LARGEST CLINICAL STUDIES TO DATE* SUPPORT CYBERKNIFE® SBRTFOR LOCALIZED PROSTATE CANCER

Two large prospective, multi-institutional clinical studies report excellent clinical outcomes and low toxicity in localized prostate cancer patients. These studies provide robust clinical data supporting the efficacy of the CyberKnife® System in delivering ultra-hypofractionated stereotactic body radiotherapy (SBRT) for patients with low- and intermediate-risk prostate cancer. The following table describes and differentiates these studies.

Study Title	High Dose "HDR-Like" Prostate SBRT: PSA 10-Year Results From a Mature, Multi-Institutional Clinical Trial	Intensity Modulated Radiotherapy Versus Stereotactic Body Radiotherapy for Prostate Cancer (PACE-B): 2 year Toxicity Results From a Randomised Open-label Phase III Non-inferiority Trial
First Author	Dr. Donald Fuller CyberKnife Centers of San Diego San Diego, CA, United States	Dr. Alison Tree The Royal Marsden Hospital London, UK
Design	Prospective; Phase II trial; 18 institutions; CyberKnife System Only	Prospective; Phase III trial; 35 centers; conventional radiotherapy vs SBRT regimen; including cohort comparing CyberKnife SBRT vs standard-linac SBRT
Number of Patients	259	874 (441 radiotherapy; 433 SBRT) SBRT cohort: • Conventional-linac 245 patients • CyberKnife 169 patients
Prescription	38 Gy in 4 fractions daily (HDR-like brachytherapy regimen)	• SBRT: 36.25 Gy–40 Gy in 5 fractions (over 2 weeks) • IMRT: 62 Gy in 20 fractions or 78 Gy in 39 fractions
Toxicity	Grade 2+ toxicity at 5 years: • GU: 16.3% • GI: 2.6% Grade 2 toxicity at 10 years: • GU: 19.2% • GI: 2.6% The toxicity profile of this SBRT regimen compares favourably with brachytherapy.	CTCAE Grade 2+ toxicity at 2 years: GU toxicity: • 5.8% CyberKnife vs 16.5% conventional linac GI toxicity: • 0.6% CyberKnife vs 5.2% conventional linac CTCAE toxicity at 2 years was significantly less frequent with CyberKnife SBRT than standard-linac SBRT (0.002)
Outcomes	10-year biochemical free recurrence: • 100% low-risk • 84.3% intermediate-risk	Primary endpoint is freedom from biochemical or clinical failure, the data of which is not yet mature
Published	https://doi.org/10.3389/fonc.2022.935310	https://doi.org/10.1016/S1470-2045(22)00517-4

*As of September 2022

CyberKnife®

CYBERKNIFE® PROSTATE SBRT

PROVEN

The CyberKnife® System is recognized and established for prostate SBRT

- Supported by the largest prospective prostate SBRT studies to date* on low- and intermediate-risk prostate cancer[1,2]
- These studies provide reassurance to patients and providers that excellent clinical results are reproducible
- Supported by extensive clinical evidence with long term follow-up demonstrating highly effective treatment outcomes at the convenience of shorter treatment schedules[1,2,3,4,5]

PRECISE

The CyberKnife System's precise robotic treatment streamlines prostate SBRT

- Automatically delivers a wide range of non-coplanar beams which improves dose minimization to surrounding organs and normal tissue compared to conventional coplanar beams[6]
- Automatically maintains sub-millimeter accuracy with continual intrafraction imaging and prostate motion adaptation, including rotation, throughout treatment delivery[7]
    - o The prostate gland is known to move unpredictably during treatment delivery but CyberKnife's robotic real-time corrections are an effective way to account for prostate motion[8]
    - o When the target volume includes the proximal seminal vesicle, 6D-rotational corrections are important to prevent under-dosing of the seminal vesicles[9]

EFFECTIVE

The CyberKnife System yields clinical outcomes that compare favorably to historical data

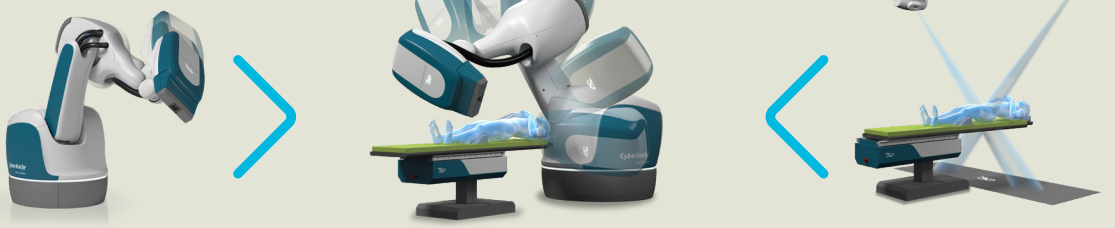
- Excellent disease-free survival rates at five and 10-years for low-intermediate risk patients[2,3,4,5,10]
- Reduced gastrointestinal and genitourinary toxicities grade 2 and above, where bladder side effects were experienced half as often with CyberKnife System[1]
- Equivalent to high dose rate (HDR) brachytherapy[2]

CONVENIENT

The CyberKnife System eases the return to daily life for patients

- Compared to surgery, this nonsurgical outpatient procedure does not require general anesthesia, invasive incisions, hospitalization, or long recovery time
- Compared to brachytherapy, this minimally invasive procedure eliminates the inconvenience and risk associated with radioactive seeds or catheter implants[2]
- Compared to conventional radiotherapy, this treatment is completed in only 4-5 sessions instead of the 20-40 sessions which offers greater convenience to patients and potential cost savings to healthcare providers[11]

CONFIDENCE IN MOTION



COMPUTER GUIDED ROBOTIC DELIVERY

AI-DRIVEN REAL-TIME TARGET TRACKING AND DYNAMIC DELIVERY

INTRAFRACTION IMAGING

1) Tree et al (2022) 'Intensity-Modulated Fractionated Radiotherapy Versus Stereotactic Body Radiotherapy for Prostate Cancer (PACE-B): 2-year Toxicity Results From an Open-label, Randomised, Phase III, Non-inferiority Trial' Lancet Oncol https://doi.org/10.1016/S1470-2045(22)00517-4
2) Fuller D.B. et al (2022) 'High Dose "HDR-Like" Prostate SBRT: PSA 10-Year Results From a Mature, Multi-Institutional Clinical Trial' Front Oncol. 12:935310.
3) Zhao, X et al (2021) Five-year outcomes of stereotactic body radiation therapy (SBRT) for prostate cancer: the largest experience in China. J Cancer Res Clin Oncol
4) Meier, RM et al (2018) Multicenter Trial of Stereotactic Body Radiation Therapy for Low- and Intermediate-Risk Prostate Cancer: Survival and Toxicity Endpoints. Int J Radiat Oncol Biol Phys 102(2):296-303
5) Voulukka, K et al (2020) Stereotactic body radiotherapy for localized prostate cancer - 5-year efficacy results. Radiat Oncol. 15(1):173
6) Rossi L. et al (2018) First fully automated planning solution for robotic radiosurgery – comparison with automatically planned volumetric arc therapy for prostate cancer (tandfonline.com) Acta Oncol. 2: 1-9
7) Xie Y. et al (2008) Intrafractional motion of the prostate during hypofractionated radiotherapy - PubMed (nih.gov). Int. J. Radiat. Oncol. Biol. Phys.72(1): 236-46
8) van de Water S. et al. (2013) Intrafraction prostate translations and rotations during hypofractionated robotic radiation surgery: dosimetric impact of correction strategies and margins Int. J. Radiat. Oncol. Biol. Phys. 2014; 88(5): 1154-60
9) Lei S, et al. (2011) Frontiers | Six-Dimensional Correction of Intra-Fractional Prostate Motion with CyberKnife Stereotactic Body Radiation Therapy Front Oncol. 1:48
10) Katz A. (2017) Stereotactic Body Radiotherapy for Low-Risk Prostate Cancer: A Ten-Year Analysis; Cureus 9(9): e1668.
11) Laviana A.A. et al.(2016) Utilizing time-driven activity-based costing to understand the short- and long-term costs of treating localized, low-risk prostate cancer. Cancer. 122: 447-55

Important Safety Information:
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), and the patient's general medical condition, to name a few. For more details about the side effects of your radiation therapy, and to see if treatment with an Accuray product is right for you, ask your doctor. Accuray Incorporated as a medical device manufacturer cannot and does not recommend specific treatment approaches. Individual results may vary.

CyberKnife®