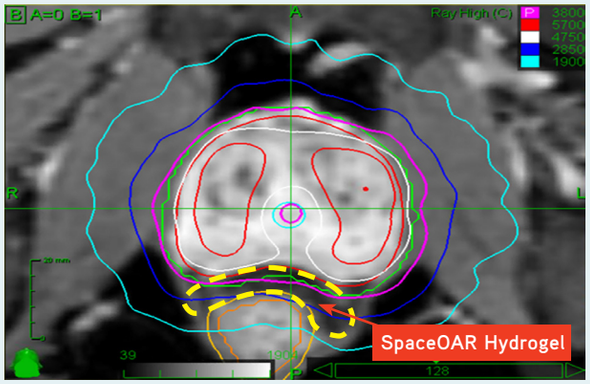
# Early Stage Disease

Due to its unique dose molding and tumor tracking capability, the CyberKnife® device has sub-millimeter accuracy and a much sharper dose fall-off beyond the prostate compared with other external radiation methods, effectively rendering the high dose radiation margin more "scalpel-like" and also, with a more concentrated dose within the prostate itself. This thin coverage margin around the prostate, which effectively reduces the risk of injury to surrounding tissues, enables the use of a short ablative dose schedule, allowing the entire treatment to be delivered in less than one week.

# Benefits of CyberKnife®

*Surgical precision* but without the hospitalization
*Far less investment of time* compared to standard radiotherapy



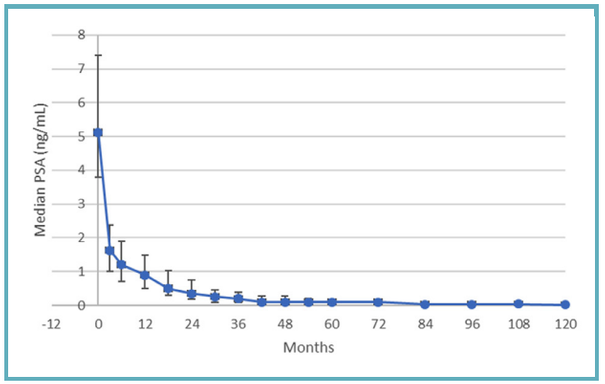

MRI defined prostate volume, treated with CyberKnife SBRT, which prints the prescribed radiation dose sharply around the margin of the prostate (purple line), with a rectal spacing gel between the prostate and rectum, to further reduce the risk of rectal injury .

Although there is ample evidence supporting the use of CyberKnife SBRT for low- and intermediate-risk disease, now including mature 10-year data, there are considerably less data regarding its use for high-risk disease. As such, we are actively investigating use of CyberKnife® SBRT in localized high-risk prostate cancer under IRB approved protocol, either as monotherapy, or combined with other therapies, depending on the severity of the case, with encouraging 5-year disease-free survival results. (2,3)

In highly selected patients, we are also investigating the use of focal CyberKnife SBRT, targeting only the region within the prostate known to contain the cancer, while sparing the rest of the "normal" prostate from full dose treatment. This is an extremely early stage research project, with the potential to reduce side effects even further, due to less adjacent bladder, urethra, rectum and nerve bundles exposed to the full dose. Due to leaving a significant part of the prostate untreated, the long-term local control with this approach is not well defined and as such, this very new approach is best done in a research setting, which we are doing, under IRB-approved protocol.

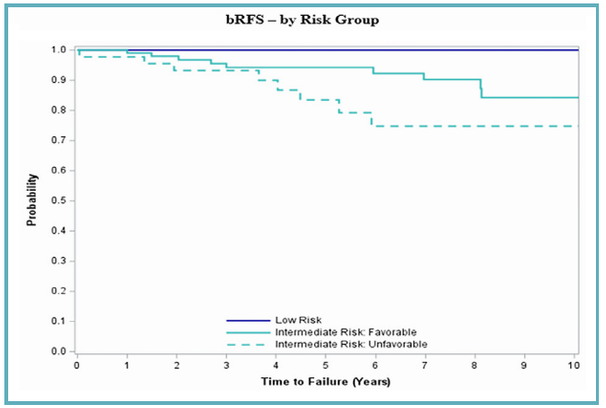
Finally, we have also reported favorable outcomes with CyberKnife SBRT for *locally recurrent prostate cancer*, for patients that have relapsed in the prostate *after prior radiotherapy* – historically, a very challenging situation, with few effective treatment options. (4)

## PSA Response: Virtual HDR® CyberKnife® Protocol

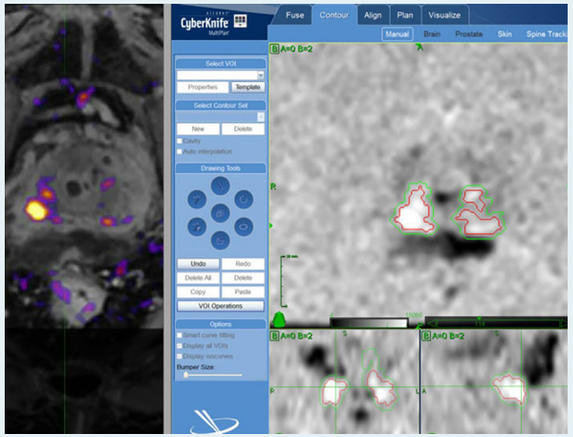



**PSA response for our Virtual HDR® protocol prostate cancer patients through the first 10 years.** A post-treatment PSA decrease to < 0.5ng/mL has been associated with a high 10-year disease-free survival rate and PSA decrease to < 0.2 ng/mL has been associated with an even higher 10-year disease-free survival rate. The median PSA nadir in this series, beyond year 6 and maintained through year 10, is < 0.1 ng/mL (ablated). (1)

## Recurrence-free survival, "Nadir + 2" Definition




Low-risk patients (Gleason score 6 and PSA < 10 ng/mL) have a 100% rate for PSA-based disease-free survival to 10 years (NOTE: Cure is not "guaranteed," in spite of this very encouraging result to 10 years). Intermediate-risk disease is broken into two subgroups. Favorable-intermediate-risk has an 84% rate and unfavorable intermediate risk has a 74% rate at 10 years.(1) All treatments (e.g. - radical prostatectomy, IMRT, brachytherapy) display this same trend, due to an increased potential for disease spread, as the risk group increases. In those who do relapse, the disease has usually spread to other areas, and typically remains very treatable even in that event. The freedom from local cancer recurrence in the prostate itself is 99% at 10 years and the prostate cancer-specific survival rate is 99.5% at 10 years. (1) Due to a less favorable outcome with unfavorable intermediate-risk disease, particularly those with primary Gleason score 4+3 disease, it is more common to combine a local treatment like CyberKnife SBRT with other forms of treatment, to improve the result in this patient subgroup.



Advanced MRI sequences now have the potential to literally map the extent of disease "voxel by voxel" within the prostate – a method that allows for the possibility of "focal" treatment, meaning to treat only the involved aspect of the prostate, as opposed to standard "whole prostate" treatment, in selected early stage patients, who wish to maximize their Quality of Life (QOL) preservation. Due to its extreme precision, the CyberKnife platform is capable of printing the dose pattern very sharply around such "MRI mapped" lesions.

# References


(1) Fuller DB, Crabtree T, Kane BL, Medbery CA, Pfeffer R, Gray JR, Peddada A, Royce TJ, Chen RC. High Dose "HDR-Like" Prostate SBRT: PSA 10-Year Results From a Mature, Multi-Institutional Clinical Trial Front Oncol. 2022 Jul 29;12:935310.

(2) Stereotactic Body Radiation Therapy in Treating Patients With Localized High-Risk Prostate Cancer. ClinicalTrials.gov Identifier: NCT02296229

(3) Ritchell van Dams, Naomi Y. Jiang, Donald B. Fuller, Andrew Loblaw, Tommy Jiang, Alan J. Katz, Sean P. Collins, Nima Aghdam, Simeng Suy, Kevin L. Stephans, Ye Yuan, Nicholas G. Nickol s, Vedang Murthy, Tejshri P. Telkhade, Patrick A. Kupelian, Michael L. Steinberg, Tahmineh Romero, Amar U. Kishan. Stereotactic Body Radiotherapy for High-Risk Localized Carcinoma of the Prostate (SHARP) Consortium: Analysis of 344 Prospectively Treated Patients. Int J Radiat Oncol Biol Phys. 2021 Jul 1; 110(3): 731–737

(4) Fuller D, Wurzer J, Shirazi R, Bridge S, Law J, Crabtree T, Mardirossian G. Retreatment for Local Recurrence of Prostatic Carcinoma After Prior Therapeutic Irradiation: Efficacy and Toxicity of HDR-Like SBRT. Int J Radiat Oncol Biol Phys. 2020 Feb 1;106(2):291-299

## COMPARISON WITH OTHER MODALITIES

| CyberKnife® Advantage | Counterpoint |
|---|---|

### *Radical Prostatectomy (RP)*

- Non-invasive outpatient treatment with rapid recovery
- No hospital admission
- No post-operative recovery
- Patient may rapidly resume normal activity
- Advanced age or coexisting medical conditions do not impede the ability to receive CyberKnife® treatment

- RP has a long-term data indicating a high cure rate for localized prostate cancer
- Of note, CyberKnife SBRT also has compelling 10-year efficacy data now (1)

### *External Beam Radiotherapy (EBRT)*

- EBRT (all forms including 3DCRT, IMRT, proton beam RT) takes approximately one to two months to complete, CyberKnife® radiosurgery takes one week to complete
- The CyberKnife® therapeutic margin is more "surgical" compared to any other form of external radiotherapy, reducing the radiation dose to surrounding tissues, and enabling more biologically powerful radiation dosing within the prostate

- EBRT methods, such as IMRT or proton beam therapy, have substantial data suggesting curative potential
- The more gradual dose delivery via standard EBRT (IMRT) has very mild side effects, whereas CyberKnife SBRT is transiently stronger, due to its compressed dose delivery schedule. Any difference of this nature is temporary

### *Permanent Seed Prostate Brachytherapy*

- The CyberKnife® approach is a non-invasive treatment
- Leaves no radioactive foreign bodies in the prostate
- The CyberKnife® urologic recovery appears more rapid
- There is less potential for long-term urinary obstruction

- Permanent source prostate brachytherapy has a large body of long- term data indicating a high cure rate for localized prostate cancer

### *HDR Prostate Brachytherapy*

- The CyberKnife® approach is a non-invasive treatment
- No hospital admission
- No painful plastic tubes
- CyberKnife® is capable of closely recapitulating HDR radiation dose sculpting noninvasively

- HDR prostate brachytherapy has data indicating a high cure rate for localized prostate cancer

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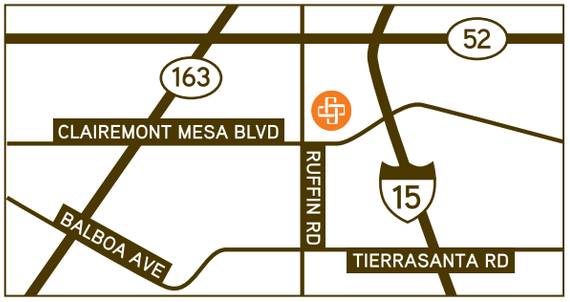


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2. Head westbound
3. Take 2nd right on Ruffin Rd
4. Destination will be on right

*From Route 163*

1. Exit Clairemont Mesa Blvd
2. Head eastbound
3. Turn left onto Ruffin Rd
4. Destination will be on right

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