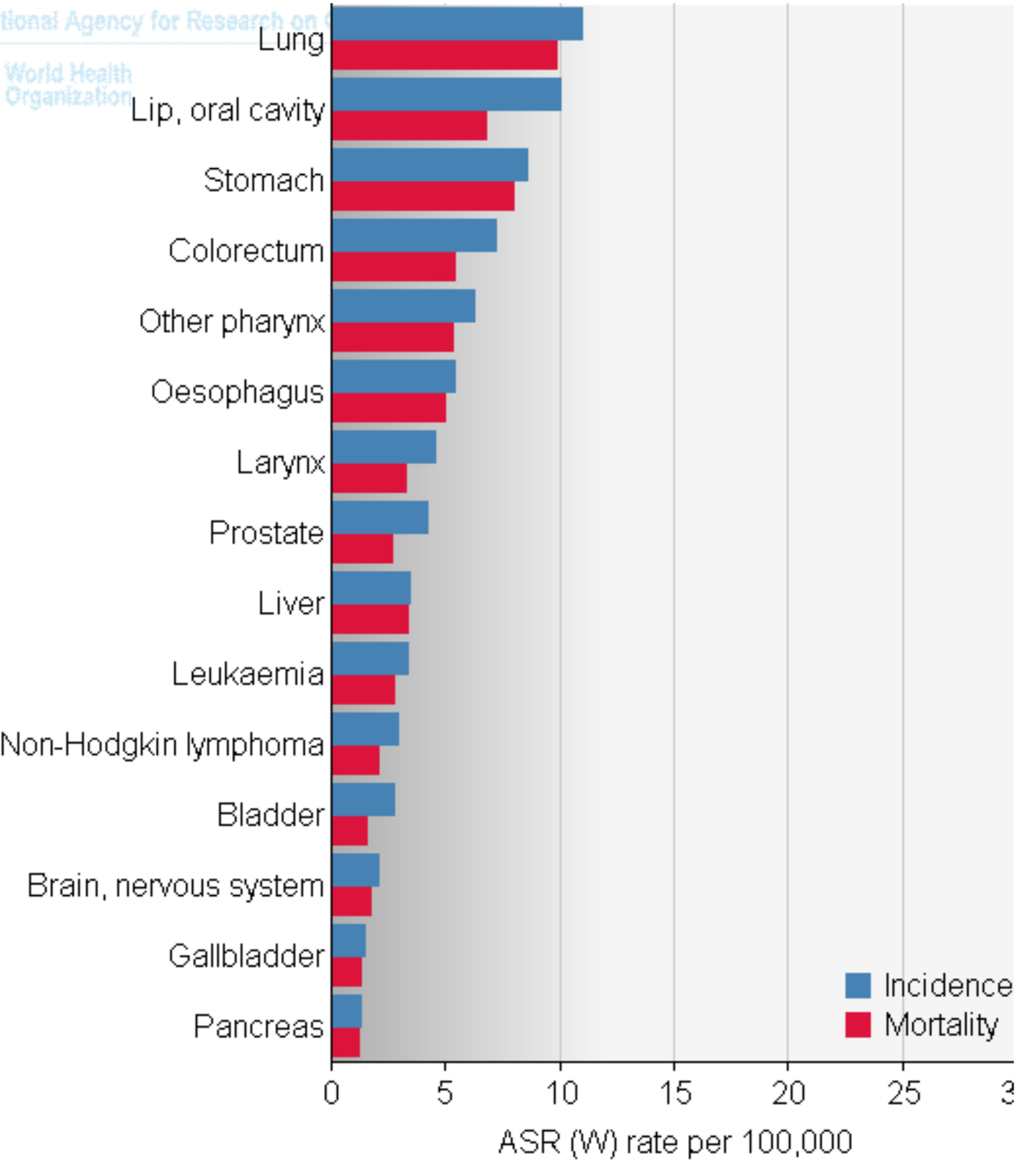
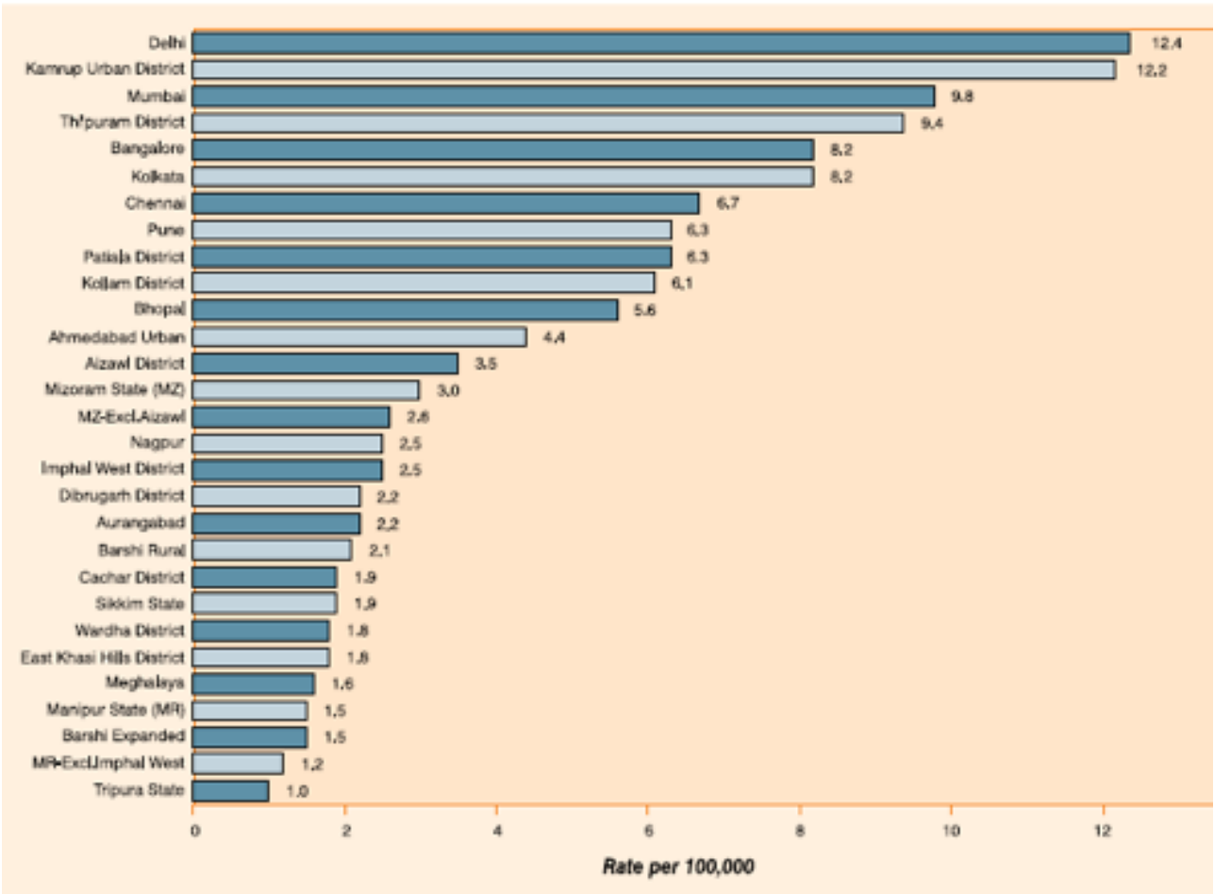
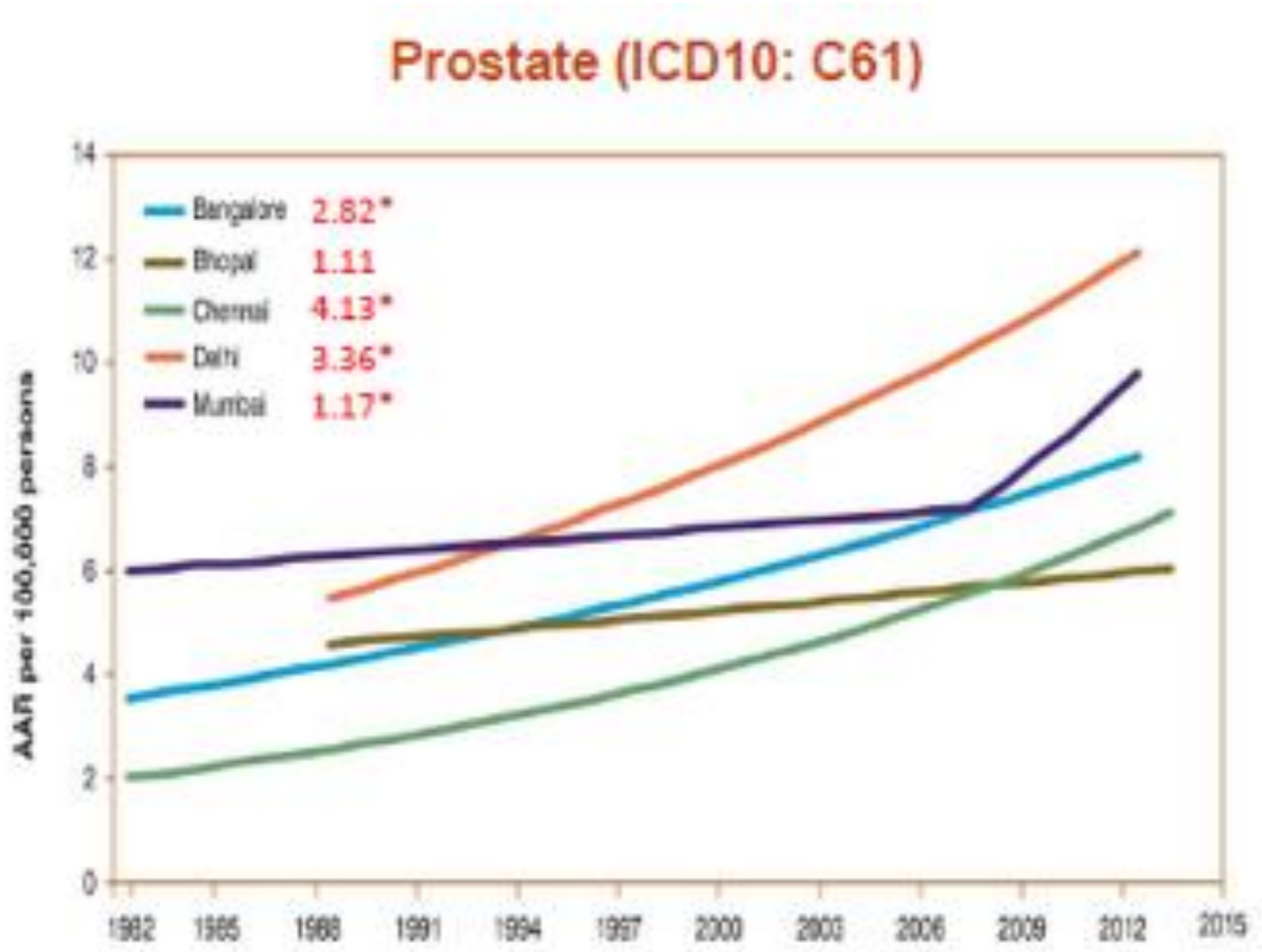
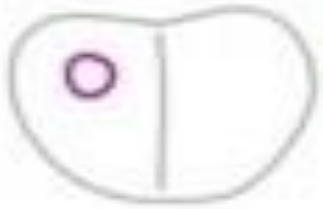


Fig. 7.17: Comparison of Age Adjusted Incidence Rates (AARs) of All PBCRs
PROSTATE (ICD-10: C61)



Time trends


Prostate (ICD10: C61)
Bangalore 2.82*
Bhopal 1.11
Chennai 4.13*
Delhi 3.36*
Mumbai 1.17*
AAR per 100,000 persons
0
2
4
6
8
10
12
14
1982
1985
1988
1991
1994
1997
2000
2003
2006
2009
2012
2015



T2a

T2b

T2c

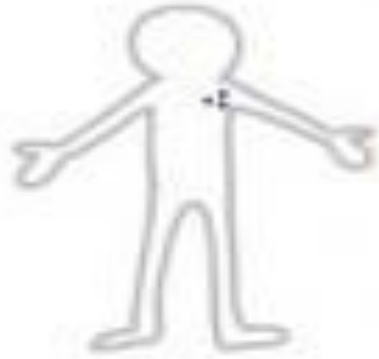
T3a

T3b

T4

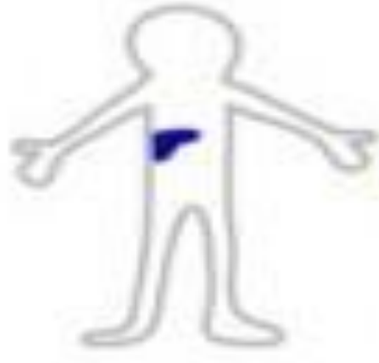
N0

N1



M1a

M1b



M1c

TNM staging for PROSTATE CA

Gleason's Pattern

1. Small, uniform glands

2. More stroma between glands

3. Distinctly infiltrative margins

4. Irregular masses of neoplastic glands

5. Only occasional gland formation

Well differentiated

Moderately differentiated

Poorly differentiated/ Anaplastic

NCCN Risk Stratification

NCCN *risk categories*	~5–10-Year bPFS/CSS
Low: T1-2a and GS ≤6 and PSA <10	80–90%/>95%
Intermediate: T2b–T2c and/or GS 7 and/or PSA 10–20	70–85%/75–90%
High: T3a or GS 8-10 or PSA >20 (very high T3b-T4)	30–60%/60–80%

(Also consider PSA kinetics, % involved biopsy cores)

D'amico AV et al. JAMA 1998,280:969–974

Prostate Treatment Options

Low Risk

- Active Surveillance
- Radical Prostatectomy ± Pelvic LN dissection
- Brachytherapy
- Radical EBRT

Intermediate Risk

- Radical EBRT + Short term ADT
- EBRT + Brachytherapy boost + Short term ADT
- Radical Prostatectomy ± Pelvic LN dissection ± Adjuvant RT
- Brachytherapy

High Risk

- Radical EBRT + long term ADT
- EBRT + Brachytherapy boost + long term ADT
- Radical Prostatectomy + Post op RT

More the Dose…Better!!!

Trial	n	Dose	FU	BCF	OS
Heemsbergen et al 2014	664	78 Gy vs 68 Gy	110 mo	+	-
Hoskin et al 2012	216	80 Gy vs 63 Gy	85 mo	+	-
Dearnaley et al 2011	843	74 Gy vs 64 Gy	120 mo	+	-
Beckendorf et al 2011	306	80 Gy vs 70 Gy	61 mo	+	-
Kuban et al 2007	301	78 Gy vs 70 Gy	114 mo	+	-

How to escalate dose?

- Conventional fractionation using high end technology like IMRT
- **Hypofractionation**
- Brachytherapy

Radiobiological Rationale for Hypofractionation

Early reactions	α/β (Gy)	Late reactions	α/β (Gy)
Skin	9–12	Kidney	2–2.4
Jejunum	6–10	Rectum	2.5–5
Colon	9–11	Lung	2.7–4
Testis	12–13	Bladder	3–7
Mucosa	9–10	CNS: brain,spinal cord	1.8–2.2

Vocal cord	~9.9 Gy	Harrison et al. 1988
Oropharynx	13–19	Rezvani et al. 1993
Larynx	25–35	Maciejewski et al 1988
Larynx	50–infinity	Chappell & Fowler 1995
Larynx	50–infinity	Roberts & Hendry 1998

Only a few types of tumor have low values of α/β:

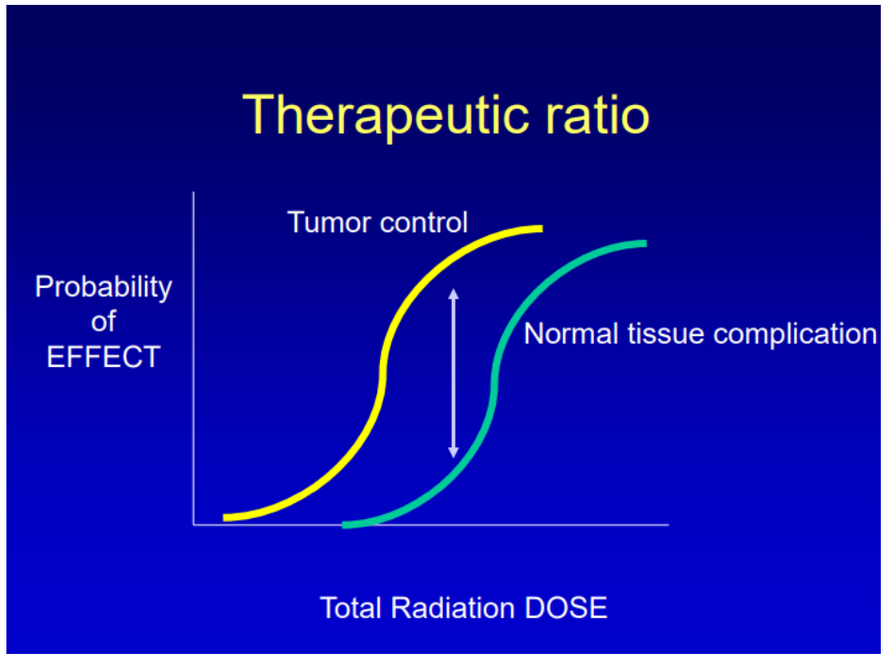
Malig. melanoma	0.6 Gy	Bentzen et al. 1989
Prostate Ca.	1.5	Brenner & Hall 1999
Prostate Ca.	1.49	Fowler et al. 2001
Prostate Ca.	1.2	Brenner . . . Martinez 2002
Rhabdomyosarcoma	2.8	Timmerman 2002

ab_rat1.jpg

J.F. Fowler. The radiobiology of prostate cancer including new aspects of fractionated radiotherapy. *Acta Oncologica*, 44(3):265-276, 2005.

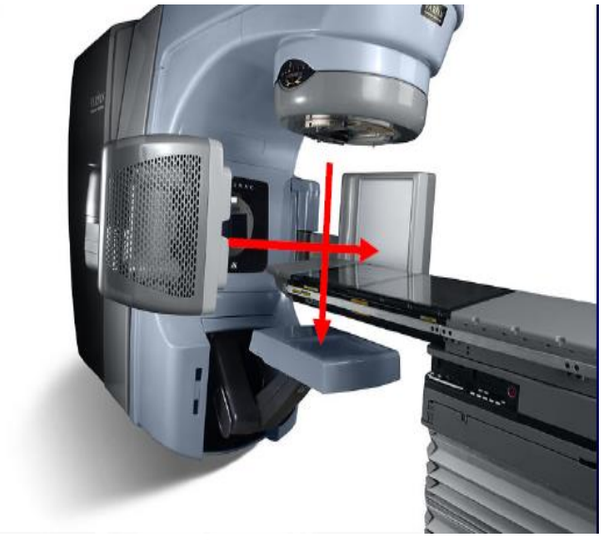
Key Points

- Margins to be kept minimal
- Metriculous planning respecting the OARs
- IGRT Mandatory—-Beware of risk of precisely missing the target and misfiring the dose to nearby normal structures
- Real time image guidance the best



High end radiation machines and High-tech image guidance (IGRT) critical for safe and effective delivery

Synergy-S

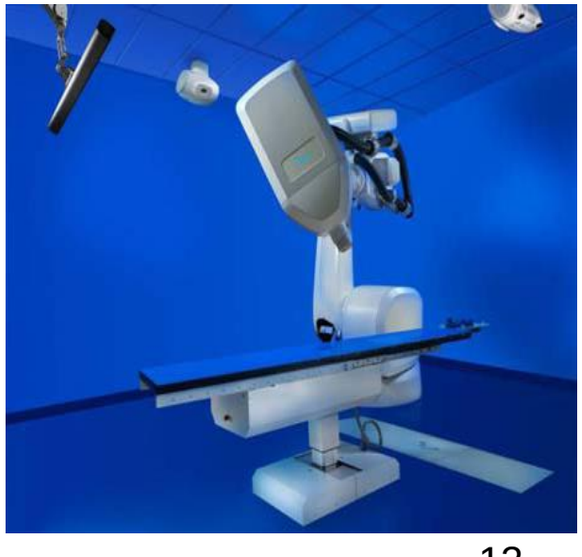


Trilogy

Artiste

Tomotherapy

Novalis with ExacTrac



CyberKnife

OLD (LOW-DOSE) EXPERIENCES: 2D, no IMRT, no IGRT

St. Thomas Hospital (London): Lloyd-Davies, Urology. 36: 107, 1990

55 Gy in 12 fractions

36 Gy in 6 fractions: **6 Gy per fraction**

Canadian randomized trial: Lukka, JCO. 23: 6132-6138, 2005

66 Gy in 33 fractions versus 52.5 Gy/20 fractions (**2.6 Gy per fraction**)

- Hypofractionated arm worse? 5yr bRFS: 53% vs. 56%; $p < 0.05$
- No difference in toxicity

Australian randomized trial:

64 Gy/32 fractions versus 55 Gy/20 fractions (**2.75 Gy per fraction**)

- Hypo arm better bRFS.
- Median FU 90 mos needed to show difference.
- GI toxicity slightly worse with hypo.

Yeoh, IJROBP, 66: 1072-83, 2006
Yeoh, IJROBP 81, 1271-8, 2011

Modern Single Arm Trials

MODERN HYPOFRACTIONATION EXPERIENCES: IMRT / IGRT

Single arm	Fraction Size(Gy)	Number	Total Dose	BED (α/β=2)	Med FU (mos) Last report
Cleveland Clinic	2.5	28	70.0	158	103
McGill	3.0	22	66.0	165	90
	2.94	22	64.7	160	59
U Wisconsin	3.63	16	58.1	163	50
	4.30	12	51.6	163	55

(Many more…)

CHHiP

Comparison of hypofractionated high-dose intensity-modulated radiotherapy schedules for prostate cancer: Results from the phase III randomized CHHiP trial (CRUK/06/016)

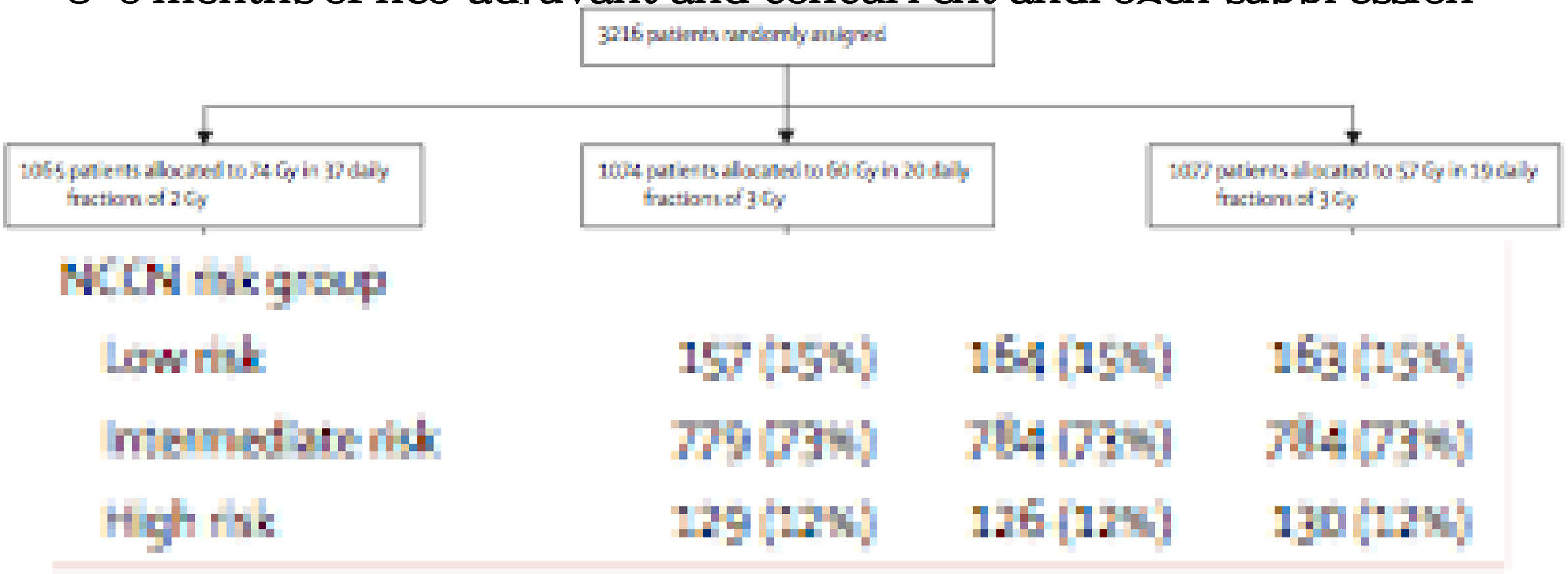
Lancet Oncol 2016; 17: 1047–60

Professor David Dearnaley

2002-2011, 71 centres, IMRT with portal imaging/IGRT

pT1b–T3aN0M0; Non Inferiority Design

3–6 months of neo-adjuvant and concurrent androgen suppression



CHHiP Results

- Biochemical or clinical failure free at 5 years

  74 Gy group: 88·3% (95% CI 86·0–90·2)

  60 Gy group: 90·6% (88·5–92·3)

  57 Gy group: 85·9% (83·4–88·0).

- 60 Gy was non-inferior to 74 Gy (HR 0·84 [90% CI 0·68–1·03], p_{NI}=0·0018)

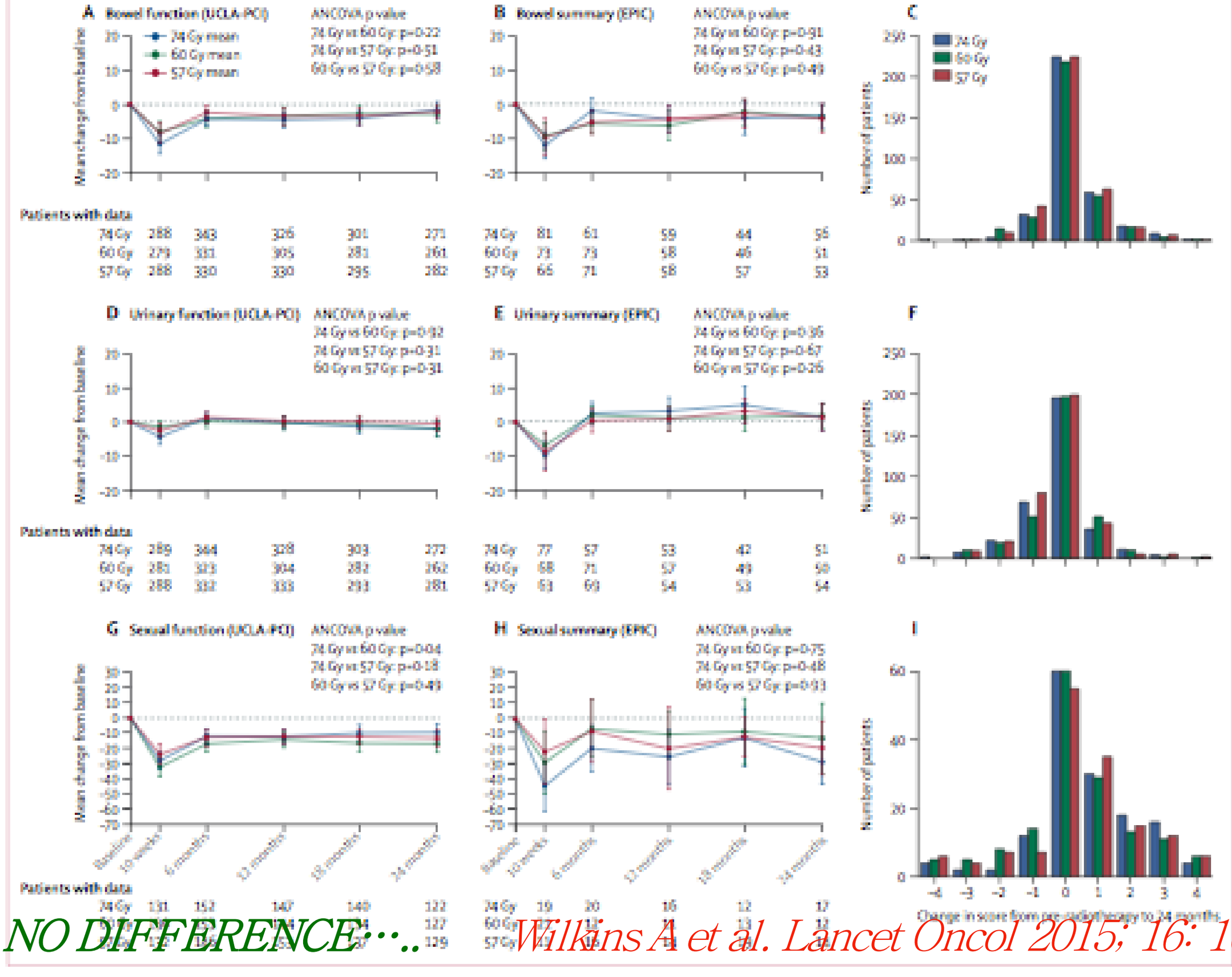
- But non-inferiority could not be claimed for 57 Gy compared with 74 Gy (HR 1·20 [0·99–1·46], p_{NI}=0·48).

- No significant differences in either the proportion or cumulative incidence of side-effects 5 years after treatment using three clinician-reported as well as patient-reported outcome measures.

- **Wave of toxicity occurs earlier in HF arms**

Lancet Oncol 2016; 17: 1047–60

2-year patient-reported outcomes



NO DIFFERENCE…. Wilkins A et al. Lancet Oncol 2015; 16: 1605–16

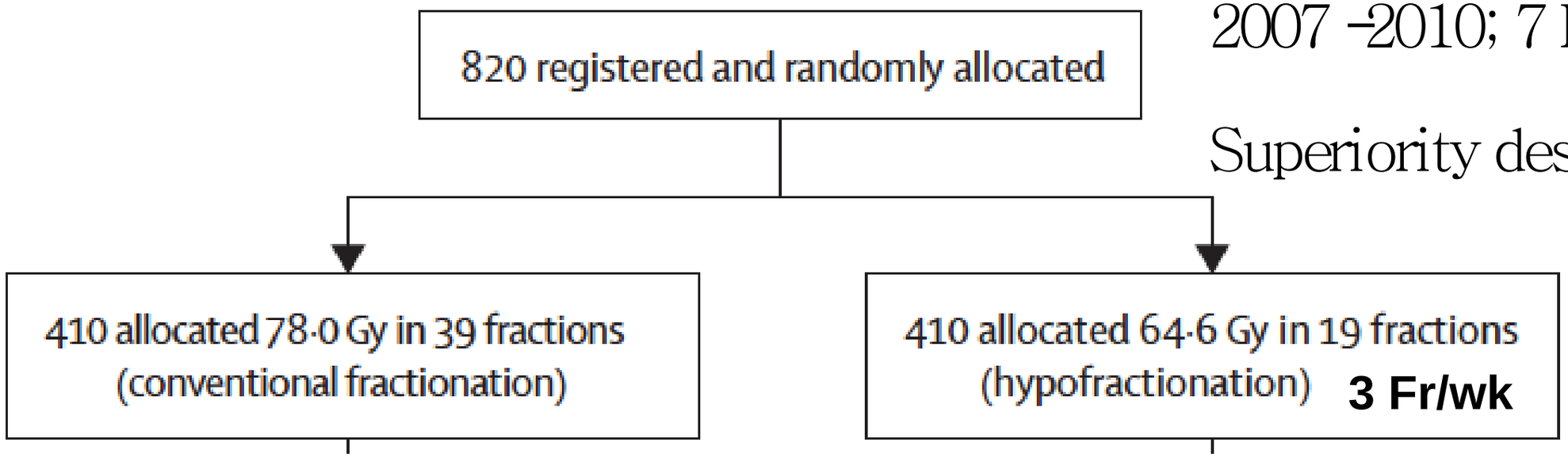
HYpofractionated irradiation for PROstate cancer (HYPRO)

Luca Incrocci et al. Lancet Oncol 2016

T1b–T4NX–N0MX–M0

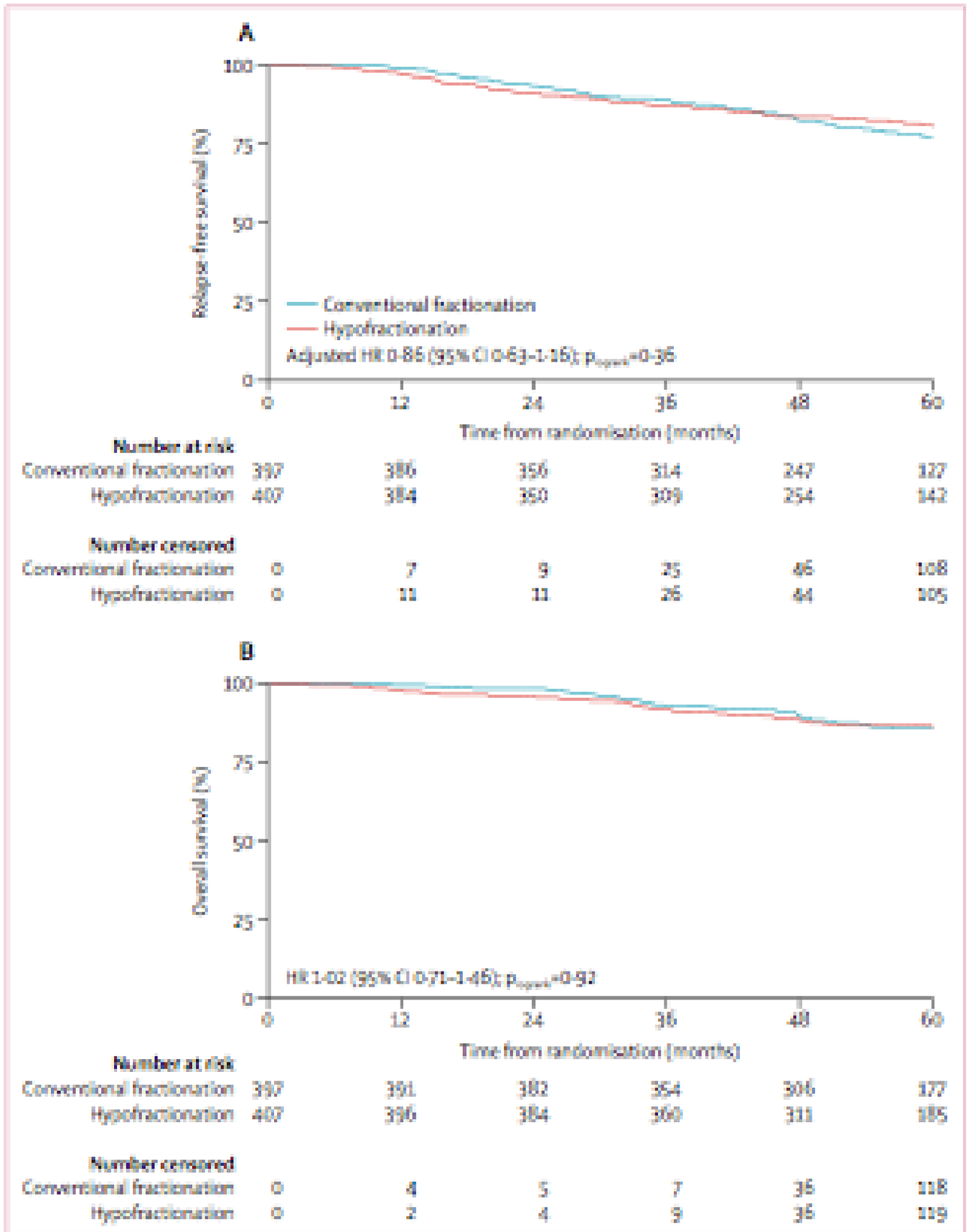
2007 –2010; 7 Dutch centres

Superiority design



Risk group**		
Intermediate	104 (26%)	107 (27%)
High	303 (74%)	290 (73%)

HYPRO Results

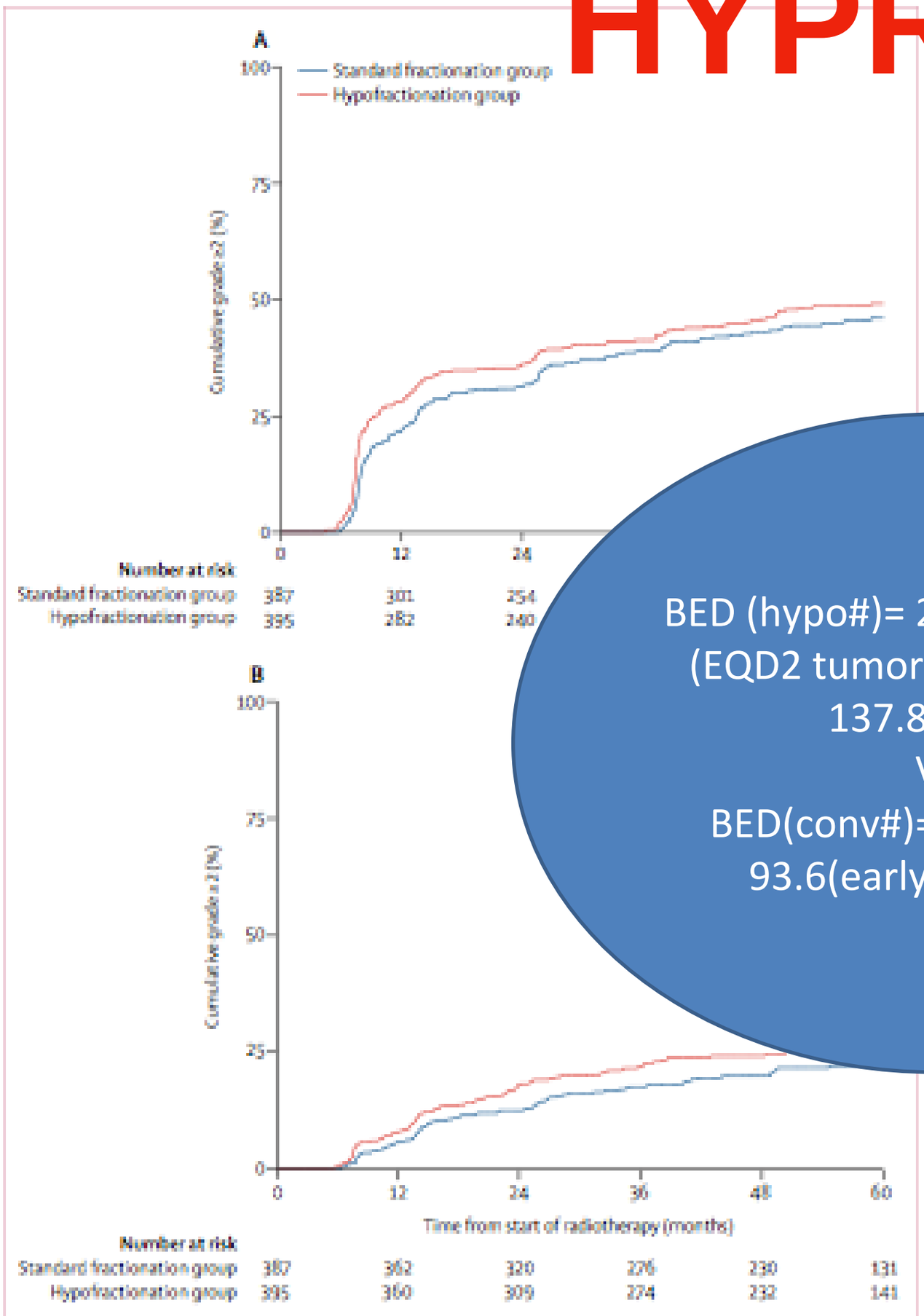


- Treatment failure:
  - 169 (21%) of 804 Pts,
  - 80 (20%) in the hypo;
  - 89 (22%) in the conv.
- 5-year relapse-free survival:
  - Hypo-80·5% (95% CI 75·7–84·4)
  - Conv-77·1% (71·9–81·5)
- No treatment-related deaths

NOT SUPERIOR

Luca Incrocci et al. Lancet Oncol 2016

HYPRO Toxicity



BED (hypo#)= 211(tumor),90.4 (EQD2 tumor), 86.56(Early), 137.81(late)
Vs
BED(conv#)= 182(tumor), 93.6(early), 130(late)

Cumulative grade ≥2 late genitourinary toxicity

At 3 years: Conv–39·0% (95% CI 34·2–44·1); Hypo–41·3% (36·6–

CI 0·98–1·38),

grade ≥2 late

~~could not be shown~~)

nal toxicity

nv–17·7% (14·1–

–21·9% (18·1–26·4)

HR of 1·19 (90% CI 0·93–1·52)

(non-inferiority could not be shown)

Shafak Aluwini, et al. Lancet Oncol 2016

HYPRO Toxicity

- Cumulative grade 3 or worse late genitourinary toxicity was significantly higher in the hypofractionation group than in the standard fractionation group (19·0% [95% CI 15·2–23·2] *vs* 12·9% [9·7–16·7], respectively; p=0·021),
- No significant difference between cumulative grade 3 or worse late gastrointestinal toxicity (2N6% [95% CI 1·2–4·7]) in the standard fractionation group and 3·3% [1·7–5·6] in the hypofractionation group; p=0·55).

Moderate Hypofractionation in High-Risk, Organ-Confined Prostate Cancer: Final Results of a Phase III Randomized Trial

Giorgio Arcangeli, Biancamaria Saracino, Stefano Arcangeli, Sara Gomellini, Maria Grazia Petrongari, Giuseppe Sanguineti, and Lidia Strigari

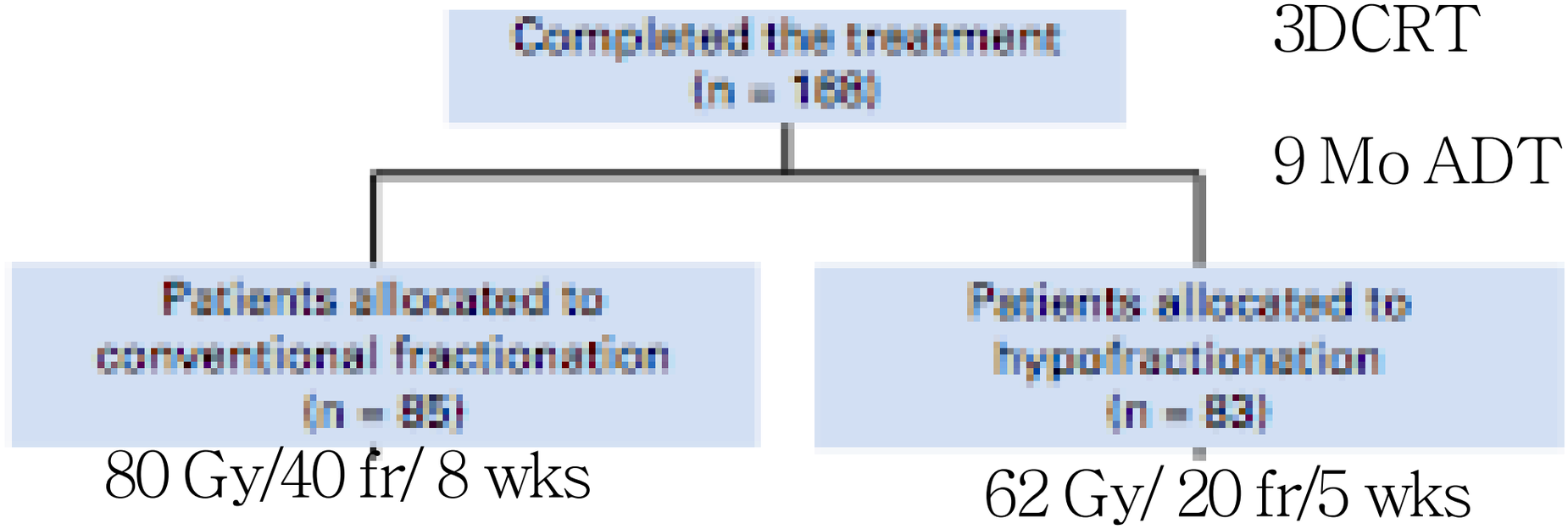
Regina Elina NCI
Italian Trial

J Clin Oncol. 2017;35:1891-1897.

High risk

2003 -2007; MFU 9 YEARS

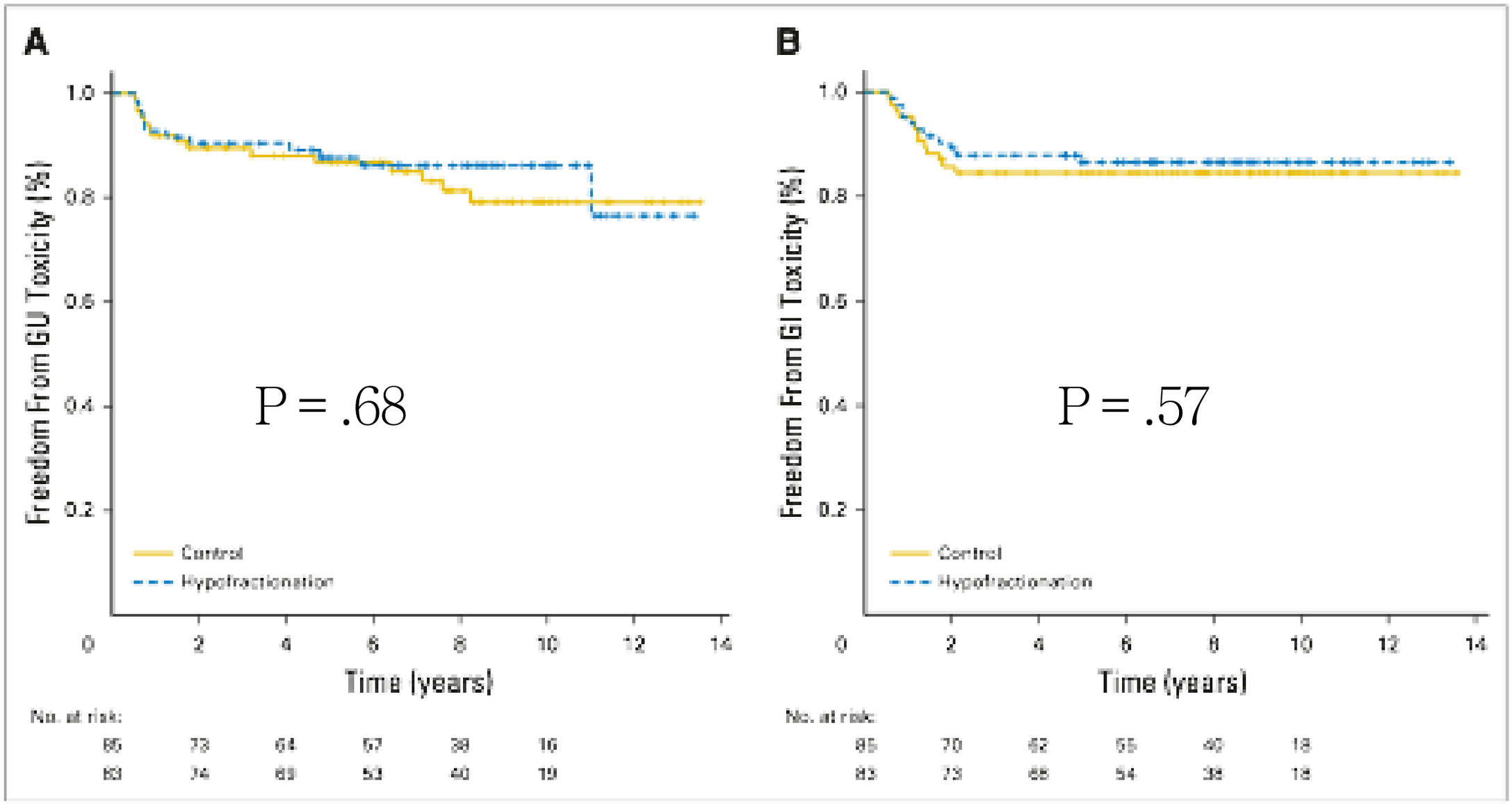
Target: prostate + SV



3DCRT

9 Mo ADT

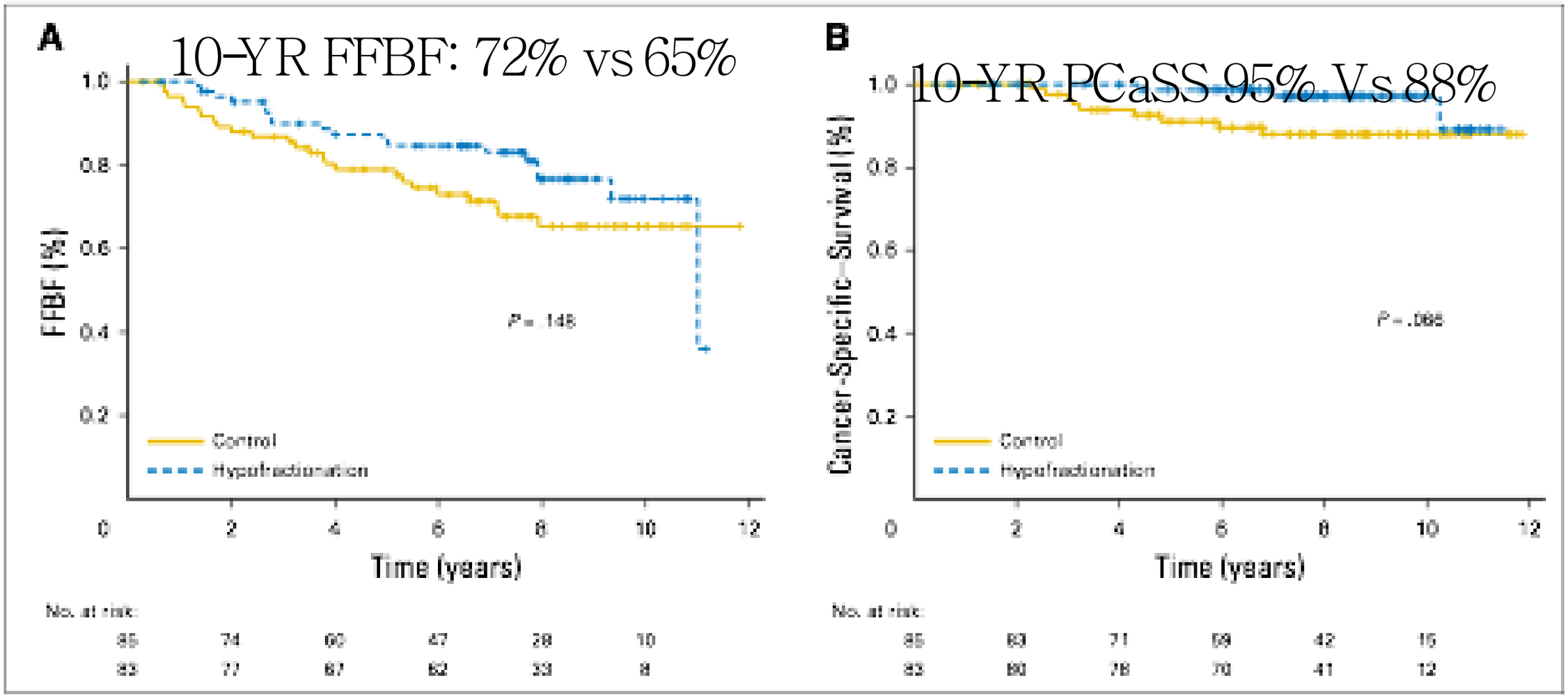
>/= Grade 2 Late Toxicities



No difference

J Clin Oncol. 2017;35:1891-1897.

Survival



Ten-year OS rates:75% in the hypofr Vs 64% in the conventional (P = .22).

Hypofractionation was a significant prognostic factor for FFBF and PCaSS, when adjusted for clinical prognostic variables

J Clin Oncol. 2017;35:1891-1897.

PROstate Fractionated Irradiation Trial (PROFIT)

Randomized Trial of a Hypofractionated Radiation Regimen for the Treatment of Localized Prostate Cancer

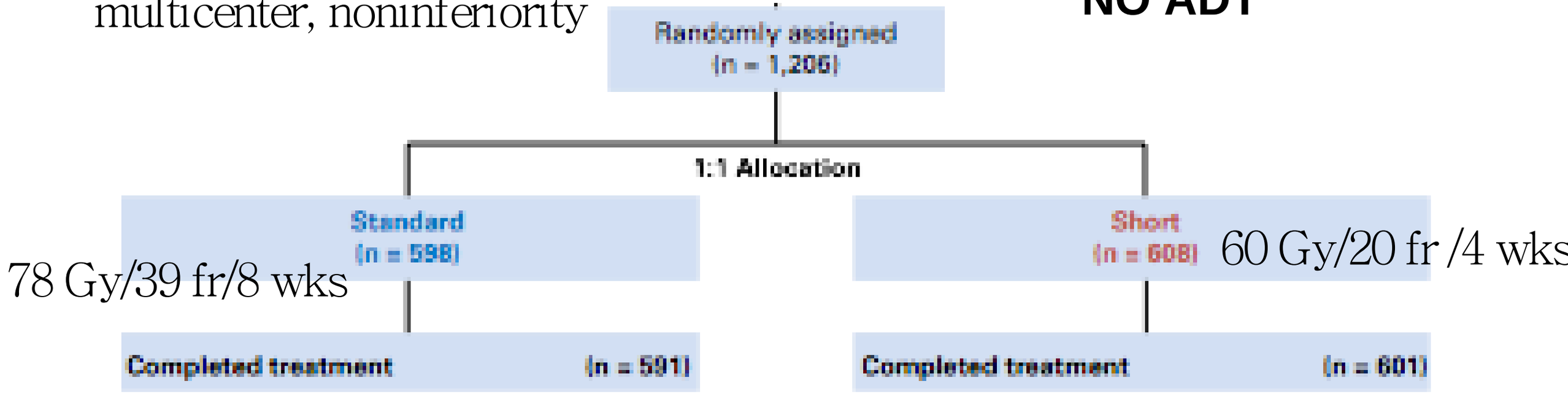
Charles N. Catton, Hima Lukka, Chu-Shu Gu, Jarad M. Martin, Stéphane Supiot, Peter W.M. Chung, Glenn S. Bauman, Jean-Paul Bahary, Shahida Ahmed, Patrick Cheung, Keen Hun Tai, Jackson S. Wu, Matthew B. Parliament, Theodoros Tsakiridis, Tom B. Corbett, Colin Tang, Ian S. Dayes, Padraig Warde, Tim K. Craig, Jim A. Julian, and Mark N. Levine

Canada

J Clin Oncol. 2017;35:1884-1890

Intermediate-risk

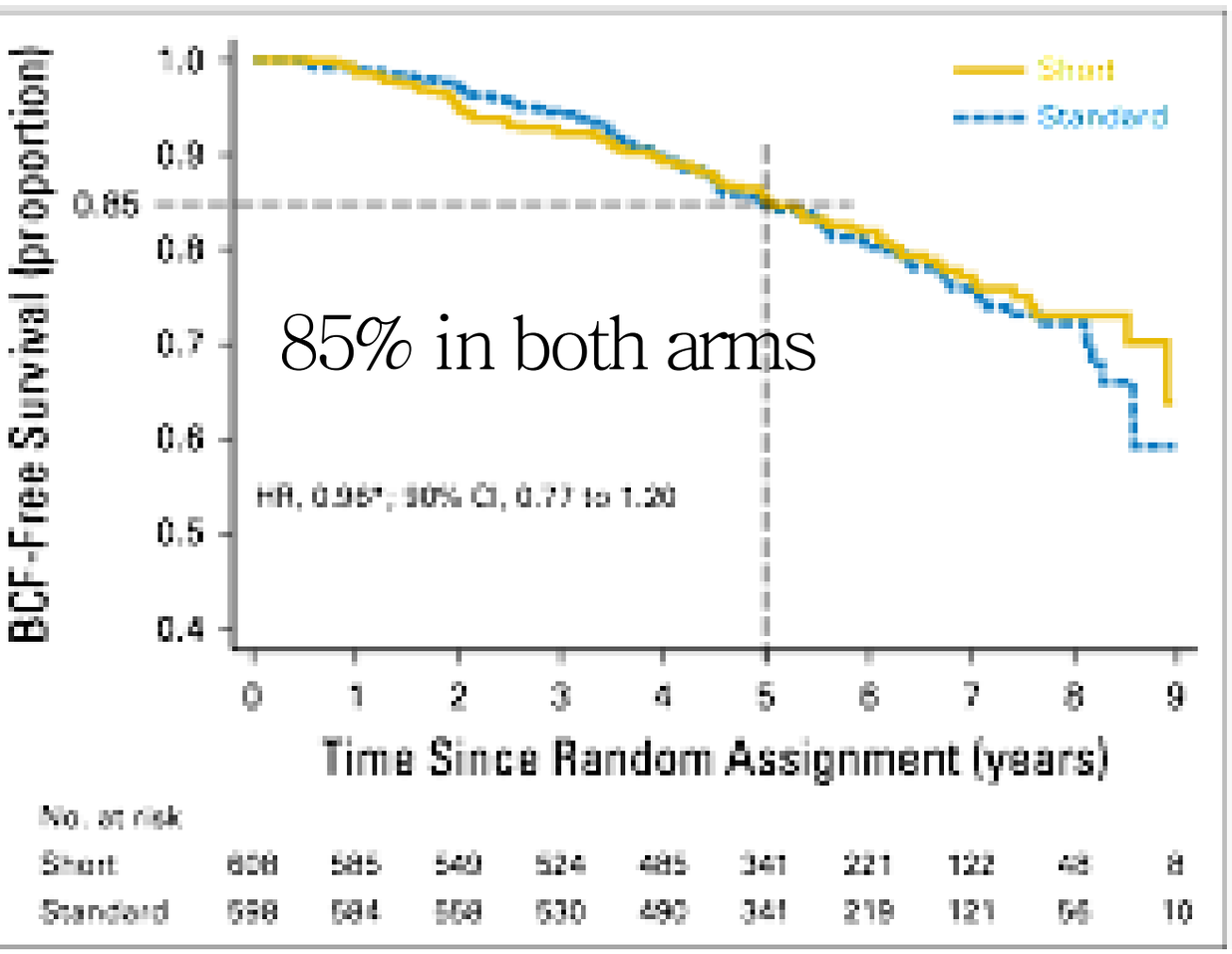
multicenter, noninferiority

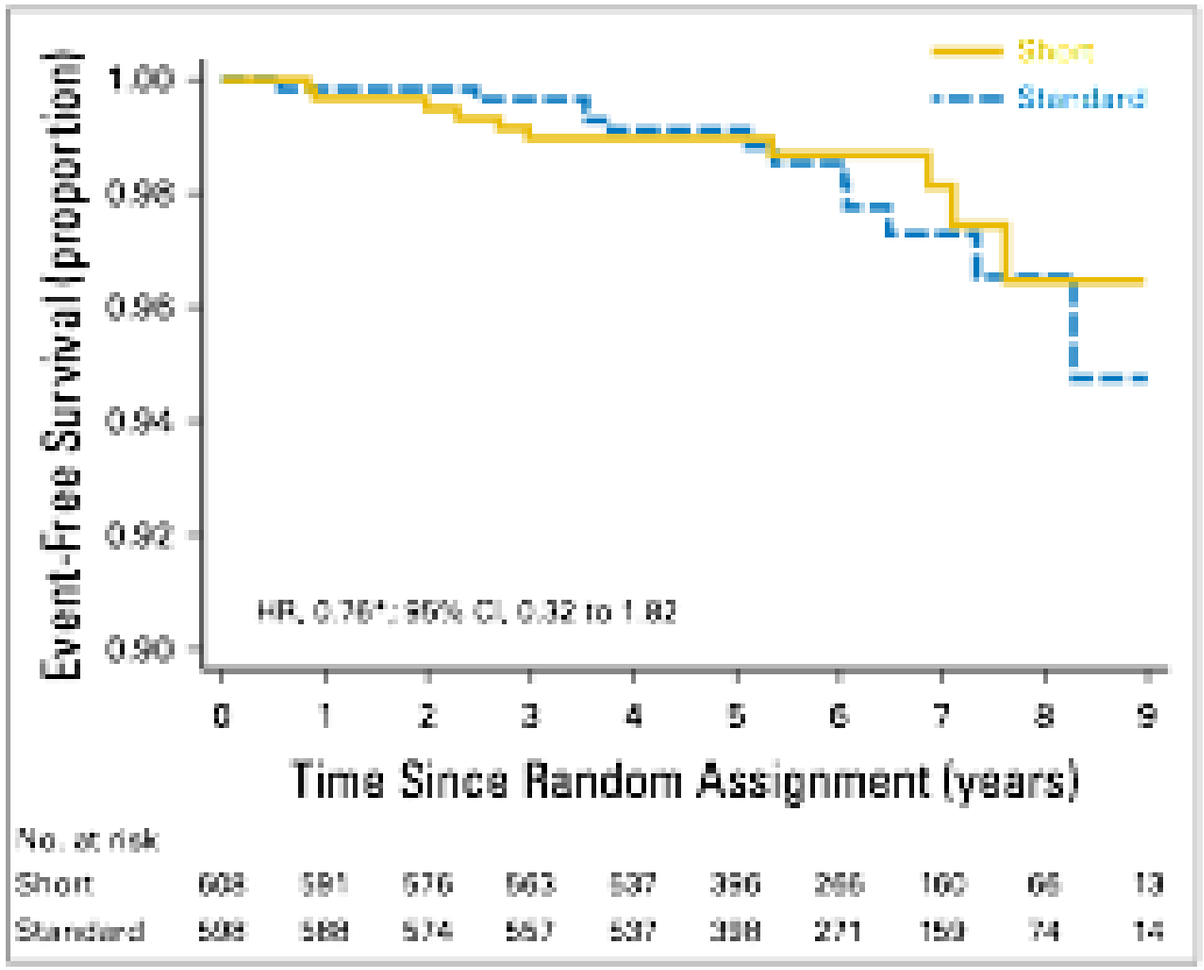


NO ADT

MFU: 6 yrs

Results





109 of 608 patients in the hypo versus 117 of 598 in the standard experienced BCF.

Ten deaths as a result of prostate cancer occurred in the short arm and 12 in the standard arm.

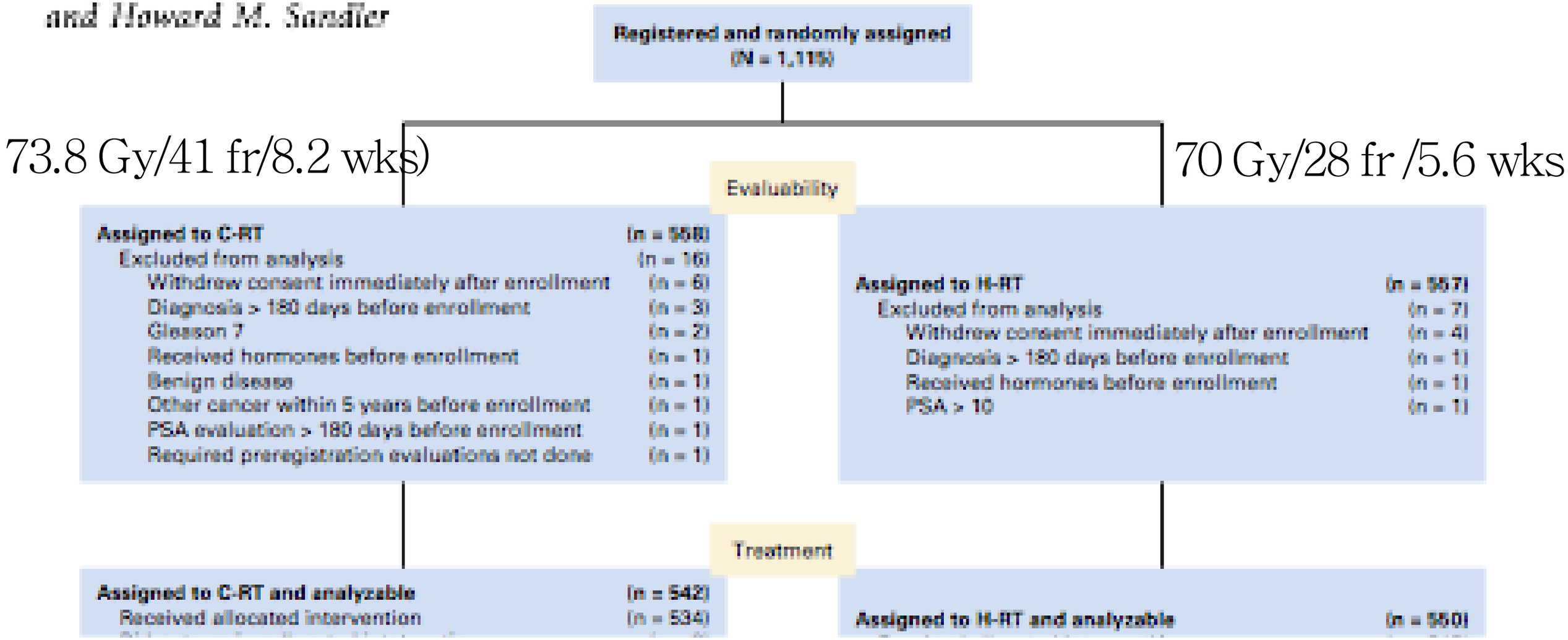
No significant differences were detected between arms for grade Gr 3 late genito-urinary and GI toxicity

J Clin Oncol. 2017;35:1884-1890

Randomized Phase III Noninferiority Study Comparing Two Radiotherapy Fractionation Schedules in Patients With Low-Risk Prostate Cancer

NRG Oncology RTOG 0415

W. Robert Lee, James J. Dignam, Mahul B. Amin, Deborah W. Bruner, Daniel Low, Gregory P. Swanson, Amit B. Shah, David P. D'Souza, Jeff M. Michalski, Ian S. Dayes, Samantha A. Seaward, William A. Hall, Paul L. Nguyen, Thomas M. Pisansky, Sergio L. Faria, Yuhchyau Chen, Bridget F. Koontz, Rebecca Paulus, and Howard M. Sandler



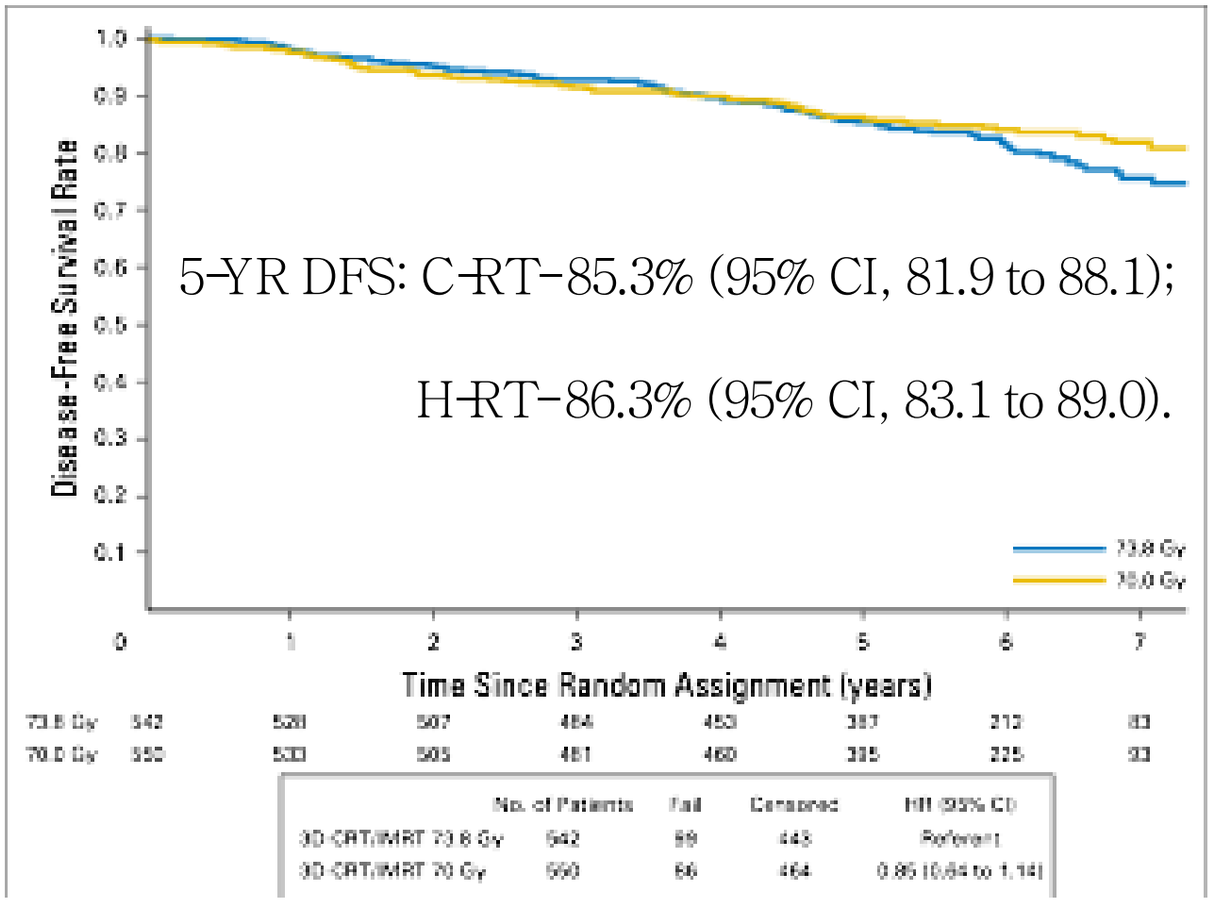
73.8 Gy/41 fr/8.2 wks)

70 Gy/28 fr /5.6 wks

MFU 5.8 YRS

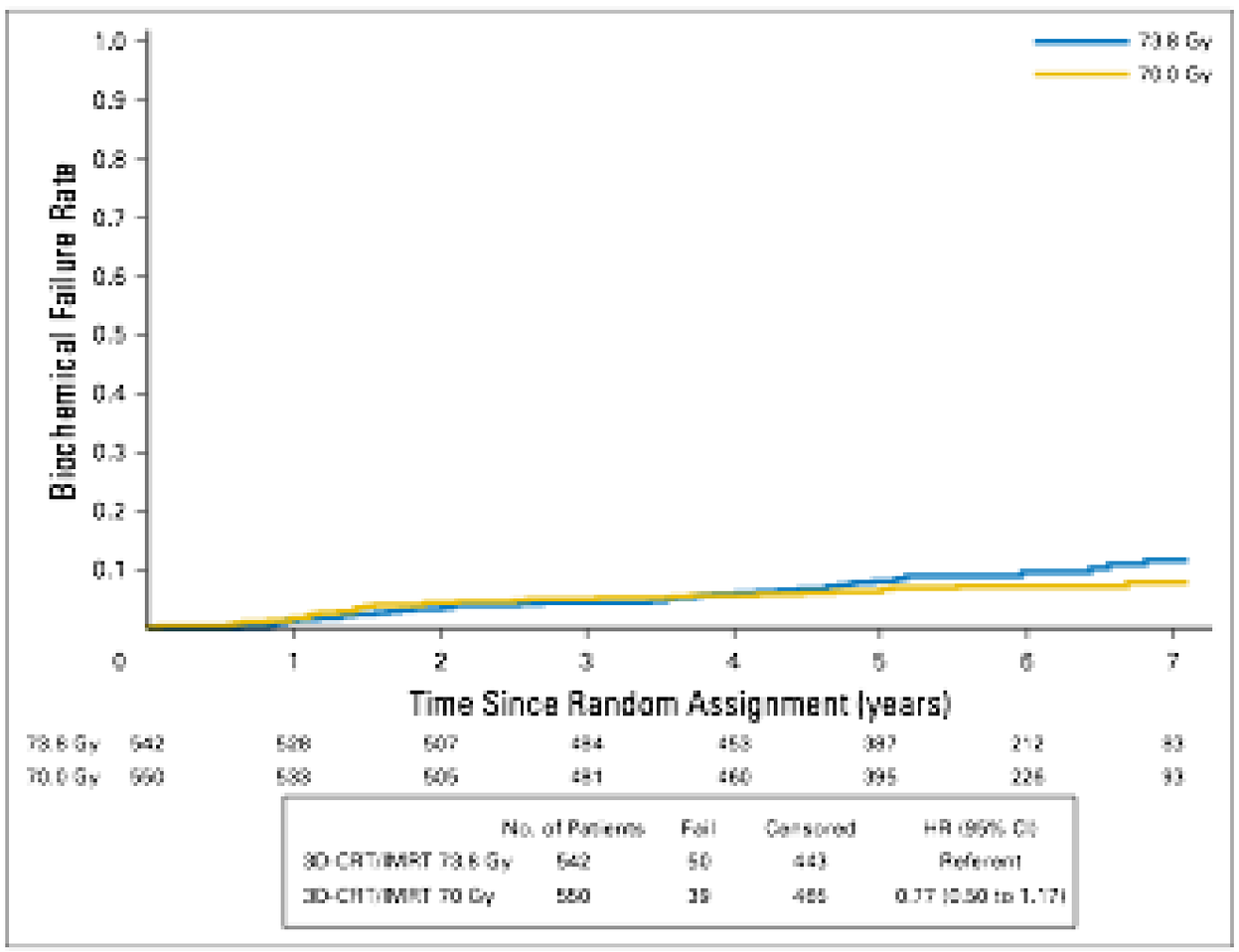
J Clin Oncol 34:2325-2332

Results



5-YR DFS: C-RT-85.3% (95% CI, 81.9 to 88.1);

H-RT-86.3% (95% CI, 83.1 to 89.0).



NON INFERIOR

Late grade 2 and 3 GI and genitourinary adverse events were increased (HR, 1.31 to 1.59) in patients who were treated with H-RT

J Clin Oncol 34:2325-2332

Hypo-fractionation RCTs- Summary

Trial	Design	HF dose	Standard dose	EQD2	Sample size	F/up	Efficacy	Acute toxicity	Late Toxicity
PROFIT (Canada)	Non-inf	60Gy/20#/4w	78Gy/39#/8w	77Gy	1206 Interm	6y	5y DFS 85% v 85%	GU same ≥G2 GI more in HF	GU same ≥G2 GI more in standard
CHHiP (UK)	Non-inf	60Gy/20# or 57Gy/19#	74Gy/37#/8w	77Gy/ 73.3G	3216 Interm	5y	5y DFS 90.6% v 85.9% v 88.3%	No diff	No diff
Italian (Arcagneli)	Non-inf	62Gy/20#/5w	80Gy/40#/8w	81.5	168 High	9y	10y DFS 72% v 65%	No diff	No diff
HYPRO (Dutch)	Sup.	64.6Gy/19#/6w	78Gy/39#/8w	90.4	820 High	5y	5y DFS 80.5% v 77.1%	GU same GI more in HF	≥G2 more in HF
RTOG 0415 (US)	Non-inf	70Gy/28#/5.6w	73.8Gy/41#/8	80Gy	1115 Low	5.8y	5y DFS 86.3% v 85.3%	No diff	G2, G3 more in HF

Hypofractionation offers equal, rates of tumor control in patients with low and intermediate risk prostate cancers with similar toxicities

www.impactjournals.com/oncotarget/ Oncotarget, 2017, Vol. 8, (No. 2), pp: 2647-2658

Research Paper

Moderate hypofractionated radiotherapy is more effective and safe for localized prostate cancer patients: a meta-analysis

Ling Cao[1], Yong-Jing Yang[1], Zhi-Wen Li[2], Hong-Fen Wu[1], Zhu-Chun Yang[1], Shi-Xin Liu[1], Ping Wang[3]

[1] Department of Radiation Oncology, Cancer Hospital of Jilin Province, Changchun 130012, People's Republic of China

9 studies with 5969 patients

H-RT group: greater improvements in

- **5-year biochemical or clinical failure-free survival (RR = 1.04, 95% CI:1.01–1.08; *P* = 0.01)**
- **5-year disease-free survival(RR = 1.04, 95% CI: 1.01–1.07, *P* = 0.02).**

5-year overall survival comparable (RR = 1.02, 95% CI: 0.99–1.04; *P* = 0.18).

Grade 2-4 acute/late gastrointestinal toxicity, grade 2–4 acute/late genitourinary toxicity- no statistical differences.

Patients with localized prostate cancer, moderate H-RT

Hypofractionated Adjuvant/ Salvage Radiotherapy

Table 2 Hypofractionated adjuvant/salvage radiotherapy

Reference	Study design	Institution	Patient collection	Fractionation (total dose/singel dose/fractions)	EQD for tumor α/β ratio 1.4Gy	EQD for normal tissue α/β ratio 3Gy	IMRT	Follow-up	Acute GU toxicitiy	Late GU toxicity	Acute GI toxicity	Late GI toxicity	Therapeutic outcomes
Cozzarini, C. [23]	Prospective phase HI for adjuvant RT	Milan, Italy	247 patients	65.8Gy/2.35Gy/28 fractions adj. RT for 117 pat.; 71.4-72.8Gy/2.55Gy/ 28 fractions salvage RT for 80 pat.; 58Gy/ 2.9Gy/20 fractions for 50 pat. Conventional arm 929 pat. 70.2Gy/ 1.8Gy/39 fractions	72.6Gy adjuvant RT; 83.0Gy salvage RT; 73.4Gy for the other 50 pat.	α/β ratio = **5Gy** for late GU toxicity! 69.14Gy adjuvant RT; 77.1Gy salvage RT; 65.5Gy for the other 50 pat.	Tomo-RT	68 months median	-	41/247 (16.5%) ≥ III° GU in hypofraction arm; 72/929 (7.7%) in conventional arm	-	-	-
Kruse, T.J. [26]	Retrospective for salvage RT	Madison, Wisconsin	108 patients	65Gy/2.5Gy/26 fractions	74.6Gy	71.5Gy	IMRT	32.4 months median	8 pat. (7%) II° and 1 pat. III° GU RTOG.	16 pat. (15%) II° GU RTOG.	15 pat. (14%) II GI RTOG.	4 (4%) pat. II° GI RTOG.	freedom from biochem. failure at 4 years 67% ± 5.3%.
Ippolito, E. [24]	Prospective phase I for dose-escalation, adjuvant RT	Campobasso, Italy	25 patients	7 pat. 56.8Gy/ 2.27Gy/25 fractions; 6 pat. 59.7Gy/2.39Gy/ 25fractions; 6 pat. 61.25Gy/2.45Gy/ 25fractions; 6 pat. 62.5Gy/2.5Gy/25 fractions	7 pat. 61.3Gy; 6 pat. 66.5Gy; 6 pat. 69.4Gy; 6 pat. 71.7Gy.	7 pat. 59.9Gy; 6 pat. 64.4Gy; 6 pat. 66.8Gy; 6 pat. 68.8Gy.	IMRT	19 months median	9/25 (36%) II° GU.	-	5/25 (20%) II° GI.	-	-
Lee, W. [52]	Retrospective for salvage RT	Manchester	37 patients	50-52.5Gy/2.5-2.63Gy/ 20 fractions	57.4-62.2Gy	55-59.1Gy	-	30.6 months median	0% II° GU.	16 pat. I° GU, 0 pat. II° GU.	0% II° GI.	4 pat. I° GI, 1 pat. II° GI.	3-year disease-free survival is 74%.

Hypo to Prostate with Conv To Pelvic Nodes

Table 3 Hypofractionated radiotherapy including pelvic nodes

Reference	Study design	Number of patients	Fractionation (total dose/singel dose/fractions)	pelvic RT dose schema	EQD for tumor α/β-ratio 1.4Gy	EQD for normal tissue α/β-ratio 3Gy	Follow-up	Acute GU toxicitiy	Late GU toxicity	Acute GI toxicity	Late GI toxicity
McDonald, A. M. [31]	Retrospective	57 PORT and 31 WPRT	70Gy/2.5Gy/28 fractions	50.4Gy/ 1.8Gy/28 fractions	80.3Gy	77Gy	41 months	18/31(58%) in PORT, 28/57 (49%) in WPRT ≥2°	4/57(7%)in WPRT, 0% in PORT ≥ III°	7/31(23%) in PORT, 23/57 (40%) in WPRT ≥ II°	0% in PORT, 10/57 (18%) in WPRT ≥ II°
McCammon, R. [30]	Retrospective	30	70Gy/2.5Gy/28 fractions	50.4Gy/ 1.8Gy/28 fractions	80.3Gy	77Gy	24 months	36.7% ≥2°	10% ≥ II°	20%	13% ≥ II°
Adkinson, J.B. [29]	Phase I prospective	53	70Gy/2.5Gy/28 fractions	56Gy/ 2Gy/28 fractions	80.3Gy	77Gy	25.4 months	20/53(38%) ≥2°	14/53(27%) ≥ II°	17/53(32%) ≥ II°	4/53(8%) ≥ II°
Pervez, N. [32]	Phase II prospective	60 high-risk	68Gy/2.72Gy/25 fractions	45Gy/ 1.8Gy/25 fractions	82.4Gy	77.8Gy	3 months	34(40%) ≥ II°	-	21(35%) ≥ II°	-
Quon, H. [33]	Prospective phase I-II	97 pat. High-risk	67.5Gy/2.7Gy/25 fractions	45Gy/ 1.8Gy/25 fractions	81.4Gy	77Gy	39 months median	50% I°, 39% II°, 4% III°	9% I°, 5% II°, 3% III°, 1% IV°.	4% pat. 0°, 59% I °, 37% II°	54% pat. 0°, 40% I°, 7% II°
Guckenberg, M. [34]	150 consecutive patients	109 PORT and 41 WPRT	73,9Gy/2,31Gy/32 fx; 76.2Gy/2.31Gy/33 fx.	45Gy/ 1.8Gy/25 fractions	80.6Gy;83.1Gy.	78.5Gy; 80.9Gy.	50 months median	85% pat. I°-II°	22.4% Pat. ≥ II° at 60 months; less than 5% pat. III°.	-	2 pat. ≥III°
Fonteyne, V. [53]	Prospective phase I	31 patients	69.3/2.77Gy/25 fractions	50Gy/ 2.0Gy/25 fractions	85Gy	80Gy	3 months median	14/31 (45%) II°, 3/31 (9.7%) III°	-	14/31 (45%) II° lower GI toxicity	-
Zilli, T. [54]	Prospective trial	78 pat.	50.4Gy/1.8Gy/28 fractions +6x4Gy boost (twice weekly)	50.4Gy/ 1.8Gy/28 fractions	85.2Gy with 1.5Gy alpha/ beta	-	57 months	~1% = III°	5 year suivival rate without II° GU toxicity 79.1 ± 4.8%	~1% = III°	5 year suivival rate without II° GI toxicity 84.1 ± 4.5%

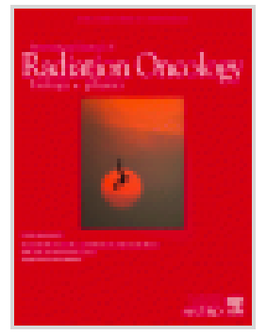
SBRT/SABR:The Extreme Hypo-fractionation

SBRT Doses

Dose ranges:	BED	
6.70 x 5 = 33.5 Gy	146	Madsen IJROBP 2007
7.25 x 5 = 36.25 Gy	168	King IJROBP 2009 King IJROBP 2011 Friedland TCRT 2009 Katz BMC Urol 2010 Wiegner IJROBP 2010 Bolzicco TCRT 2010 Aluwini J Endourol 2010 Freeman RO 2010 Townsend AJCO 2011 Kang Tumori 2011 Jabbari IJROBP 2011 Mantz IJROBP 2011
7.5 x 5 = 37.5 Gy	178	
9.0 x 4 = 36.0 Gy	198	Fuller IJROBP 2008
8.0 x 5 = 40.0 Gy	200	King RO 2013
9.0 x 5 = 45.0 Gy	248	Boike JCO 2011 / Kim ASTRO 2013
9.5 x 5 = 47.5 Gy	273	
10.0 x 5 = 50.0 Gy	300	
24 x 1 = 24 Gy	312	Greco, Lisbon

International Journal of Radiation Oncology*Biology*Physics

Volume 82, Issue 2, 1 February 2012, Pages 877–882



Clinical Investigation

Long-Term Outcomes From a Prospective Trial of Stereotactic Body Radiotherapy for Low-Risk Prostate Cancer

This paper was presented at the 52nd Annual Meeting of the American Society for Radiation OncologySan Diego Convention Center, San Diego, CA. November 2010

Christopher R. King, Ph.D., M.D.*, , James D. Brooks, M.D.†, Harcharan Gill, M.D.†, Joseph C. Presti Jr., M.D.†

- Low-risk prostate cancer
- 67 patients
- 36.25 Gy in 5 fractions with CyberKnife system
- Median follow-up of 2.7 years
- Low rates of Late rectal and urinary toxicity - >G2 in 1 & 5 pts respectively
- The 4- year Kaplan-Meier PSA relapse-free survival was 94% and is similar to other definitive treatments

SABR Results

Phase II trial

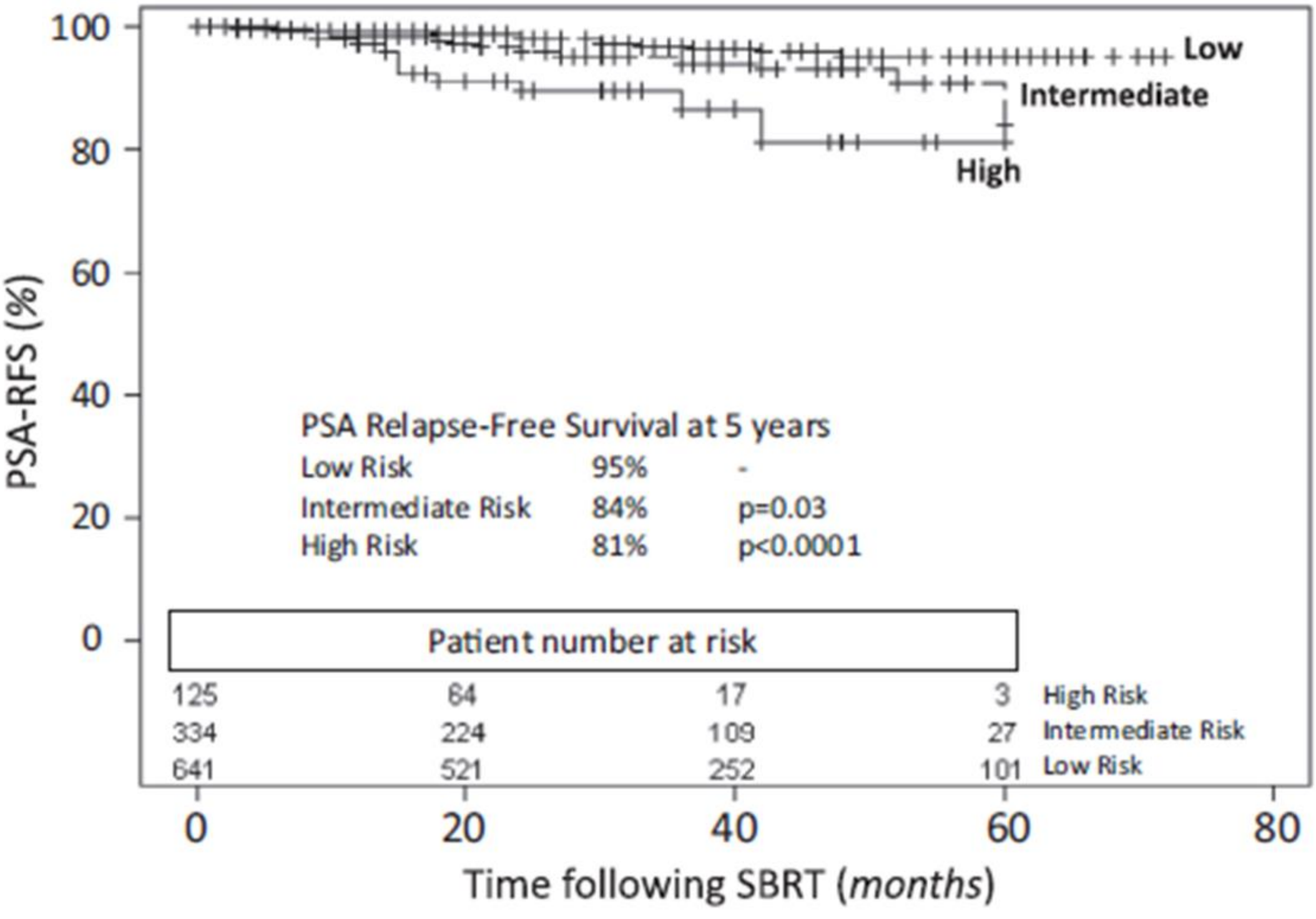
Stereotactic body radiotherapy for localized prostate cancer: Pooled analysis from a multi-institutional consortium of prospective phase II trials ☆,☆☆

Christopher R. King [a,*], Debra Freeman [b], Irving Kaplan [c], Donald Fuller [d], Giampaolo Bolzicco [e], Sean Collins Robert Meier [g], Jason Wang [a], Patrick Kupelian [a], Michael Steinberg [a], Alan Katz [h]

- Multi-institutional pooled data
- N – 1100
- Median dose – 36.25 Gy in 5 fractions (35-40 Gy/4-5#)
- 3 yr median FU, 335 cases with a >4 years follow-up (median 53 mos)
- Risk group
  - Low risk – 59%
  - Intermediate risk – 30%
  - High risk – 11%
- ADT – 14%

King et al Radiother Oncol 2013; 109:217-21

SBRT Results



King et al Radiother Oncol 2013; 109:217-21

SABR Advantage

Conv
- 8 weeks

Moderate Hypo
- 4 weeks

SABR- 5 days

- Safe and Effective treatment
- Short treatment
- Convenient for patient
- Less Hospital visits
- Less waiting times
- Non Invasive
- No Anaesthesia
- No Hospital stay
- May be less cost

ASTRO Model Policies

STEREOTACTIC BODY RADIATION THERAPY (SBRT)

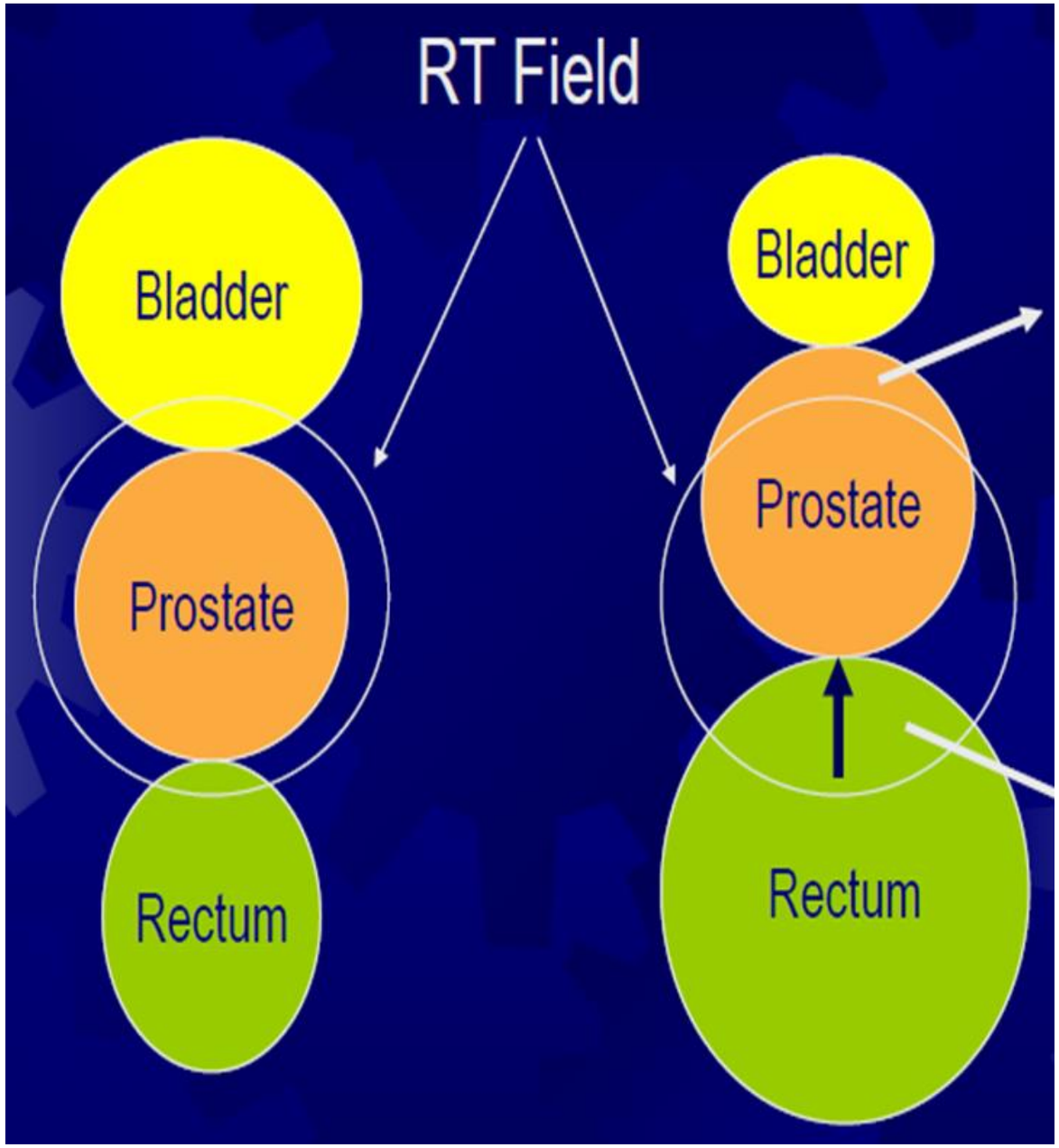
Prostate Cancer:

Many clinical studies supporting the efficacy and safety of SBRT in the treatment of prostate cancer have been published. At least one study has shown excellent five year biochemical control rates with very low rates of serious toxicity. Additionally, numerous studies have demonstrated the safety of SBRT for prostate cancer after a follow-up interval long enough (two to three years) to provide an opportunity to observe the incidence of late GU or GI toxicity. While it is necessary to observe patients treated for prostate cancer for extended intervals to gauge the rate of long term (beyond 10 years) biochemical control and overall survival, the interim results reported appear at least as good as other forms of radiotherapy administered to patients with equivalent risk levels followed for the same duration post-treatment.

It is ASTRO's opinion that data supporting the use of SBRT for prostate cancer have matured to a point where SBRT could be considered an appropriate alternative for select patients with low to intermediate risk disease.

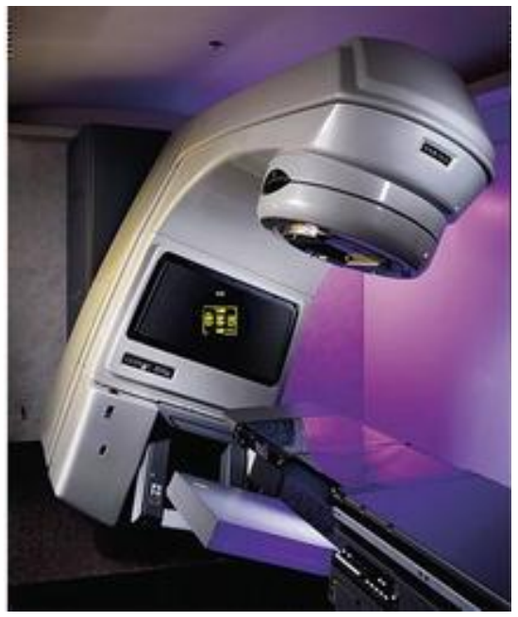
Image Guidance Very Critical

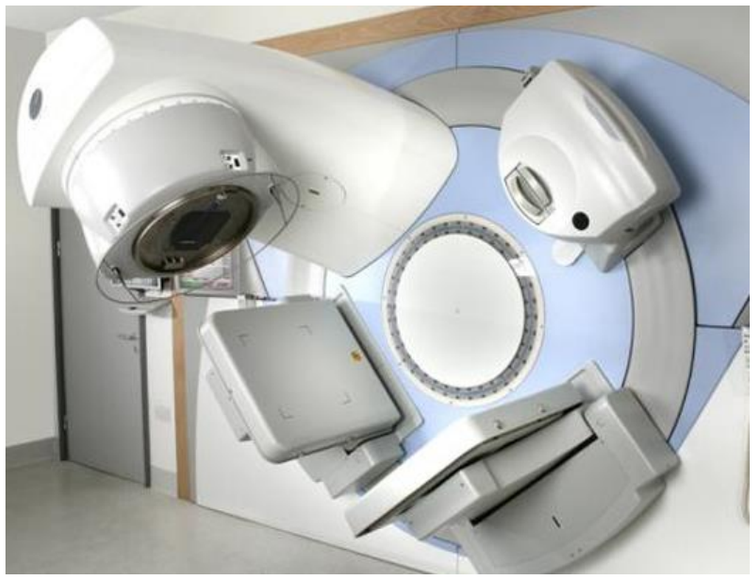
- Prostate motion
  - Inter-fraction
  - Intra-fraction
- Bony Anatomy as surrogate for prostate location
  - Not reliable
  - Significant variation
- Advantage
  - Tight margin
  - Better sparing
  - Improved treatment delivery
- Real time Guidance best

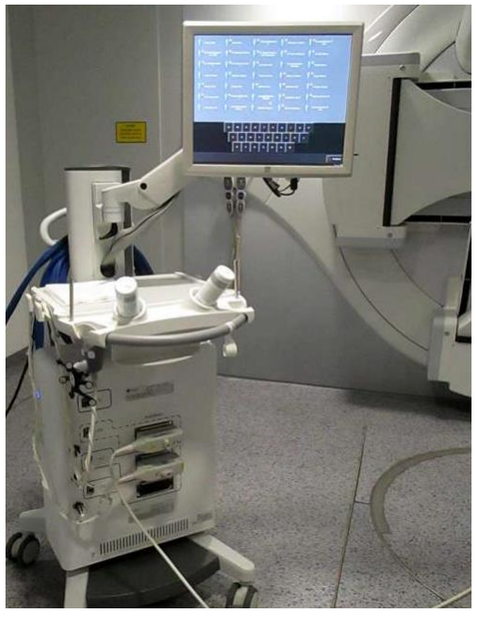


IGRT Technologies

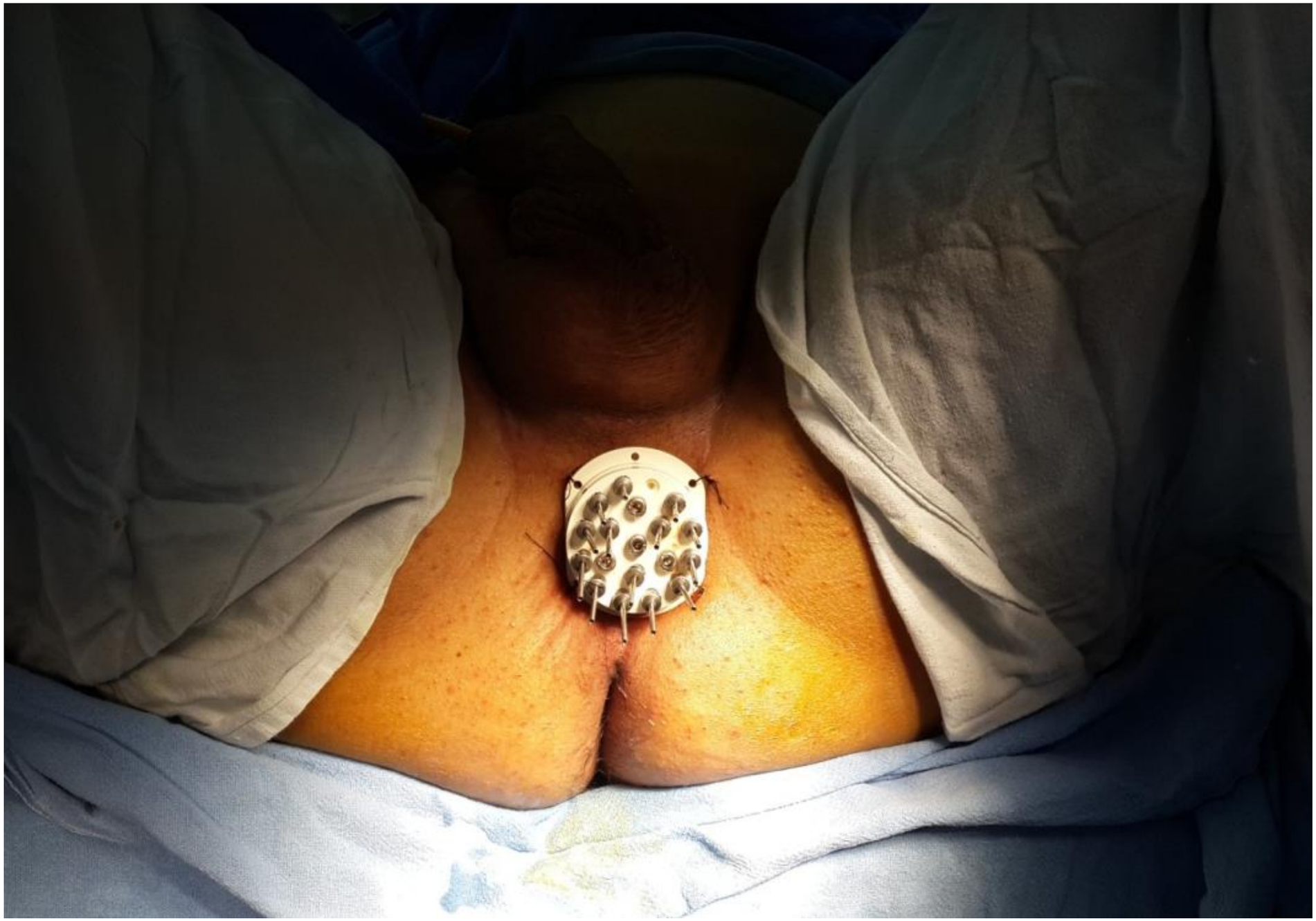
- Electronic Portal Imaging
- Cone Beam CT
- **Ultrasound (CLARITY)**
- Orthogonal X rays
- Tomotherapy







Brachytherapy: Intrinsically HypoFr



Randomised trial of external beam radiotherapy alone or combined with high-dose-rate brachytherapy boost for localised prostate cancer

Peter J. Hoskin[a], Ana M. Rojas[a,*], Peter J. Bownes[b], Gerry J. Lowe[a], Peter J. Ostler[a], Linda Bryant[a]

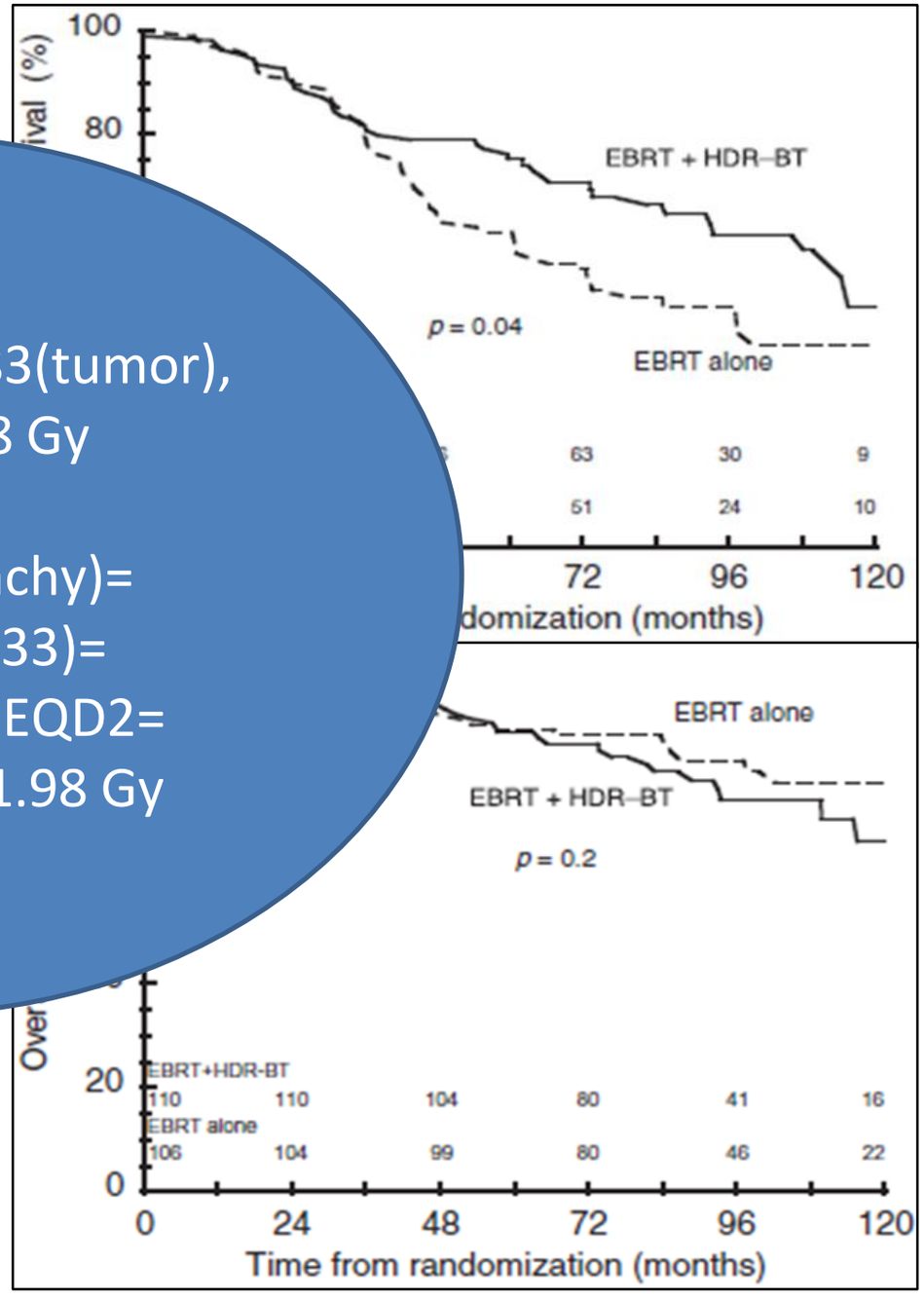
- n= 218
- T1-T3 and PSA <50 ng/mL
- Radiotherapy
  - EBRT alone – 55 Gy/20#
  - EBRT 35.75 Gy/13# → HDR Brachytherapy 8.5 Gy x 2#
- ADT – 76%
- Primary end point - bRFS

Hoskin et al Radiother Oncol 2012; 103:217-22

Brachy Results

- 10 yr bRFS
  - EBRT only – 39 %
  - EBRT + Brachy boost –
    (p=0.04)
- 10 yr OS
  - EBRT only – 7
  - EBRT + Brac
    (p=0.2)
- GU and GI toxic
  - Similar
- Risk of relapse
  - Treatment arm
  - Risk category
  - ADT

BED (EBRT)= 155.83(tumor), EQD2= 66.78 Gy
Vs
BED(EBRT+Brachy)= (101.29+113.33)= 214.62(tumor), EQD2= 43.41+48.57=91.98 Gy



How I do It ? (Photos, Videos)

CT simulation with Clarity USG
Contouring
Planning
Plan Evaluation
Treatment set up with Clarity
Treatment

Conclusions

- Dose escalation important for disease control in prostate cancers
- Dose escalation can be achieved by Hypofractionation
- Moderate hypo fractionated radiotherapy offers equal rates of tumor control with similar toxicities
- Extreme hypofractionation by SBRT an appropriate alternative
- Brachytherapy also helps in dose escalation and better disease outcomes

THANK YOU