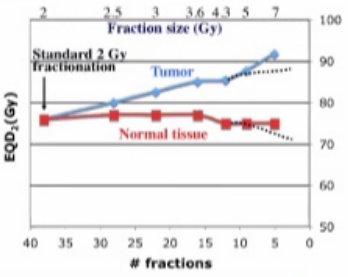
SBRT PROSTATE -BECOMING A STANDARD OPTION WORLDWIDE

Practical applications in radiotherapy have developed considerably over the past 60 years. Medical imaging, immobilization techniques and advances in computer soft ware programs enable the use of broad-based stereotactic body radiotherapy (SBRT). SBRT is a special type of external radiation therapy that is irradiated with a high radiation dose of 1 to 5 fractions with smaller safety margins than the target conventional irradiation.By condensing the course of therapy to four or five treatments, SBRT — also known as extreme hypofractionation or stereotactic ablative therapy — has pushed the hypothesis that short-term, high-dose treatments can be effective and safe against some forms of prostate cancer Although different from traditional radiobiological concepts, SBRT is a promising treatment model with a high local control rate, low normal tissue toxicity, and short treatment duration compared with conventional radiotherapy. Stereotactic radiotherapy can be used in various parts of the body due to noninvasive stabilization methods and the availability of taking target images during treatment. It has been started to be used in primer lung cancers and lung metastases, primary liver cancers and liver metastases, pancreatic cancers, prostate cancer.

Fifteen years ago a handful of researchers began investigating stereotactic body radiation therapy (SBRT) for low- and medium-risk prostate cancer. The basis for the research was a theoretical radiobiological advantage.Large fraction doses are biologically superior in prostate cancer to small fraction doses. Due to the low α/β ratio (1.4-3 Gy) of tumor cells in prostate cancer, high doses can be achieved. Therapeutic rate is also increased with hypofractionational application.

Biological Rationale

- **Prostate α/β : 1.5 to 1.8**



Parameters	Conventional fractionation	Moderate hypofractionation	Extreme fractionation/ SBRT
Equi-effective dose	74Gy/37#	60Gy/20#	36.25Gy/5#
Dose/#	2Gy	3 Gy	7.5Gy
Rectum BED (α/β :3)	**123 Gy**	**120 Gy**	**106 Gy**
Prostate BED			
α/β = 10	89 Gy	78 Gy	62 Gy
α/β = 2	148 Gy	150 Gy	168 Gy
α/β = 1.5	173 Gy	180 Gy	210 Gy

A major advantage exploiting the radiobiological advantage which prostate cancer SBRT offers is that the BED -Biological Equivalent Dose to prostate increases as the fractions are reduced with higher dose per fraction and Rectal BED s decrease there by increasing the therapeutic ratio and lesser toxicities to rectal tissue by treating with extreme hypofractionation.

The initial investigation to Prostate SBRT dates back to 2004 wheb Bent et al group studied SBRT with 33.5Gy in 5 fractions -SHARP Trial which set the pace for furture trials. Though this was a phase 1/2 trial , it had promising results with comparable GI and GU toxicities to conventional hypofractionation.

Currently there are many Phase 3 trials which are recruting patients and few of the trials like HYPO RT -PC which has been published. PACE -B study has also recently published the toxicity data and the results have been extremely good and the evidence is in and there is good news favoring prostate SBRT.

Trial Name	NRG-GU 005	PACE B	HYPO RT-PC	PACE C	PRIME
Study/Group	NRG Oncology	Royal Marsden NHS	Scandinavia	Royal Marsden NHS	TMH & TMCK, India
Stage/ Eligibility	Low Risk (cT1a-T2b)	Low risk- favorable Intermediate risk (cT1-T2c, GS ≤7)	Intermediate risk	Unfav. intermediate risk / Fav High risk	High risk / Very high risk / Node +ve
Target Accrual	606	1716	1200	1182	464
Interventions	36.25 Gy/5# 70 Gy/28#	36.25 Gy/5# 78 Gy/39#	42.7 Gy/7# 78 Gy/39#	36.25 Gy/5# 60 Gy/20#	36.25 Gy/5# 68 Gy/25#
Primary end point	DFS, 2-yr EPIC-26 bladder/rectal toxicity	5-yr BCF	5-yr FFBF	5-yr bPFS	5-yr BFFS
Estimated completion	Dec 2025	Sept 2021	Completed	Sept 2026	March 2024
Status	Enrolling	Accrual completed, **Acute toxicity results published**	**Results published**	Enrolling	Enrolling (200+)

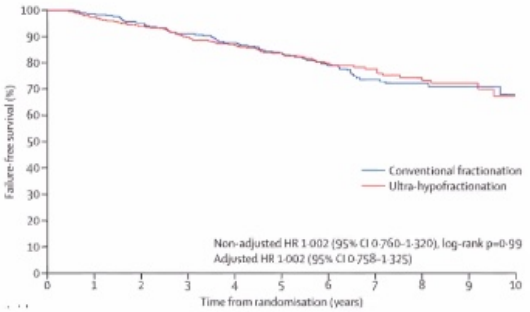
HYPO-RT SCANDINAVIAN PHASE 3 trial has published 5 year data and the results are extremely in favour of SBRT.

Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer: 5-year outcomes of the HYPO-RT-PC randomised, non-inferiority, phase 3 trial

Lancet 2019; 394: 385-95

Anders Widmark, Adalsteinn Gunnlaugsson, Lars Beckman, Camilla Thellenberg-Karlsson, Morten Hoyer, Magnus Lagerlund, Jon Kindblom, Claes Ginman, Bengt Johansson, Kirsten Björnlinger, Mihajl Seke, Måns Agrup, Per Fransson, Björn Tavelin, David Norman, Björn Zackrisson, Harald Anderson, Élisabeth Kjellén, Lars Franzén, Per Nilsson

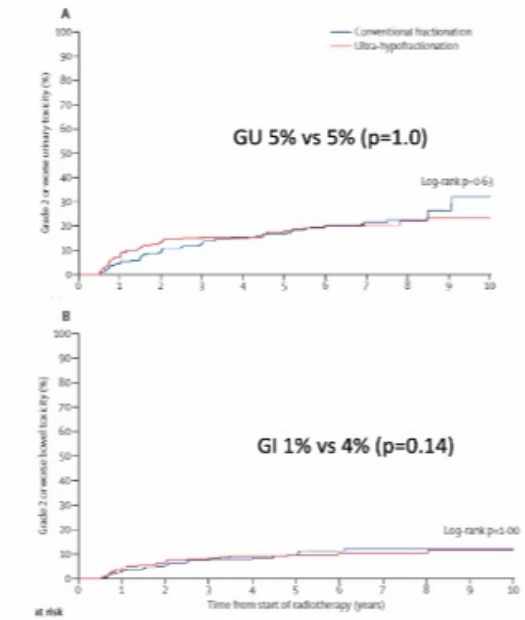
- **N= 1200, IR (89%)**
- No ADT
- **78 Gy/39# daily vs 42.7 Gy/7# alternate day**
- 3DCRT (80%) or IMRT (20%)
- Non-inferiority margin: 4% for 5-yr FFS



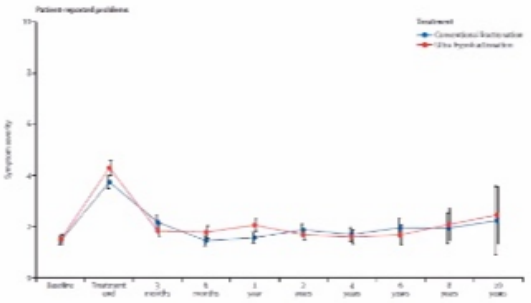
- **5-yr FFS 84% vs 84%** (HR: 1.002, p=0.99)
- **5-yr OS 96% vs 94%** (HR 1.1)

Toxicity data of HYPO-RT shows comparable results to conventional fractionation regimens.

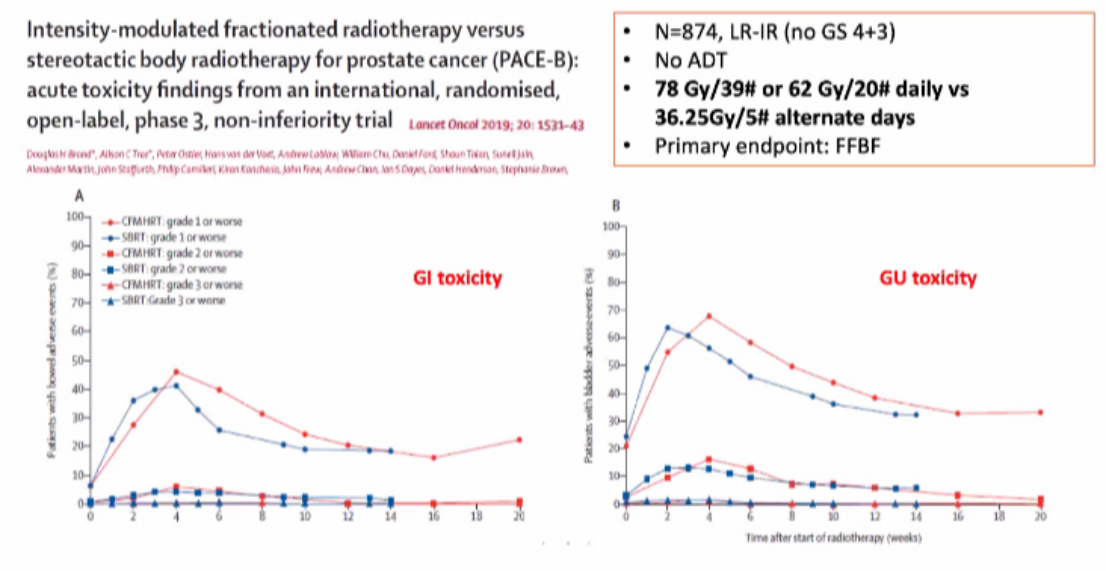
Physician reported cumulative RTOG gr II+ toxicity



PROs similar



Recently completed PACE-B studies has published the data on toxicities in 2019 which has shown similar comparable toxicity profile which has reiterated the feasibility of SBRT.



As more long-term data emerges on the viability of stereotactic body radiation therapy (SBRT, also referred to as SABR or stereotactic ablative radiotherapy), advances in linac-based treatment delivery technologies have created a significant uptick in the demand for prostate SBRT.

In Indian context the challenges of node positive diseases to be treated with SBRT and post TURP cases for RT warrants more caution to select the patients for SBRT . TMH and TMC jointly are recruiting patients and we will have our own data by 2024.