ACCURAY

Prostate SBRT and the PACE-B trial

Alison Tree, MBBS, BSc, FRCR, M.D.(Res)

Consultant Oncologist, Royal Marsden Hospital and Institute of Cancer Research, London, U.K.



Prostate SBRT and the PACE trial

Dr Alison Tree Consultant Oncologist, Royal Marsden Hospital and Institute of Cancer Research



Life demands excellence

Accuray Disclaimers and Disclosure

Disclosure

The views contained and expressed in this presentation, including any accompanying oral commentary, are those of the presenter and do not necessarily reflect the views or policies of Accuray Incorporated or its subsidiaries. No official endorsement by Accuray Incorporated or any of its subsidiaries of any vendor, products or services contained in this presentation is intended or should be inferred.

An honorarium is provided by Accuray for this presentation.

Medical Advice Disclaimer

Accuray Incorporated as a medical device manufacturer cannot and does not recommend specific treatment approaches. Individual results may vary.

Safety Statement

Most side effects of radiotherapy, including radiotherapy delivered with Accuray systems, are mild and temporary, often involving fatigue, nausea, and skin irritation. Side effects can be severe, however, leading to pain, alterations in normal body functions (for example, urinary or salivary function), deterioration of quality of life, permanent injury and even death. Side effects can occur during or shortly after radiation treatment or in the months and years following radiation. The nature and severity of side effects depend on many factors, including the size and location of the treated tumor, the treatment technique (for example, the radiation dose), the patient's general medical condition, to name a few. For more details about the side effects of your radiation therapy, and if treatment with an Accuray product is right for you, ask your doctor.

Potential conflicts of interest

Research funding:

- Elekta, Varian, Accuray

Honoraria/travel grants:

- Elekta, Accuray, Janssen





The PACE trials

Overview of the PACE trials so far

Results from PACE B

Where next?



"The Stanford SBRT programme began in 2003..."





			Acute (≤	(3 mo)	highest g	grade			I	Late (>3	3 mo) hi	ghest	grade				
		Grade 1		Grade 2		Grade 3-5		Grade 1		Grade 2		Grade 3		Grade 4 or 5			
	Adverse event	n	%	n	%	n	%	n	%	n	%	n	%	n	%		
	Genitourinary																
	Any GU toxicity*	182	59	79	26	0	0	87	28	38	12		12	0	0		
	Frequency and/or urgency	151	49	49	16	0	0	50	16	22	7.1			0	0		
	Dysuria	118	38	26	8.4	0	0	27	8		3.2	0		0	0		
	Urinary retention	102	33	27	8.7	0	0	28	9.		2.9	1	0.3	0	0		
	Pelvic pain	31	10	4	1.3	0	0	9	2.9		0	0	0	0	0		
	Hematuria	5	1.6	3	1.0	0	0	21	6.8		2.9	2	0.6	0	0		
	Incontinence	7	2.3	0	0	0	0	10	3.2		1.6	0	0	0	0		
	Prostatitis	0	0	1	0.3	0	0	4	1.3		1	0	0	0	0		
	Urinary tract infection	0	0	3	1.0	0	0	0	0		3	1	0.3	0	0		
		~	~	^	~	^	^	^	^				~ ~	^			
	Gastrointestinal																
	Any GI toxicity*	169	55	25	8.1	0	0	38	12	6	2	0	0	0			
	requent and/or roose stoors	12	50		2.0	~		12	5.7		0.5			~			
	Proctitis	42	14	9	2.9	0	0	7	2.3	3	1.0	0	0	0	0		
	Rectal blood	34	11	8	2.6	0	0	11	3.6	1	0.3	0	0	0	0		
	Hemorrhoid	34	11	0	0	0	0	11	3.6	0	0	0	0	0	0		
	Flatulence	23	7.4	0	0	0	0	0	0	0	0	0	0	0	0		
	Constipation	17	5.5	3	1.0	0	0	3	1.0	0	0	0	0	0	0		
	Nausea and/or anorexia	10	3.2	0	0	0	0	2	0.6	0	0	0	0	0	0		
	Rectal urgency	5	1.6	0	0	0	0	1	0.3	1	0.3	0	0	0	0		
	Pain	4	1.3	0	0	0	0	1	0.3	0	0	0	0	0	0		
2	Rectal incontinence	1	0.3	0	0	0	0	2	0.6	0	0	0	0	0	0		
花	Ulcer	1	0.3	0	0	0	0	0	0	0	0	0	0	0	0		
	Other events																
	Fatigue	87	28	11	4	0	0	4	1.3	0	0	0	0	0	0		
	Dermatitis	5	1.6	0	0	0	0	0	0	0	0	0	0	0	0		

The value of randomised data: Bladder side effects





Dearnaley et al, Lancet Oncology 2016 Meier et al, IJROBP 2018

Why do we deliver Prostate SBRT?



6116 men

Med FU 39 months

5 year RFS 95.3%

Jackson et al, IJROBP 2019; 104 (4) 778-789

Planning

- Entire PACE C RTQA pack is available open access at
- <u>https://www.icr.ac.uk/our-research/centres-and-collaborations/centres-at-the-icr/clinical-trials-and-statistics-unit/clinical-trials/pace</u>
- (or google PACE trial prostate radiotherapy ICR and you should find it)



What dose is given?

Most international experience with 36.25 Gy in 5 fractions (with or without 40 Gy to CTV)







Allowable margins in PACE

PTV=CTV+4-6mm

Most commonly used margins in PACE:

5mm except 3mm posteriorly





PACE B results so far



PACE B trial schema





>90% patients intermediate risk, 82% Gleason 3+4, 31% PSA >10 ng/ml

Acute RTOG Gastrointestinal Toxicity





Brand et al 2019 Lancet Oncology

Acute RTOG Genitourinary Toxicity





Brand et al 2019 Lancet Oncology

Articles

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, Peter Ostler, Hans van der Voet, William Chu, Andrew Loblaw, Daniel Ford, Shaun Tolan, Suneil Jain, Alexander Martin, John Staffurth, John Armstrong, Philip Camilleri, Kiran Kancherla, John Frew, Andrew Chan, Ian S Dayes, Aileen Duffton, Douglas H Brand, Daniel Henderson, Kirsty Morrison, Stephanie Brown, Julia Pugh, Stephanie Burnett, Muneeb Mahmud, Victoria Hinder, Olivia Naismith, Emma Hall*, Nicholas van As*, on behalf of the PACE Trial Investigators







Tree et al, Lancet Oncology 2022

What do the patients say?



EPIC 26 bowel MCID (+/-5 points)

Proportion of patients with a change in EPIC 26 bowel composite score which exceeds the MCID threshold



Overall bowel bother

🔲 No problem 🔄 Very small problem 🦳 Small problem 🔲 Moderate problem 📕 Big problem



CRT baseline 1.6% At 2 years 3.7%

SBRT baseline 1.6% At 2 years 4.6%





Tree et al, Lancet Oncology, 2022

Time to occurrence of Grade 2+ GU toxicity; CRT (red) and SBRT (green)



CRT 430 (0) 430 (7) 423 (10) 413 (8) 405 (5) 400 (2) 398 (6) 392 (2) 390 (6) 384 SBRT(B) 414 (0) 414 (8) 406 (15) 391 (17) 374 (17) 357 (7) 350 (5) 345 (3) 342 (3) 339

CRT 430 (0) 430 (19) 411 (23) 387 (9) 375 (7) 366 (4) 361 (6) 353 (10) 337 (6) 329 SBRT(B) 414 (0) 414 (9) 405 (37) 368 (27) 340 (21) 316 (16) 298 (11) 285 (5) 274 (6) 268



Tree et al, Lancet Oncology, 2022



What do the patients say?



Proportion of patients with a change in EPIC 26 urinary irritative/obstructive composite score which exceeds the MCID threshold



Tree et al, Lancet Oncology, 2022

Overall bladder bother



CRT baseline 7.1% At 2 years 5.2%

SBRT baseline 7.9% At 2 years 10.4%

SBRT









What determines GU toxicit

Clinical Investigation

Radiation Dose to the Intraprostatic Ureth Correlates Strongly With Urinary Toxicity A Prostate Stereotactic Body Radiation Thera A Combined Analysis of 23 Prospective Clinical Trials

Jonathan E. Leeman, MD,* Yu-Hui Chen, MS,[†] Paul Catalano, S Jeremy Bredfeldt, PhD,* Martin King, MD, PhD,* Kent W. Mouw, MD, PhD,* Anthony V. D'Amico, MD, PhD,* Peter Orio, DO,* Paul L. Nguyen, MD,* and Neil Martin, MD, M

*Department of Radiation Oncology, Dana-Farber Cancer Institute/Brigham and Women Harvard Medical School, Boston, Massachusetts; and [†]Department of Data Science, Dana Cancer Institute, Boston, Massachusetts





GU flare not universally seen with SBRT

– Urethra (catheter) +3mm = urethral PRV







Zilli et al, 2020. Cancer Medicine (9) 3097-3106

Is there a difference between CyberKnife (CK) and conventional linac (CL) SBRT?









Baseline characteristics	SB	RT-CK	SB	RT-CL	Test for differences between groups		
	0	N=170)	(N	=244)	(N=414)		
	n	%	n	%			
Γ-Stage ¹							
Tlc	19	(11.2)	58	(23.8)			
T2a	47	(27.6)	56	(23.0)	0.00097 (T1 vs T2)		
T2b	40	(23.5)	40	(16.4)			
T2c	64	(37.6)	87	(35.7)			
Risk group ¹							
Low	21	(12.4)	14	(5.7)	0.017		
Intermediate	149	(87.6)	230	(94.3)	0.017		
JICASUII SCULC							
3+3	36	(21.2)	25	(10.2)	0.0020		
3+4	134	(78.8)	219	(89.8)			
Prostate volume ²							
<40 mL	69	(40.6)	96	(39.30)			
40 - <80 mL	76	(44.7)	98	(40.2)	0.50		
80+ mL	10	(5.9)	11	(4.5)	0.59		
Unknown	15	(8.8)	39	(16.0)			
Alpha blockers at randomisation'	_						
Yes	18	(10.6)	52	(21.3)			
No	150	(88.2)	191	(78.3)	0.0046		
Unknown	2	(1.2)	1	(0.4)			
Yes	15	(8.8)	54	(22.1)			
No	151	(88.8)	190	(77.9)	0.00050		
Unknown	4	(2.4)	0	(0.0)			
· · · ·							

But...

But are cancer control outcomes similar with 5 fraction SBRT?





PACE B 5-year data due to mature 2023...

HYPO - not technically SBRT but UHF



78 Gy in 39 fractions vs 42.7 Gy in 7 fractions

Both groups = 84% 5-year failure-free survival

> Widmark et al, Lancet Oncology 2019



The Royal M The ROYAL Can we treat higher risk men with 5-fraction SBRT? MARSDEN Cancer Charity PACE A PACE B PACE C 234 1182 patients 874 PACE C **CI** Alison Tree 5 days 4 weeks 5 days 5 days 4-8 weeks SBRT and Surgery and ADT SBRT SBRT ADT varian ACCURAY

PACE C recruitment

Acute toxicity data available 2023





Can we treat the nodes with 5 fractions?



Alayed et al, IJROBP 104 (1) 36-41 Murthy et al, Clinical oncology 30 (2018) 442-447

PACE-NODES: A randomised trial of 5 fraction prostate radiotherapy (SBRT) or 5 fraction prostate and pelvic nodal SBRT in patients with high risk localised prostate cancer

> High risk, localised prostate cancer suitable for 5 fraction SBRT requiring at least 18m androgen deprivation therapy (ADT)





Late toxicity assessment (6, 12, 18, 24, 36, 48 and 60 months) QoL at 6, 12, 24 and 60 months

Conclusions regarding the PACE trial so far

- Toxicity low for both SBRT and CRT to 2 years
- Increase in grade 2 GU toxicity up to 24m with SBRT compared to CRT
- Frequency and urgency the most commonly reported GU toxicities
- Some corresponding differences seen in PROs
- SBRT delivered in a CyberKnife centre is associated with fewer G2 GU toxicities than SBRT on a conventional linac



- Data on 5 fraction SBRT for higher-risk patients awaited

Thank you for listening

Thanks to Accuray, Varian, RMCC, ICR-CTSU, RTTQA and all the men who participated in PACE

Happy to take questions



