



VIRGINIA PROSTATE CENTER Newsletter

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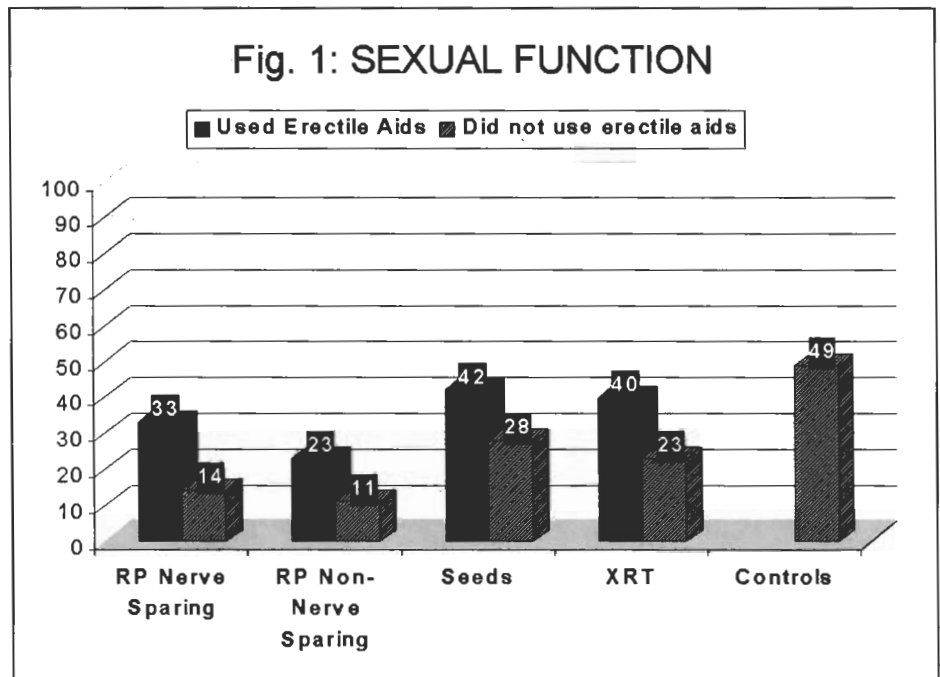
Virginia Prostate Center physicians study quality of life after treatment for localized prostate cancer

Comparing brachytherapy, radical prostatectomy and external beam radiation therapy

BY JOHN W. DAVIS, MD

Prostate cancer is the most common cancer in men and second to lung cancer as a cause of cancer death. Urologists and radiation oncologists have a significant challenge in treating prostate cancer patients: to cure the disease while minimizing the side effects from therapy. Radical prostatectomy and radiation therapy have been available for decades and their improved techniques have continued towards the goal of higher cure rates with fewer side effects. Urologists have developed nerve-sparing techniques, bladder-neck sparing techniques, and careful dissection of the urethra, which have combined to improve post treatment erectile and urinary function. Radiation oncologists are utilizing more sophisticated imaging techniques that allow them to deliver higher doses of therapeutic radiation to the prostate, while minimizing the effects on the nearby rectum.

In the last five years, brachytherapy, also known as 'seeds' or 'implant therapy,' has become an increasingly popular treatment choice for men with localized prostate cancer. Brachytherapy, in theory, allows the



placement of high doses of therapeutic radiation to the prostate, while minimizing radiation to surrounding structures such as the rectum, bladder, and nerves controlling erectile function, and therefore minimizing the side effects of treatment. Does brachytherapy provide the best chance of curing prostate cancer? Unfortunately, prostate cancer has such a slow rate of growth that studies comparing the cure rates are several years away from completion. Does brachytherapy lessen the side effects of treatment compared to radical prostatectomy and XRT? Virginia Prostate Center physicians John Davis, Donald Lynch, and Paul Schellhammer worked

together to answer just that question.

The study of quality of life after prostate cancer treatment

After treatment for prostate cancer, physicians often ask their patients how they are doing with respect to side effects of treatment. The three most commonly discussed side effects are erectile, urinary, and bowel function. While the patient's answers are important to the physician's desire to improve patient outcomes, prior studies have shown that patients are often uncomfortable telling their physicians about their side effects. Therefore, a patient may tell his

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Quality of life after treatment for localized prostate cancer.

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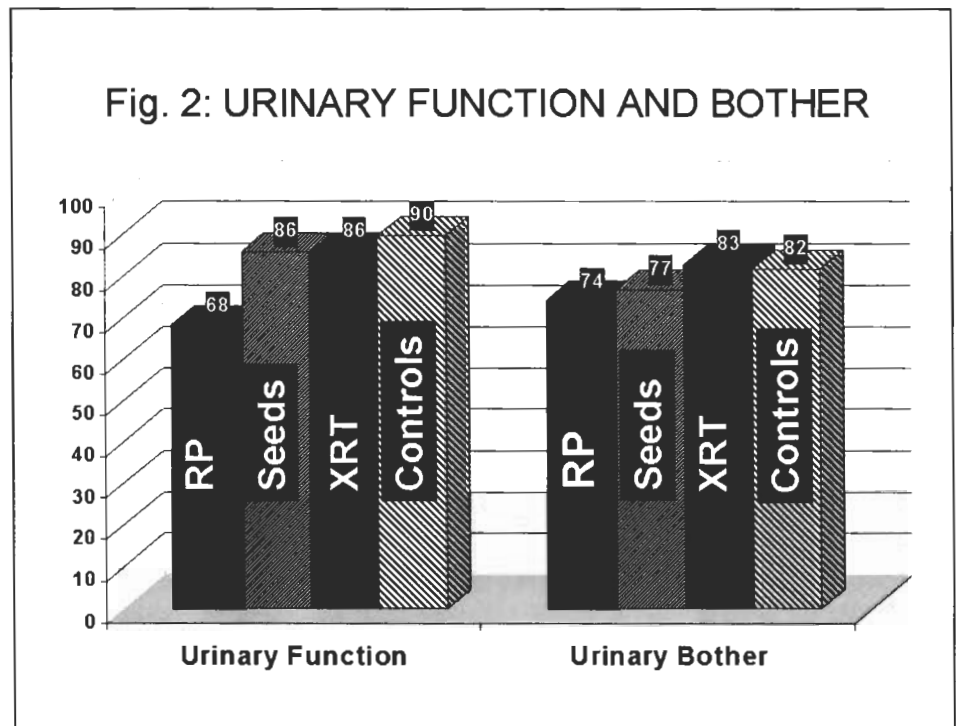
physician he is doing fine with his sexual function, but when asked to answer the same questions on an anonymous survey he may report more severe loss of function. As a result, the most meaningful way to study quality of life issues is through written surveys, which are mailed to, and completed by, patients in the privacy of their home.

Virginia Prostate Center physicians recently mailed over 600 quality-of-life surveys to men treated in the last five years by radical prostatectomy, brachytherapy, or XRT. Greater than 80% of men in each treatment group returned these surveys, which asked numerous questions ranging from physical and emotional health, to sexual/urinary/bowel function, to overall satisfaction with their treatment selection. Other researchers have used these same survey instruments to test men in the same age group (approximately 50-70) who have not been treated for prostate cancer (called "controls" from here on), thus allowing us to see what aspects of quality of life may be affected by prostate cancer treatment.

Quality of life survey results.

General health was assessed with a 36-item survey instrument, which assesses physical function, emotional issues, social interactions, energy, and pain. Men in all three treatment groups reported scores which were equal to and sometimes greater than the control group.

The prostate cancer specific side effects-sexual, urinary, and bowel function - were assessed by questions that not only asked about the details of these body functions, but also asked patients how much they are bothered by the changes in these functions. Before reporting sexual function scores,



it was interesting to find that our control population reported a mean sexual function score of 48 on a 0-100 point scale, indicating that many men already experienced some loss of sexual function prior to prostate cancer treatment. All treatment groups experienced a decrease in sexual function and more bother, compared to controls. The final outcome for sexual function, however, also depended upon whether RP was performed with the nerve-sparing technique, as well as whether or not patients elected to use erectile aids. Figure 1 shows that all groups' sexual function scores improved significantly with erectile aid use, and that RP nerve sparing patients who used erectile aids were similar to seeds and XRT groups. Thus, the final outcome of sexual function can vary significantly by nerve sparing surgery and erectile aid use. Figure 2 shows that urinary function (assessing incontinence) scores for seeds and XRT were similar to controls, while RP patients' scores were significantly less. However, urinary bother

scores for all groups were similar. A separate survey was used to assess urinary frequency and irritation symptoms. These surveys showed that seeds patients report higher urinary frequency, urgency, and irritation in the first year after therapy, but after one year they normalize to the same low levels as the other groups.

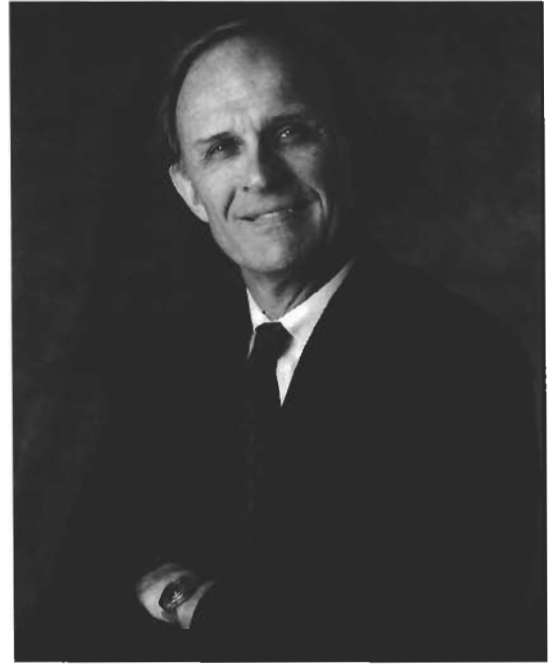
Overall satisfaction with treatment was assessed by asking patients which therapy they would choose today if they could re-select their therapy. Approximately 75% of each group said they would re-select their same therapy, with the remaining 25% of answers spread between watchful waiting and the other treatments.

In summary, prostate cancer patients treated in our community by RP, seeds, or XRT reported satisfactory overall health and function. The majority of patients were satisfied with their treatment modality and would select it again if given the chance. Differences in specific side effects were

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Paul F. Schellhammer, M.D. concludes two-year term as President of the Society of Urologic Oncology

In 1999, Paul Schellhammer was elected President of the Society of Urologic Oncology, a national organization of urologic surgeons dedicated to the clinical care and research support that benefits the treatment of patients with malignancies of the genetic urinary system. A national conference was held in conjunction with the Society and the National Cancer Institute, December 2-3, 2000, and his term will conclude at the annual meeting in June 2001.



Good News!

BY PAUL F. SCHELLHAMMER, M.D.

The most recent national American Cancer Society and National Tumor Registry reports indicate a decrease in prostate cancer mortality of 16% among Caucasians and 11% among Afro-Americans. This indeed is encouraging information. The first evidence of decrease in prostate cancer mortality came with the analysis of the five-year interval of 1990-1995. The fact that the trend continues through the five-year analysis of 1996-2000 supports that this is a real and sustained trend and not just an aberration of a statistical miscalculation at one interval. Parenthetically a decline in mortality from other cancers occurred for the first time as well. The National Cancer Act had declared "war" on cancer mortality in 1971. Twenty years of effort and billions of dollars of expense have shown cancer to be a difficult and tenacious adversary! This decrease in prostate cancer mortality is attributed to the use of the PSA (prostate specific antigen) blood test for early detection of prostate cancer when it is still in a localized state and, therefore, more

amenable to cure by surgery or irradiation. Support for this conclusion

comes from a recently reported observation from Austria. A section of Austria,
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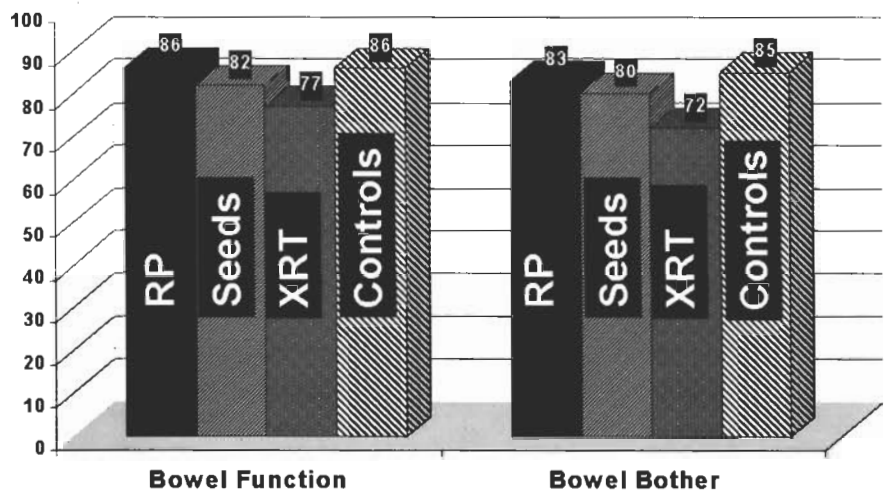
Quality of life

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evident from the surveys, which newly diagnosed patients may find useful in selecting their treatment for prostate cancer. Quality of life will continue to

be an important part of prostate cancer research. We are currently collecting surveys from patients before treatment and at several intervals after treatment to allow a more detailed analysis of quality of life changes after prostate cancer treatment. ■

Fig. 3: BOWEL FUNCTION AND BOTHER



Herbal Treatment for Prostate Cancer

BY PAUL F. SCHELLHAMMER, M.D.

PC-SPES (PC=prostate cancer; SPES=hope in Latin) is a Chinese preparation containing eight different herbal substances. When it was first introduced several years ago, it was looked upon askance by most of the medical community. However, clinical trials have demonstrated its benefits, specifically in patients who are experiencing a relapse after receiving traditional hormone or androgen deprivation therapy. Significant decreases in PSA have been observed with PC-SPES therapy. A recently presented clinical trial from Memorial-Sloan Kettering Cancer Center at the American Society for Clinical Oncology (ASCO) meeting in May reported a greater than 80% fall in PSA in 33 patients with previously untreated prostate cancer; in another study 52% of 23 patients who had progression of disease after other hormone therapy application had a greater than 50% decline.

The exact mechanism of PC-SPES action is unknown. It is a strongly

estrogenic compound as evidenced by the appearance of breast enlargement, and the risk of side effects associated with estrogenic therapy: namely thrombophlebitis and pulmonary embolus. Part of the beneficial effect and perhaps the most important component of the beneficial effect of PC-SPES is its estrogenic activity. Estrogens are important in the treatment of prostate cancer for two reasons: 1) They drive the male hormone, testosterone, to castrate range; i.e. they negate testosterone's effect, and 2) estrogens have a direct toxic effect on prostate cancer. Therefore, the explanation of further activity of PC-SPES even in men who have been treated with other means of androgen deprivation and who have a castrate testosterone level might be the additional direct toxic effect of estrogen on the cancer cell.

A number of studies are ongoing to clarify the specific mechanisms of PC-SPES and to explore its use in combination with other therapies.

One of the major drawbacks at

present is cost (anywhere from \$100 to \$300 a month) and mail-order house availability to anyone who wishes to purchase the compound. With regard to the latter, it is often learned that a patient is taking PC-SPES through casual conversation. Many patients do not view it as an "official" medicine. Obviously if it is being taken and other therapies are employed it is difficult to separate the effect of one from the other. Therefore, patients, if they are taking PC-SPES, should be certain that their physicians are aware. In addition, measures to minimize the complications of thrombophlebitis, including daily aspirin or low dose Coumadin, are warranted. Other so called "second line" hormone therapy can be employed with some success. Again, at the ASCO Conference, favorable reports using a synthetic female hormone, diethylstilbesterol (DES), Ketoconazole and soy products, which can have estrogenic activity, were reported. This information expands the options available for patients with prostate cancer. ■

Good News!

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the Tyrol, was the center of a large scale government-supported PSA screening program. As a result, the prostatic cancer mortality rate decreased 30-40% in 1998 when compared to the mortality rate recorded before 1990 when no PSA screening was offered. Furthermore, this difference held when the Tyrol mortality was compared with the rest of Austria, i.e. a 30-40% difference in favor of the Tyrol. It is my personal opinion that early detection or screening, as has been practiced for the past 8-10 years in the United States, is

largely responsible for the decrease in mortality. However, a randomized clinical trial, the gold standard for assuring that this correlation is justified, is still pending completion. And there is uncertainty as to whether these screening trials conducted by the NCI in the USA will provide accurate outcomes. The reason for this is that most men, due to media publicity in our information age, are aware of the potential value of PSA testing and therefore, 'control' arms of trials are actually impossible to maintain, i.e. patients in the control arm are

seeking PSA monitoring outside the trial protocol. Actually a large European screening trial centered in Rotterdam may ultimately provide the information that is necessary. In Europe, routine PSA testing is much less frequent, much less emphasized, and much less publicized. It may be that our intuitive explanation for the welcome information of a decrease in prostate cancer deaths due to early detection by PSA in the USA may rely on scientific confirmation from the Rotterdam trial. ■

The American Cancer Society and National Tumor Registry reports indicate a decrease in the prostate cancer mortality rate.

BREAKING NEWS

BY PAUL F. SCHELLHAMMER, M.D.

One of the uncertainties revolving around the treatment of prostate cancer has been the timing of androgen deprivation, which is achieved by medication or a surgical procedure to lower the levels of the male hormone, testosterone. Prostate cells, both malignant and benign, rely on testosterone for growth and support. Lowering testosterone levels, whether accomplished by surgical or pharmacological means, will result in prostate cell death. Intuitively it would seem that the earlier such a therapy could be applied, the more complete and effective the therapy may be. Concerns regarding the early application of testosterone deprivation are centered on two areas: namely interference with quality of life and altering the biology of the cancer. Quality of life is significantly affected by androgen deprivation; side effects include loss of vim, vigor, and vitality; and acceleration of such natural consequences of aging as loss of bone strength and density, loss of muscle mass, and occasionally, alterations in overall mental health. In addition, very annoying hot flashes, often suffered by females during menopause, are now endured by the male during this physician-induced "male" menopause, or andropause.

A second area of concern is the possible adaptation or redirection that the tumor cells might assume as a result of exposure to the androgen deprived environment. This change in biology would encourage the appearance and growth of cancer cells resistant to further hormonal manipulations. The vexing question presented by this possibility could be stated, "Would successful initial therapy result in the subsequent development of more aggressive cancer that would be less susceptible to further

therapy?" In fact this question enters into the decision process of many pharmaceutical agents directed at the treatment of malignancy. An analogy could be drawn from the world of infectious diseases; e.g. the development of resistant bacteria after prolonged exposure to a particular antibiotic.

Only carefully conducted clinical trials can satisfy the relative risk/benefit profile of therapeutic maneuvers like early androgen deprivation in the treatment of prostate cancer. Several months ago, a report of a clinical trial in the *New England Journal of Medicine* (*N Engl J Med* 1999;341:1781-8) provided information concerning the timing of androgen deprivation therapy. Approximately ten years ago, a clinical trial was initiated by the National Cancer Institute in cooperation with the Southwest Oncology Group which randomized patients who had undergone a radical prostatectomy and in whom metastases to the pelvic lymph nodes were found to receive either immediate treatment with hormonal therapy or to receive treatment with hormonal therapy at some later date at the time of disease recurrence. The endpoint of the study was to determine if a survival benefit was associated with initial continuous androgen deprivation therapy. After prolonged follow up which extended beyond seven years, the survival outcome did indeed benefit those patients receiving initial therapy. Therefore, in the situation where lymph node metastases are found at the time of surgical removal of the prostate, there is now very strong support for early initiation of hormonal therapy. While it is tempting to extrapolate this finding to a number of other circumstances of uncertainty with regard to early hormone therapy, namely the

finding of any adverse pathologic features after radical prostatectomy, a rising PSA after surgery or irradiation, these situations require specific testing in similarly constructed randomized trials to determine benefit. Appropriate trials addressing these questions are in process. One worth describing is the recently analyzed RTOG 92-02 trial which tested long term (2 years) vs. short term (4 months) androgen deprivation among men with high-risk prostate cancer receiving irradiation therapy. There were advantages in the long-term therapy for the endpoints of local, distant, & PSA response. Further follow up in this trial will provide the necessary data regarding survival advantage.

The clinical trial process by which critical questions are identified by physicians and in which patients participate, provides data which is factual, unencumbered by bias, and invaluable in directing care. Patients participating in a clinical trial are assured of periodic physical and laboratory examinations and access to new therapies monitored by physicians and clinical trial nurses.

The statement "cold facts are a welcome alternative to heated opinion" applies to the information garnered through the clinical trial process. ■

Volunteers Needed

Men age 40 and older who have a diagnosis of prostate disease (prostatitis, benign prostate hyperplasia, or prostate cancer), and men who do not have prostate disease are needed to donate body fluids for the SELDI Biomarker study. A payment for the donation will be provided. Those interested should call 757-446-7910.