A retrospective analysis by researchers at the UCLA Jonsson Comprehensive Cancer Center has concluded that high-dose radiation therapies may be as effective as radical prostatectomy for treating very aggressive prostate cancer — Gleason score (GS) 9-10. The Gleason score is a grading system of how aggressive tumor tissue appears on microscopic examination.

Researchers analyzed 487 patients with biopsy GS 9-10 treated between 2000 and 2013. Of these, 230 had external beam radiation therapy (EBRT) and 87 were treated with EBRT plus brachytherapy (BT), the use of high-dose radiation sources implanted directly into the prostate gland. Most radiotherapy patients also received androgen deprivation therapy (ADT) to prevent male hormones from stimulating prostate cancer growth. The average duration of ADT with radiation alone was two years; patients receiving radiation plus BT had about nine months of ADT.

Of the patients studied, 170 were treated with radical prostatectomy. Nearly 40 percent of these ultimately received post-operative radiotherapy.

The UCLA Prostate Cancer Program offers a number of clinical trials for very-high-risk patients. These include two multi-modality trials, one that combines the newest targeted therapies with surgery and a second combining precise stereotactic body radiation therapy (SBRT) and surgery sequentially.

Also ongoing is a trial that abbreviates the typical course of extremely dose-escalated external beam radiotherapy to five treatments. All patients involved so far have reported quality of life comparable to those treated with longer-course radiation. “This would be an excellent option to deliver dose-escalated radiation for patients with Gleason score 9-10 disease,” says Christopher King, MD, PhD, professor of clinical radiation oncology and urology.
Among other issues, the study looked at the impact of treatment options on distant metastasis-free survival (a distant metastasis refers to cancer that has spread from the original tumor to distant organs or lymph nodes). One particularly intriguing finding that the analysis showed was that patients with the lowest rates of metastasis received extremely dose-escalated radiotherapy (delivering a higher total dose of radiation beyond that given with conventional radiotherapy) combined with BT and short-term ADT.

The study, published in *European Urology* in August 2016, is the first to directly compare outcomes between radiation-based treatments and surgery for patients with GS 9-10 — the highest Gleason scores.

### Highest score, highest risk

Prostate cancer is the most common cancer among men in the United States, and the second-leading cause of cancer death following lung cancer. About 180,000 men are diagnosed with prostate cancer each year in the U.S. Prostate cancer, which tends to be slow growing, is highly curable when diagnosed and treated early.

However, this profile does not typically apply to GS 9-10 cases, which represent about 5 to 10 percent of all men with prostate cancer and has been associated with a higher risk of recurrence after treatment, along with an increased risk of developing metastatic disease.

Prostate cancer's typical slow growth makes it difficult to accumulate sufficient data on modern therapies to compare the long-term effectiveness of different treatments. High-risk and aggressive GS 9-10 cancers, however, typically follow a shorter time course, allowing for comparative analysis as treatment methods evolve.

Study authors drew patient records from UCLA and two collaborating medical centers to compare five-year and 10-year rates of metastasis-free survival, cancer-specific survival and overall survival. Within this initial patient population, radiotherapy (typically with ADT) and radical prostatectomy provided equivalent cancer-specific survival and overall survival.

### Full-spectrum prostate-cancer program

Ultimately, many patients with prostate cancer — in particular those with high-risk, aggressive forms of the disease — will require multiple forms of treatments. Within the UCLA Prostate Cancer Program, part of the UCLA Institute of Urologic Oncology, treatment decisions are made on a case-by-case basis to optimize individual care.

The UCLA program is among the nation’s most active centers for prostate-cancer treatment. Treatment options are available for all stages of the disease, including the most aggressive forms. For some patients, including young men concerned about the potential impact of hormone treatment on sexual performance, surgery may be the most appropriate first-line therapy. Surgical patients rarely receive ADT until they experience a recurrence or metastasis.

Study authors are continuing their outcomes analysis — collaborating with more medical centers nationwide to generate additional data — inspired by questions raised in the initial retrospective study.