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HOW TO USE THIS MONOGRAPH

This is a CME activity that contains both audio and print components. To receive credit, the participant should listen to the CDs or tapes, review the monograph and complete the post-test and evaluation form located in the back of this monograph or on our website. This monograph contains edited comments, clinical trial schemas, graphics and references that supplement the audio program. ProstateCancerUpdate.net includes an easy-to-use interactive version of this monograph with links to relevant full-text articles, abstracts, trial information and other web resources indicated here in red underlined text.

Prostate Cancer Update: A CME Audio Series and Activity

STATEMENT OF NEED/TARGET AUDIENCE

Prostate cancer is one of the most rapidly evolving fields in urology. Published results from clinical trials lead to the emergence of new surgical and radiation therapy techniques and therapeutic agents, along with changes in the indications for existing treatments. In order to offer optimal patient care — including the option of clinical trial participation — the practicing urologist and radiation oncologist must be well-informed of these advances. To bridge the gap between research and patient care, *Prostate Cancer Update* utilizes one-on-one discussions with leading urologic oncology investigators. By providing access to the latest research developments and expert perspectives, this CME program assists urologists and radiation oncologists in the formulation of up-to-date clinical management strategies.

GLOBAL LEARNING OBJECTIVES

Upon completion of this activity, participants should be able to:

- Critically evaluate the clinical implications of emerging clinical trial data in prostate cancer treatment.
- Inform patients about the specific risks and benefits of local and systemic therapies.
- Provide individualized counseling to patients regarding the choice and timing of endocrine therapy.
- Offer patients information regarding their prognosis with and without various therapeutic options.

SPECIFIC LEARNING OBJECTIVES FOR ISSUE 6

Upon completion of this activity, participants should be able to:

- Consider the use of neoadjuvant and adjuvant hormone manipulation in addition to radiation therapy in the management of patients with locally advanced prostate cancer.
- Discuss recent and ongoing clinical trials of brachytherapy in the management of patients with prostate cancer.
- Describe the results of the Early Prostate Cancer trial and the implications for clinical practice.
- Counsel patients with prostate cancer about the morbidities associated with brachytherapy.

ACCREDITATION STATEMENT

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

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Research To Practice designates this educational activity for a maximum of 3 category 1 credits toward the AMA Physician's Recognition Award. Each physician should claim only credits that he/she actually spent on the activity.

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Gregory S Merrick, MD	Grants/Research Support: Theragenics Corporation, Amersham Health
Judd W Moul, MD, FACS	Grants/Research: AstraZeneca Pharmaceuticals LP Honorarium: AstraZeneca Pharmaceuticals LP, Aventis Pharmaceuticals
Colleen A Lawton, MD, FACR	No financial interests or affiliations to disclose

Pharmaceutical agents discussed in this program

GENERIC	TRADE	MANUFACTURER
bicalutamide	Casodex®	AstraZeneca Pharmaceuticals LP
estramustine phosphate	Emcyt®	Pharmacia & Upjohn SpA
etoposide VP-16	VePesid®	Bristol-Myers Squibb Company
finasteride	Proscar®	Merck and Company Inc
flutamide	Euflex®, Eulexin®	Schering-Plough Corporation
goserelin acetate implant	Zoladex®	AstraZeneca Pharmaceuticals LP
leuprolide acetate implant	Viadur™	ALZA Corporation
	Lupron Depot®	TAP Pharmaceuticals Inc
mitoxantrone	Novantrone®	Lederle Labs
paclitaxel	Taxol®	Bristol-Myers Squibb Company
prednisone	Various	Various
sildenafil citrate	Viagra®	Pfizer Inc [generics by many others]
tamsulosin	Flomax®	Boehringer Ingelheim Pharmaceuthicals Inc

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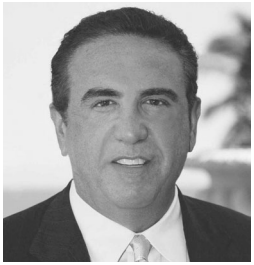

Editor's Note

The Waiting Room

"You tell a patient that they have cancer and they don't hear anything else. Sometimes you see a glazed-over expression — they're just overwhelmed. Also, as a female physician trying to deal with a cancer in a sexual organ in a man, I tread very lightly. A lot of men say, "Honey, what do you know about what I'm going through?" And slowly, but surely, I've developed a better sense of what it's like for men dealing with prostate cancer. And the wives deal with it differently than their husbands, even though they're dealing with the same cancer. I don't think we ever really understand what patients go through, although we try hard. There are certain common situations where we think we have a sense of what patients face, but until you walk in those shoes, you never really know."

Colleen A Lawton, MD, FACR

Recently, I accompanied a close friend to Mark Soloway's office at the University of Miami, Department of Urology, for a second opinion on a complex and serious condition. The waiting room — filled with anxious couples and men by themselves — was virtually silent. "I'm so scared," my friend whispered as she clung to me in a trembling embrace. There was nothing I could say or do to alleviate her totally understandable fear.

As we waited in silence, I began to imagine Mark, calmly going from room to room, seeing mainly prostate cancer patients, and I realized that for almost every person visiting his clinic that day, this was a seminal moment in their lives. Doing my best to comfort my terrified companion, I thought about some of the patients discussed in this audio program and the thoughts they might have had as they waited to be evaluated.

How did Greg Merrick's patient feel as he waited for the results of his most recent PSA assay? Having been through brachytherapy for Gleason 6 disease two years previously, successive rises in his PSA levels had convinced Dr Merrick that this man likely had recurrent and probably systemic disease.

The patient had undoubtedly learned of the potential side effects of androgen deprivation, and might have believed that this was the visit that treatment would begin. I wonder if he or Dr Merrick would have predicted that the elevation was a post-radiation "PSA bounce" and that six years later the patient would remain untreated with an undetectable PSA.

What was Judd Moul's patient thinking as he pondered the dilemma of a less than definitive but concerning prostate biopsy, which was complicated by an eight-year history of androgen replacement therapy for hypogonadism? After suffering through a miserable experience when the testosterone was withdrawn, would this

man and Dr Moul risk restarting androgens and stimulating what seemed to be a low-grade tumor?

How would Colleen Lawton's patient with locally advanced prostate cancer react, as he waited for his initial treatment with an LHRH agonist and bicalutamide, which would precede by two months, intensity-modulated radiation therapy? This educated man and his wife knew what to expect in terms of side effects from this therapy. What were their thoughts and feelings about how treatment might affect their relationship and family?

Thinking about these different scenarios, I realized how difficult it can be for a physician to understand the true human impact of a serious illness like prostate cancer. In this program, Dr Lawton shares with us a personal experience that clearly changed her perspective.

Three years ago, her father was diagnosed with locally advanced prostate cancer, and she accepted the role of a family member, and provided support and advice. How did her father feel as he sat in the waiting room of his treating radiation oncologist's office, knowing that his daughter had a central role in developing and testing the therapy that would render him biochemically free of recurrence?

Mark Soloway's clinic was bustling with residents and medical students who filtered through the waiting area. I remembered a scene from the movie, "The Doctor." In the lead role, William Hurt is a somewhat gruff surgeon whose personal experience with his own cancer dramatically changes his perspective on medicine and patient care, which he expresses to medical students on rounds.
"Doctors, you have spent a lot of time learning the Latin names for diseases your patients might have. Now it's time to learn something simpler about them. Patients feel frightened, embarrassed and vulnerable, and they feel sick. Most of all, they want to get better. Because of that, they put their lives in our hands. I could try to explain what that means until I'm blue in the face, but you know something? It wouldn't mean a thing. It sure as hell never did to me."

Experienced physicians usually develop an empathetic connection with patients and family members that assists them in understanding the human experience of a cancer diagnosis. We owe it to future generations of patients to allow training residents and students the opportunity to explore this essential part of medical care.

My friend and I followed Mark's nurse into the exam room, and once again I realized how different it feels at the other end of the doctor-patient relationship. The exam table looked cold and clinical, and it seemed as if there was not enough air to breath. We anxiously waited for the door to open.

—Neil Love, MD

Gregory S Merrick, MD

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Edited Comments by Dr Merrick

Ongoing clinical trials of brachytherapy

Kent Wallner at the University of Washington and I are currently completing two brachytherapy trials. The first randomly assigns patients with low-risk prostate cancer (i.e., pretreatment PSA <10 ng/mL, Gleason score ≤6 and T1-T2 disease) to brachytherapy with either iodine 125 (I 125) or palladium 103 (Pd 103). The goal of this trial is to determine whether there is a difference in biochemical outcome or quality-of-life parameters (i.e., urinary, bowel and sexual function). The trial will eventually accrue 660 patients. Currently, around 600 patients are enrolled in that study.

The second trial is for patients whose disease has higher risk features (i.e., PSA = 10-20 ng/mL, Gleason score ≥7 and T1-T2 disease). The standard of care for these patients has been five weeks of supplemental external beam radiation (45 Gy) followed by a palladium implant. In our series of patients, supplemental external beam radiation adversely affected long-term urinary function based on the Expanded Prostate Cancer Index Composite (EPIC) survey. External beam radiation can also increase the risk of rectal bleeding and erectile dysfunction.

Hence, the second trial in patients with higher-risk features will compare high and low doses of external beam radiation therapy followed by a brachytherapy implant. This trial will determine whether the dose of the external beam radiation can be reduced. It will have the same endpoints as the first trial: biochemical outcome and quality of life (i.e., urinary, bowel and sexual function). The trial will eventually accrue 680 patients; currently, around 600 patients are enrolled.

In the same patient population, RTOG recently opened a Phase III trial (RTOG-0232) comparing traditional external beam radiation therapy (45 Gy) plus an implant to an implant alone. RTOG-0232 will determine whether external beam radiation therapy is truly needed.

As we develop trials, we're looking for ways to further reduce morbidity, because we know the cure rates are very good. Early next year, we're hoping to begin a Phase III trial that will evaluate dose de-escalation in brachytherapy. Everything in radiation therapy — both for external beam and brachytherapy — has been about dose escalation. We think that with very careful intraoperative evaluation, we will be able to reduce the dose of the palladium implant by 10 to 15 percent without compromising cure, while further improving quality of life.

Phase III Randomized Study of Interstitial Brachytherapy with or without External Beam Radiotherapy in Patients with Intermediate-Risk Prostate Cancer
Open Protocol

Protocol ID: RTOG-0232
Projected Accrual: 1,520

Eligibility: Patient with intermediate-risk prostate cancer (T1c-T2b, NX/N0, M0)

ARM 1: External beam radiation therapy + brachytherapy with I 125 or Pd 103
ARM 2: Brachytherapy with I 125 or Pd 103

Study Contact:
Radiation Therapy Oncology Group
Bradley Prestidge, MD, Protocol Chair
Tel: 210-949-7522

SOURCE: NCI, Physician Data Query, November 2003.

Hormonal therapy plus brachytherapy and external beam radiation

In patients with intermediate- or high-risk prostate cancer, a Phase III trial was going to compare six months of hormonal therapy combined with external beam radiation therapy and an implant to an implant and external beam radiation therapy alone. Unfortunately, that study accrued about 90 patients over three or four years and was closed.

At the present time, the only proven role for hormonal therapy with brachytherapy is to reduce the size of very large glands. Total androgen suppression is proven to shrink glands 35 to 45 percent. Some of our data in press will show that the response of the transition zone to hormonal therapy may be the best predictor of long-term urinary morbidity.

We do not have strong data to indicate that hormonal therapy alters biochemical outcome following brachytherapy. The Stock and Stone data show some suggestion for improvements; however, the follow-up in patients who are hormone-naïve has been significantly longer. Those curves will have to mature before making any definitive conclusions.

In our series, we have not found any improvement in biochemical outcome for patients with intermediate-risk disease treated with hormonal therapy. In patients with high-risk disease, we found a small but statistically significant improvement with the addition of hormonal therapy. The shortcomings of our

data are the same as those of Stock and Stone's data: (1) it's not randomized, and (2) the follow-up of the patients who were hormone-naïve is significantly longer.

Part of the problem is that we have tried to extrapolate the results of conventional doses of external beam radiation therapy with hormones to brachytherapy. Determining the role of hormonal therapy will require much better studies than we have done to date. A population of patients will probably benefit from hormonal therapy administered in combination with brachytherapy. This is a question that will be best answered in a prospective randomized trial.

Total androgen suppression

I always utilize an LHRH agonist in combination with an antiandrogen for cytoreduction. Data indicate that slightly more downsizing occurs with total androgen suppression — at least at three months — and we don't want to keep patients on hormones longer than necessary. In our series, we have demonstrated about 45 percent downsizing with an LHRH agonist and bicalutamide 50 mg per day.

When treating patients with external beam radiation therapy, I always start with total androgen suppression and usually continue the antiandrogen for four months. If the PSA is undetectable at four months, I stop the bicalutamide; if the PSA remains elevated, I continue it. After bicalutamide is discontinued, if the PSA creeps back up, I put them back on it.

Hormonal therapy after biochemical failure following brachytherapy

We manage patients with biochemical failure by instituting hormonal therapy when the PSA doubling time becomes less than 12 months, the PSA reaches an arbitrary level (e.g., 15 ng/mL), or both. In our series, the patients who failed frequently had very rapid PSA doubling times. We always begin with total androgen suppression. I continue the antiandrogen for four months and, if the PSA is undetectable, I consider discontinuing it. Some of those patients, however, are very nervous and say, "I don't want to quit taking the antiandrogen," and we certainly don't encourage them to quit.

Intermittent androgen suppression

I believe intermittent androgen suppression is a marvelous treatment approach for patients who are not overly sensitive to changes in PSA. We use it occasionally to treat patients with metastatic disease or biochemical failures. We usually treat with about nine to 12 months of hormonal therapy — I generally utilize an antiandrogen, bicalutamide, at least for the first four months. If the patient has a good PSA response, we stop the hormonal therapy and wait until the PSA approaches some arbitrary level. The quality of life for these men is very good. Patients are usually off of hormonal therapy for 12 to 18 months. When I reinstitute hormonal therapy, I always reinitiate bicalutamide.

Influence of Hormonal Therapy on Six-Year Biochemical Disease-Free Survival in Patients Treated with Brachytherapy with and without External Beam Radiation Therapy

	No hormonal therapy	Cytoreductive hormonal therapy	Adjuvant hormonal therapy	*p*-value
High-risk prostate cancer	79%	94%	92%	0.046
Intermediate-risk prostate cancer	98%	96%	100%	0.693

SOURCE: Merrick GS et al. **Does hormonal manipulation in conjunction with permanent interstitial brachytherapy, with or without supplemental external beam irradiation, improve the biochemical outcome for men with intermediate or high-risk prostate cancer?** *BJU Int* 2003; 91(1):23-9. **Abstract**

Short-term morbidities following brachytherapy

The usual short-term side effects associated with brachytherapy involve very intense prostatitis with symptoms of urgency, frequency, burning and nocturia. We demonstrated that the prophylactic use of alpha blockers, primarily tamsulosin, initiated before the implant and continued at least until the International Prostate Symptom Score (IPSS) was normalized, significantly lessened the irritative urinary symptoms and led to a more rapid return to the baseline IPSS. Short-term rectal morbidity following brachytherapy is minimal.

Prophylactic versus Therapeutic Use of Alpha-blockers After Brachytherapy

"Prophylactic use of alpha-blockers results in significantly less urinary morbidity than either the absence or therapeutic use of alpha-blockers. In patients receiving prophylactic alpha-blockers, the IPSS normalized significantly faster but had no impact on urinary retention or the ultimate need for postimplant surgical intervention."

SOURCES: Merrick GS et al. **Prophylactic versus therapeutic alpha-blockers after permanent prostate brachytherapy.** *Urology* 2002;60:650-55. **Abstract**

Long-term urinary outcomes following brachytherapy

We recently published a paper about the long-term urinary outcomes following brachytherapy as measured by the Expanded Prostate Cancer Index Composite (EPIC). We chose the EPIC instrument because it evaluates the irritative component that we're most concerned with following brachytherapy. Compared to a matched control group, the long-term EPIC scores were identical for the men treated with brachytherapy.

Surprisingly, patients treated with short-term (e.g., six months or less) hormonal therapy had slightly, though not statistically significant, better urinary function compared to men who did not receive hormones. However, men treated with hormones for more than six months had significantly poorer outcomes with

regard to irritation and function. The strongest predictor of late urinary function was tobacco consumption. It affected all of the domains of the EPIC survey and the IPSS. The use of supplemental external beam radiation therapy also predicted long-term urinary morbidity; it had a deleterious effect on incontinence and function.

Factors Affecting Urinary Outcomes After Brachytherapy

"With a median follow-up of 64.0 months, no significant difference was noted in overall urinary QOL when brachytherapy patients were compared with a group of newly diagnosed prostate cancer patients of comparable demographics. Of the multiple clinical, treatment, and dosimetric parameters evaluated, tobacco consumption was the single strongest predictor of late urinary function."

SOURCES: Merrick GS et al. **Long-term urinary quality of life after permanent prostate brachytherapy.** *Int J Radiation Oncology Biol Phys* 2003;56(2):454-61. **Abstract**

Long-term bowel function following brachytherapy

Brachytherapy also effects long-term bowel function. Using the Rectal Function Assessment Score (R-FAS), which is graded from zero (best function) to 27 (worst function), patients with newly diagnosed prostate cancer have a score of 1.6. Three years after brachytherapy, they have a score of approximately 4.2, and at eight years, they have a score of about 3.9.

Although there are changes in long-term bowel function following brachytherapy, they're relatively minor and may improve slightly with time. The best predictors of long-term morbidity following brachytherapy are the number of pretreatment bowel movements per day, the use of supplemental external beam radiation, the rectal dose, and tobacco consumption. The external beam data is beginning to show that long-term hormonal therapy (nine months or more) causes more rectal bleeding following external beam radiation. We evaluated that but did not find that hormonal therapy had any effect on rectal function following brachytherapy.

Sexual function following brachytherapy

Erectile function is one of the most overestimated outcomes. The Internet and individual publications report that brachytherapy results in potency preservation in 80 percent of patients. We did not believe those numbers, and we published the first data using a validated instrument, the International Index of Erectile Function (IIEF).

Using the IIEF-5, our six-year potency preservation rate after brachytherapy was 39 percent. The Cleveland Clinic data, using the IIEF-6, found only 19 percent of patients maintained potency after brachytherapy. Our potency rates also fall to 25 percent if we use comparable scoring. Fortunately, sildenafil is very effective for these gentlemen. In our series, the use of sildenafil increased the six-year potency preservation rate to about 90 percent.

Postbrachytherapy PSA spikes

Prostate-specific antigen (PSA) spikes — usually defined as increases in PSA greater than or equal to 0.2 ng/mL followed by a durable decline — occur in 23 percent of our patients. In our series, most PSA spikes occurred between 12 and 30 months after an implant; however, they may still occur as much as five years later. We believe PSA spikes are a result of compromised cell-membrane integrity — a radiation-induced prostatitis.

Younger men are more likely to experience a PSA spike, possibly because they're sexually active. The first postimplant PSA level is a strong predictor of PSA spike. In our series, the first postimplant PSA level in men with PSA spikes was 1.2 ng/mL compared to 0.6 ng/mL in men without a PSA spike. Also, patients treated with an I 125 implant were twice as likely to have a PSA spike as those treated with Pd 103 implant (33 percent versus 17 percent, respectively).

It is important that patients, radiation oncologists, urologists and primary care physicians be aware of this PSA spike phenomenon so that we do not rush into a salvage prostatectomy or hormonal therapy in these men.

Kent Wallner and I recently published a report in *Urology* on a series of eight patients who had PSA spikes and biopsies that were positive for prostate cancer. It was recommended that all eight patients undergo salvage prostatectomy, but nothing was done and all the men had a subsequent decrease and normalization in their PSA level. Therefore, biopsies, at least in those first couple of years, are probably of limited utility in determining subsequent treatment.

Clinical Significance of Postbrachytherapy PSA Spikes

"The most important lesson to be learned from the data from these patients is that transient PSA rises can occur even in the presence of a persistently positive biopsy and that patients and physicians should not feel compelled to rush ahead with salvage therapy. …

"… here, it appears that a PSA spike of up to 10 ng/mL is still consistent with cancer eradication. Because spikes have been reported to occur as long as 5 years after implantation, we believe that a spike peak occurring at any time may still be followed by a subsequent spontaneous drop to very low levels. …

"The relationship between PSA spikes and inflammatory changes, dose distribution, or molecular markers should be subjects of future investigations. It has been informally suggested to us that spikes are associated with intraprostatic postimplant necrosis, but we found no evidence of such in the patients reported here."

SOURCES: Reed D et al. **Clinical correlates to PSA spikes and positive repeat biopsies after prostate brachytherapy.** *Urology* 2003;62:683-88. [citations omitted] **Abstract**

Case discussion: 52-year-old man with a postimplant PSA spike that resolved without intervention

Approximately eight years ago, we had a patient with a PSA of 4.6 ng/mL and a Gleason 6 prostate cancer whom we treated with an I 125 implant. At that time, he was about 52 years of age. He had a poor initial PSA response with a PSA nadir of about 2.5 ng/mL approximately 18 to 24 months after the implant. Three and a half to four years after the implant, his PSA began to rise and went up to approximately 5.2 ng/mL. I was confident that he had failed. I did not recommend any additional intervention at that time and continued to watch him. He was very comfortable with this approach. His PSA went down to 4.8 ng/mL, and six months later, it went to about 0.3 ng/mL. Eight years after his initial implant, his PSA is zero. This is a unique case, and we don't usually see patients who are cured when the initial PSA nadir is that high. This patient was not overly concerned with his PSA. Fortunately, we did nothing and he's been fine.

Select publications

Publications discussed by Dr Merrick

Lee LN et al. **Role of hormonal therapy in the management of intermediate- to high-risk prostate cancer treated with permanent radioactive seed implantation.** *Int J Radiat Oncol Biol Phys* 2002;52(2):444-52. **Abstract**

Merrick GS et al. **Does hormonal manipulation in conjunction with permanent interstitial brachytherapy, with or without supplemental external beam irradiation, improve the biochemical outcome for men with intermediate or high-risk prostate cancer?** *BJU Int* 2003;91(1):23-9. **Abstract**

Merrick GS et al. **Erectile function after permanent prostate brachytherapy.** *Int J Radiat Oncol Biol Phys* 2002;52(4):893-902. **Abstract**

Merrick GS et al. **Late rectal function after prostate brachytherapy.** *Int J Radiat Oncol Biol Phys* 2003;57(1):42-8. **Abstract**

Merrick GS et al. **Long-term urinary quality of life after permanent prostate brachytherapy**. *Int J Radiat Oncol Biol Phys* 2003;56(2):454-61. **Abstract**

Merrick GS et al. **Prophylactic versus therapeutic alpha-blockers after permanent prostate brachytherapy.** *Urology* 2002;60(4):650-5. **Abstract**

Merrick GS et al. **Prostate-specific antigen spikes after permanent prostate brachytherapy**. *Int J Radiat Oncol Biol Phys* 2002;54(2):450-6. **Abstract**

Merrick GS et al. **Rectal function following prostate brachytherapy.** *Int J Radiat Oncol Biol Phys* 2000;48(3):667-74. **Abstract**

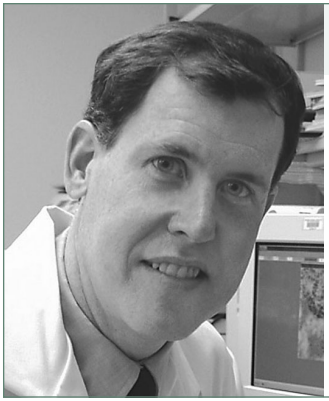
Reed D et al. **Clinical correlates to PSA spikes and positive repeat biopsies after prostate brachytherapy.** *Urology* 2003;62(4):683-8. **Abstract**

Roach M 3rd et al. **Phase III trial comparing whole-pelvic versus prostate-only radiotherapy and neoadjuvant versus adjuvant combined androgen suppression: Radiation Therapy Oncology Group 9413.** *J Clin Oncol* 2003;21(10):1904-11. **Abstract**

Schover LR et al. **Defining sexual outcomes after treatment for localized prostate carcinoma.** *Cancer* 2002;95(8):1773-85. **Abstract**

Wernicke AG et al. **Radiation dose delivered to the proximal penis as a predictor of the risk of erectile dysfunction after three-dimensional conformal radiotherapy for localized prostate cancer**. *Int J Radiat Oncol Biol Phys* 2003;57(2S):S274;**Abstract 1022.**

Stone NN, Stock RG. **Neoadjuvant hormonal therapy improves the outcomes of patients undergoing radioactive seed implantation for localized prostate cancer**. *Mol Urol* 1999;3(3):239-244. **Abstract**



Judd W Moul, MD, FACS

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Edited comments by Dr Moul

Intergroup S9921 adjuvant trial of hormonal therapy with or without chemotherapy

We have not yet proven whether adding adjuvant chemotherapy to hormonal therapy makes a difference. Intergroup trial SWOG-S9921 is enrolling patients who have undergone a radical prostatectomy and whose tumors have adverse pathologic features.

This trial evaluates whether the combination of hormonal therapy plus chemotherapy is better than hormonal therapy alone. We desperately need to complete this trial, but it's accruing slowly. After completing this study, we need to evaluate some of the potentially more effective chemotherapies along with hormonal therapy in the adjuvant setting.

Phase III Randomized Study of Adjuvant Androgen Deprivation Therapy with or without Mitoxantrone and Prednisone after Radical Prostatectomy in Patients with High-Risk Adenocarcinoma of the Prostate **Open Protocol**

Protocol IDs: SWOG-S9921, CALGB-99904, CTSU
Projected Accrual: 1,350 within 9.5 years

Eligibility: Postprostatectomy with at least one of the following pathologic critera: Gleason 8; pT3b (seminal vesicle), pT4 or N1; Gleason 7 and positive margin; preoperative PSA > 15 ng/mL, Gleason > 7, or PSA > 10 ng/mL and Gleason > 6.

ARM 1: Goserelin q 12 weeks + bicalutamide qd x 2 years
ARM 2: (Mitoxantrone d1 + prednisone BID d1-21) every 3 weeks x 6 plus hormonal therapy as in ARM 1

SOURCE: NCI, Physician Data Query, November 2003.

Nonprotocol options for patients with high-risk disease after prostatectomy

In a nonprotocol setting, the standard approach to patients with high-risk prostate cancer has been close monitoring. In light of the Early Prostate Cancer trials with bicalutamide 150 mg monotherapy, some clinicians utilize this approach. Others put these patients on traditional hormonal therapy, such as LHRH agents plus or minus an antiandrogen, even though it's not considered the standard yet.

Many patients undergoing radical prostatectomy are younger and have a successful nerve-sparing procedure. Many of these men have regained or are regaining sexual function. The Intergroup trial has a control arm of traditional hormonal therapy, which has a profound effect on their sexual function. Some men who don't enroll on the Intergroup trial are opting for bicalutamide monotherapy as opposed to the traditional hormonal therapy.

RTOG Trial 85-31: Immediate versus delayed hormonal therapy in patients with locally advanced disease

RTOG-85-31 randomly assigned patients with locally advanced prostate cancer who were going to receive external beam radiotherapy to radiotherapy alone versus radiotherapy plus immediate traditional hormonal therapy.

The data presented from RTOG-85-31 at ASCO 2003 demonstrated an overall survival advantage for patients who received immediate versus delayed hormonal therapy. These findings confirm the results of the Bolla trial.

Many people criticized the Bolla trial because it was a single study and patients in the delayed treatment arm probably were treated later than in North America, magnifying the difference between early and the delayed treatment. RTOG-85-31 is more representative of North American practice patterns and demonstrates a survival benefit to androgen ablation.

Phase III Comparison of Adjuvant Therapy with Goserelin versus Observation Only Following Definitive Radiotherapy for Unfavorable Prognosis Adenocarcinoma of the Prostate **Closed Protocol**

Protocol ID: RTOG-85-31
Projected Accrual: 977

Eligibility: Clinical Stage C prostate cancer or Stage A2 or B with positive lymph nodes

ARM 1: Radiotherapy → goserelin at relapse
ARM 2: Radiotherapy + adjuvant goserelin

SOURCE: NCI, Physician Data Query, November 2003.

Prostate Cancer Prevention Trial (PCPT): Interpreting the results

The Prostate Cancer Prevention Trial was designed to determine whether finasteride prevents prostate cancer. The trial enrolled over 18,000 men from across the United States. It had a very simple design that randomly assigned men 55 years of age or older — all of whom had a PSA of 3 ng/mL or less — to finasteride or placebo. The plan was for a seven-year follow-up. Any man who developed an abnormal digital rectal exam or a PSA that rose significantly underwent a prostate biopsy. The men who maintained a normal PSA or who did not develop a change in their digital rectal exam were asked to undergo a prostate biopsy at the end of seven years.

Men who received finasteride, compared to those who received placebo, had a 24.8 percent reduction in the "period" prevalence of prostate cancer — patients who developed prostate cancer during the seven years plus patients who were diagnosed with prostate cancer at the end of seven years. The study was stopped because the primary endpoint was achieved and the safety monitoring committee believed it would be unethical to continue the study because the reduction in prostate cancer had been met.

The bad news was that tumors in men who developed prostate cancer on finasteride had a higher rate of Gleason scores of seven, eight, nine or 10 compared to those in the men on placebo. When I explain these results to patients, I say, "If you take this drug, your chance of developing prostate cancer appears to be less, but if you develop prostate cancer, the cancer may appear more aggressive under the microscope."

Urologic pathology involves considerable debate. One school of thought contends finasteride actually changes the appearance of the cancer, making the Gleason scoring more difficult. The other school of thought says the change in Gleason score is a real biological phenomenon. Is it an epiphenomenon — the drug just changes appearances under the microscope — or a real phenomenon in which the drug actually increases the aggressiveness of prostate cancer? We don't know.

Overall Rates and Rates of Gleason 7-10 Prostate Cancer in Men Receiving Prophylactic Finasteride Compared to Placebo

	Finasteride (n = 4,368)	Placebo (n = 4,692)	*p*-value
Prostate cancer	803 (18.4%)	1,147 (24.8%)	<0.001
Gleason 7-10	280/757 (37.0%)	237/1,068 (22.2%)	<0.001

SOURCE: Thompson IM et al. **The influence of finasteride on the development of prostate cancer.** *N Engl J Med* 2003;349(3):215-24. **Abstract**

Case discussion: 67-year-old man on testosterone replacement with abnormal prostate biopsy

Treated for hypogonadism since 1995, this man had five sets of prostate biopsies between 1995 and 2002 with a reference diagnosis of probable cancer, not yet definitive. In February 2002, he was taken off of testosterone replacement therapy. The problem is that he's becoming more symptomatic from hypogonadism. His current testosterone level is 30 ng/dL — significantly lower than the normal level of greater than 250 ng/dL. The question is: How do we treat this man?

He has a few cells on one of five biopsies that have been interpreted as "prostate cancer," yet he doesn't want anything definitive done for this condition. He's in excellent health, and his attitude is that "life goes on." We've been equivocating as to whether or not he has cancer. He's probably had about 60 cores removed from his prostate over the last six years. One or two cores show a few isolated cells suggestive of cancer.

He's miserable because he has gained weight and has poor muscle tone, mood swings and no libido. He wants to go back on testosterone replacement therapy and says he'll shop around until he finds a physician who will restart therapy.

This issue may become more common in light of discussions of "andropause" among the aging male population. Is it truly wrong to maintain a normal testosterone in some of these men? The conventional wisdom is that prostate cancer is fueled by testosterone, and testosterone replacement should not be given. The reality is that more recent studies suggest men with low testosterone levels may have more advanced prostate cancer.

One recommendation would be to tell this patient, "Unless you have your prostate removed, you should not go on testosterone replacement therapy." Is that too Draconian for this man? I don't know the answer, but it's a real dilemma, including from a medicolegal perspective.

Prostatectomy versus radiotherapy for men with lower-risk disease

I recently had the fortunate opportunity to collaborate with Anthony D'Amico and Peter Carroll to combine our CPDR database with the CaPSURE database. We were able to amass over 6,000 patient records, asking the simple question of whether stratifying patients by the D'Amico risk stratification schema predicts death from prostate cancer. We found that in patients who underwent either surgery or radiation, this schema predicted death from prostate cancer at 10 years. Stratified by age, men with low-risk disease — PSA of 10 or less, Gleason score of 6 or less, T1C, T2A — who underwent surgery had a lower chance of death from prostate cancer than those who underwent primary radiation therapy.

The caveats are that this is not a randomized trial and the radiotherapy was predominantly conventional external beam radiation. Some would argue that with higher doses of radiation — intensity modulated or brachytherapy — it is reasonable to offer radiotherapy to younger men with low-risk disease.

Prostate Cancer-Specific Mortality (PCSM) and Non-PCSM after Surgery or Radiation Therapy: Analyses of 7,316 Patients from 44 Institutions

	Surgery	Radiation	*p*-value
Estimated Non-PCSM 8 y after PSA failure for men <70 y (%)	4%	15%	0.002
Estimated Non-PCSM 8 y after PSA failure for men ≥70 y (%)	13%	18%	0.35
PCSM (RR)			
Low risk	1.0	1.0	
Intermediate risk	4.9 (95% CI 1.7-8.1)	5.6 (95% CI 2.0-9.3)	
High risk	14.2 (95% CI 5.0-23.4)	14.3 (95% CI 5.2-24.0)	

PCSM = prostate cancer-specific mortality

SOURCES: D'Amico AV et al. **Cancer-specific mortality after surgery or radiation for patients with clinically localized prostate cancer managed during the prostate-specific antigen era.** *J Clin Oncol* 2003;21:2163-72. **Abstract**

Use of bicalutamide 150 mg monotherapy in clinical practice

In the EPC trials, bicalutamide 150 mg monotherapy resulted in a clinical progression benefit. When it was published by Dr See in the *Journal of Urology*, there was a greater magnitude of benefit in patients with high-risk disease, and there was a lot of skepticism. Even though there was statistical benefit, the clinical benefit in individuals at low risk was not great.

Another concern is that compared to placebo, bicalutamide delayed the onset of clinical metastases, but there was no survival benefit observed. Additionally, in the North American trial made up of mostly radical prostatectomy patients, many men had organ-confined prostate cancer and would be considered at low risk for progression.

These patients, who were probably included in the low-risk group, may have diluted the overall effect. The bottom line is immediate adjuvant bicalutamide 150 mg makes sense for patients who are risk-stratified and may be at higher risk for progression.

The EPC trial did not evaluate therapy at PSA progression. It compared men who were treated adjuvantly to men who underwent watchful waiting, external beam radiation or radical prostatectomy. It's speculative to extrapolate the use of bicalutamide to biochemical recurrence. Many physicians use it in that setting and assume the benefits will be the same, but we have to be academically honest: The trial did not look at biochemical recurrence.

The use of bicalutamide 150 mg has increased in younger men who experience a biochemical recurrence, or men who fall into the very high-risk postoperative group. This is particularly true for men who are recovering sexual potency after a successful nerve-sparing prostatectomy.

Those men are reluctant to use traditional hormonal therapy because they know it will hinder their sexual rehabilitation and further recovery of their erectile function. They've been more willing to take bicalutamide monotherapy, hoping it will have less impact on their sexual function. The problem is that we don't have long-term data to know whether sexual function is truly maintained. We believe it will be, but we don't have data on men in their forties and fifties who have been through a nerve-sparing procedure.

Tolerability of bicalutamide monotherapy

In the short-term, breast irradiation seems to eliminate the breast enlargement and most of the tenderness associated with bicalutamide. Many patients will still have mild nipple tenderness without a great deal of breast growth.

Patients receiving bicalutamide alone do not develop hot flashes. I've carefully questioned patients on bicalutamide who have been through a nerve-sparing prostatectomy about their experiences, and they tell me their sexual libido is maintained and they still respond to sildenafil. Men who were regaining natural potency continue to do so. I have to admit, I have fairly short follow-up and I have not used an objective questionnaire to systematically evaluate sexual function in these patients.

Canadian Public Advisory on Bicalutamide

"The Early Prostate Cancer (EPC) trial compared bicalutamide 150 mg to placebo, when given in addition to standard care (i.e., radiation therapy, radical prostatectomy or watchful waiting) in men (N = 8,113) with localized or locally advanced nonmetastatic prostate cancer. In a planned second analysis (median follow-up 5.4 years), there continues to be a significant reduction in the risk of disease progression with bicalutamide (HR = 0.73, p < 0.0001); no differences were found in overall survival. ...

"In an exploratory subgroup analysis, however, trends were noted in the subgroup of patients managed by watchful waiting. Patients with localized disease treated with bicalutamide in addition to watchful waiting showed a trend towards decreased survival (25.2% versus 20.5%, HR = 1.23, 95% CI = 1.00-1.50). Conversely, in patients with locally advanced disease, those treated with bicalutamide in addition to watchful waiting showed a trend towards increased survival (33.7% versus 41.3%, HR = 0.80, 95% CI = 0.62-1.04). As a result of this second analysis, Canada and the United Kingdom have withdrawn the approval for bicalutamide 150 mg in patents with localized prostate cancer."

SOURCES:

Public Advisory: Important safety information regarding Casodex 150 mg. Health Canada Health Products and Food Branch. 18 August 2003. Accessed November 19, 2003.

Casodex 150 mg (bicalutamide): No longer indicated for treatment of localized prostate cancer. Committee on Safety of Medications (UK). 28 October 2003. Accessed November 19, 2003.

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Bolla M et al. **Long-term results with immediate androgen suppression and external irradiation in patients with locally advanced prostate cancer (an EORTC study): A phase III randomised trial.** *Lancet* 2002;360(9327):103-6. **Abstract**

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See W et al. **Immediate treatment with bicalutamide 150 mg as adjuvant therapy significantly reduces the risk of PSA progression in early prostate cancer.** *Eur Urol* 2003;44(5):512-8. **Abstract**

See WA et al. **Bicalutamide as immediate therapy either alone or as adjuvant to standard care of patients with localized or locally advanced prostate cancer: First analysis of the early prostate cancer program.** *J Urol* 2002;168(2):429-35. **Abstract**

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Immediate versus delayed hormonal therapy

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Walsh PC et al. **A structured debate: Immediate versus deferred androgen suppression in prostate cancer-evidence for deferred treatment.** *J Urol* **2001;166(2):508-15. Abstract**

Colleen A Lawton, MD, FACR

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Edited comments by Dr Lawton

RTOG-85-31: Radiation therapy and androgen deprivation for locally advanced prostate cancer

Trial design and efficacy data

RTOG-85-31 was a prospective, randomized trial for patients with locally advanced disease. The trial began in 1985 and compared radiation alone to radiation plus indefinite hormone manipulation in the form of an LHRH agonist. Patients on the radiation-only arm received an LHRH agonist at the time of failure — generally biochemical failure.

When the results of RTOG-85-31 were first published, a significant benefit was seen in local control, distant disease and biochemical control for patients receiving adjuvant hormone therapy. We believed we would eventually see a survival advantage, but we did not see it at that early analysis.

The long-term data for RTOG-85-31 was presented at the 2003 ASTRO meeting and showed 10-year overall and cause-specific survival advantage for patients receiving adjuvant hormone therapy. I believe patients are more concerned about cause-specific survival than overall survival. Patients want to know if they are going to die of prostate cancer, not whether they are going to die of a heart disease or stroke in the interim.

Hormone therapy appears to do two things: It shrinks the volume of the cancer in the area, making it easier to radiate the prostate bed, and it treats micrometastases.

Dose escalation in radiation therapy

We are learning that for patients with locally advanced disease, we need to add hormones and to dose-escalate radiation therapy. The million-dollar question from RTOG-85-31 is whether the hormone therapy compensated for inadequate radiation therapy. Data suggests that we need to deliver higher

doses of radiation than those administered in any of the RTOG trials, which was essentially a boost dose of 70 Gy to the isocenter, with the prostate itself receiving about 68 to 69 Gy. Probably the best prospective, randomized data regarding the need for dose escalation in patients with intermediate- and high-risk tumors comes from MD Anderson, but what advantage we obtain by adding that higher dose in addition to the hormones is still an unanswered question.

Osteoporosis and fractures while on long-term hormonal therapy

In RTOG-85-31, the length of hormone therapy was indefinite, so some of the patients are still on treatment 15 years later. Currently RTOG is developing a protocol to study the relationship between long-term hormone therapy and osteoporosis and fractures. We are hoping to accrue 700 patients within 12 to 18 months, and we expect to have an answer in the next two years. We will evaluate Dexascans to assess osteoporosis and T-spine films to evaluate the rate of fractures.

Multiple studies have demonstrated an increased rate of osteoporosis with long-term hormonal therapy, and I think this study will confirm that, but there's very little data on whether that translates into an increased fracture risk. There will be a quality-of-life instrument in this protocol, and I suspect we'll see more fractures and a decrement in the quality of life. If so, we need to determine what to do to avoid this toxicity for patients on long-term hormone therapy.

RTOG-86-10: Neoadjuvant androgen blockade for locally advanced disease

In RTOG-86-10, approximately 450 patients with locally advanced disease were randomly assigned to receive either no hormone treatment or total androgen suppression neoadjuvantly — two months prior to radiation therapy and then again during radiation versus radiation alone. Patients with lower Gleason Grades (six or less) benefited from radiation therapy.

One could postulate the hormone therapy shrank the lesions that weren't likely to metastasize, allowing the radiation to do its job. In contrast, the patients with high-grade tumors had too much micrometastatic disease and really needed long-term hormone therapy.

RTOG-92-02: Short-term versus long-term total androgen suppression for locally advanced disease

Patients in this trial received total androgen suppression in a neoadjuvant fashion, as in the treatment arm of RTOG-86-10, with or without two years of an adjuvant LHRH agonist. The data showed an advantage in local control, distant disease and biochemical-free survival for patients treated with long-term therapy, and a survival advantage in patients with high-grade disease. As the data matures, I believe we will see a cause-specific survival advantage as we did in RTOG-85-31.

Both trials RTOG-85-31 and 92-02 indicate, and it's generally accepted, that we need to include some degree of long-term hormone manipulation in treating patients with locally advanced disease, high-grade tumors and possibly patients with a high PSA.

Phase III Randomized Trial of Long-Term Adjuvant Total Androgen Suppression with ZDX versus No Subsequent Treatment following Neoadjuvant FLUT/ZDX and Radiotherapy for Locally Advanced Carcinoma of the Prostate **Closed Protocol**

Protocol ID: RTOG-92-02
Projected Accrual: 1,554

Eligibility: Locally advanced prostate cancer

ARM 1: Goserelin/flutamide x 4 m + radiation therapy
ARM 2: Goserelin/flutamide x 4 m + radiation therapy → goserelin x 24 m

Study Contact:
Radiation Therapy Oncology Group
Gerald Hanks, Chair. Tel: 215-728-2940

5-year treatment outcomes estimated rate

Endpoint value	Arm 1	Arm 2	*p*-value
Local progression	12.3 (95% CI 10-15)	6.4 (95% CI 4-8)	p = 0.0001
Distant metastasis	17.0 (95% CI 14-20)	11.5 (95% CI 8-14)	p = 0.0035
Disease-free survival	28.1 (95% CI 24-32)	46.4 (95% CI 42-50)	p < 0.0001
Cause-specific survival	91.2 (95% CI 89-93)	94.6 (95% CI 93-96)	p = 0.006

SOURCE: NCI Physician Data Query, November 2003.

Hanks GE et al. **Phase III Trial of Long-Term Adjuvant Androgen Deprivation After Neoadjuvant Hormonal Cytoreduction and Radiotherapy in Locally Advanced Carcinoma of the Prostate: The Radiation Therapy Oncology Group Protocol 92-02.** *J Clin Oncol* 2003;21(21):3972-8. **Abstract**

RTOG-99-02: Adjuvant chemotherapy for patients with high-risk prostate cancer

RTOG has an ongoing trial looking at the value of chemotherapy in patients with aggressive disease — high PSAs, locally advanced disease and high-grade tumors. Patients are randomized between hormones and radiation versus hormones, radiation and chemotherapy.

It's an uphill battle to enter patients on study because of biases against chemotherapy, but we need to remember that just 15 years ago we thought there was no role for chemotherapy in non-small-cell lung cancer, and look at us today. I believe that slowly but surely we'll define a role for adjuvant chemotherapy, but it's going to take some time.

Phase III Randomized Study of Androgen Suppression and Radiotherapy with or without Subsequent Paclitaxel, Estramustine, and Etoposide in Patients with Localized High-Risk Prostate Cancer **Open Protocol**

Protocol ID: RTOG-99-02
Projected Accrual: 1,440

Eligibility: Prostate cancer at high risk for relapse, negative lymph nodes

ARM 1: Androgen suppression* x 4 m → radiotherapy → androgen suppression** x 20 m
ARM 2: Androgen suppression* x 4 m → radiotherapy → androgen suppression** x 20 m + [(estramustine + etoposide days 1-14) + paclitaxel on day 2] q 3 w x 4

*Androgen suppression consists of (goserelin OR leuprolide) AND (bicalutamide OR flutamide).
**Goserelin or leuprolide.

Study Contact:

Radiation Therapy Oncology Group
Howard Sandler, Chair. Tel: 734-936-9338

SOURCE: NCI, Physician Data Query, November 2003.

Case study: Patient presenting with locally advanced prostate cancer

History

This patient was in his mid-fifties when he had his first screening PSA, which was in the high forties. He was diagnosed with a T3, Gleason 7 (4+3), prostate cancer.

Follow-up

When I saw the patient, I recommended radiation therapy and androgen deprivation. I treated him with two months of neoadjuvant hormonal therapy to cytoreduce the tumor. Essentially, his therapy was the same as the long-term treatment arm in RTOG-92-02. He received bicalutamide and a LHRH agonist. The tumor responded nicely after two months and then we began radiation treatment.

I treated the nodes and pelvis, and to maximize his chance for survival, I used a higher boost dose to the prostate than in any of the RTOG studies. The patient tolerated treatment well and we will continue hormone therapy for two years. He's still receiving the LHRH agonist; his PSA is undetectable and he feels well.

Screening for prostate cancer

When this patient was diagnosed, he had a sense of anger that his doctor had never recommended PSA screening. It was his wife who suggested he should be screened during an annual exam. I believe it's unusual for patients to be well-screened for prostate cancer in the community.

Quality of life versus survival from the patient's perspective

I explained to this patient that when we use hormone therapy for such a long period of time, the likelihood is high that he will have erectile dysfunction. I do have a few patients who have regained sexual function after extended hormonal manipulation, but it's uncommon. Potency was a huge issue for this young patient, but survival was more important.

Patients have different goals. In this case, the disease was so advanced that the issue was survival. Patients at low risk realize they probably won't die of their disease, so quality of life becomes more important.

I didn't discuss the alternative of bicalutamide monotherapy with this patient, because I don't have data that shows it's as efficacious as an LHRH agonist and he was focused on survival. For the patient who wants to be treated with hormone therapy, but values quality of life as much as survival, I consider bicalutamide monotherapy.

"PSA bounce"

The biggest issue with "PSA bounce" is defining it. For the longest time we used the ASTRO definition for biochemical recurrence, which is three consecutive rises in PSA, but data from MD Anderson has demonstrated this probably isn't the best definition. If a patient has a rising PSA and then it goes down and subsequently rises two or three times, where do you count the first rise in PSA? It's difficult to determine, and we've all known patients with courses like that. Interesting new data suggests that an absolute rise of 2.0 ng/mL may be a better definition of recurrence, which is certainly a very clear definition.

Patients are so anxious about their PSA that they often want it tested during treatment; however, we can see fluctuations then, so I discourage testing. In the past, I checked the PSA on all my patients one month after treatment, but in five to 10 percent of cases, the PSA rose before it ultimately went down. That upset everyone, including me, so now I encourage patients to wait longer. With a patient like this, after the LHRH agonist is stopped, we may see a bounce at some point, and then hopefully a leveling off or maybe even a drop. That's something we carefully walk the patient through.

A father with locally advanced prostate cancer

Three and a half years ago when my father was almost 70 years old, he was diagnosed with a Gleason 7, locally advanced prostate cancer. His PSA was 93. He had not had routine screening but he was having some clinical symptoms. He was treated at my institution, and although I didn't treat him, I was in the background. He received radiation therapy and hormone therapy. At the outset, he received total androgen suppression with bicalutamide and an LHRH agonist, followed by long-term LHRH agonist therapy.

This experience certainly gave me a different perspective on being a doctor versus a daughter. There was a lot of tap dancing between those two roles when I spoke with him. My dad is a very traditional man, and he didn't know much about my work before that, but at the end of the day he respected what I did. It was difficult for my friends and family to believe he developed the disease — and in fact the very stage of the disease — I've spent my career investigating.

I'm a very religious person, as is my father, and I think that the good Lord had something to do with this. I had a chance to do something very meaningful for my father, not so much in instituting treatment, but in helping him cope with the side effects, obtain information and line up physicians. It brought us closer. I don't think it was an accident that this related to my life's work and that my father was among the men who benefited from it.

Select publications

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Post-test: Prostate Cancer Update, Issue 6, 2003

Conversations with Urologic Oncology Leaders

Bridging the Gap between Research and Patient Care

QUESTIONS (PLEASE CIRCLE ANSWER):

1. In patients with prostate cancer, prospective randomized trials have demonstrated a benefit for the addition of hormonal therapy to brachytherapy plus external beam radiation therapy.
   a. True
   b. False

2. Hormonal therapy can be used to reduce the size of the prostate prior to brachytherapy.
   a. True
   b. False

3. Which of the following may have an impact on long-term urinary outcomes following brachytherapy?
   a. Use of supplemental external beam radiation
   b. Tobacco consumption
   c. Hormonal therapy
   d. All of the above
   e. None of the above

4. Which of the following may have an impact on long-term bowel function following brachytherapy?
   a. Use of supplemental external beam radiation
   b. Tobacco consumption
   c. Number of pretreatment bowel movements per day
   d. All of the above
   e. None of the above

5. Following brachytherapy, long-term potency preservation rates without the use of sildenafil approaches 80 percent.
   a. True
   b. False

6. SWOG-S9921 will evaluate whether hormonal therapy plus chemotherapy is better than hormonal therapy alone after radical prostatectomy in men whose tumors have adverse pathologic features.
   a. True
   b. False

7. Trial RTOG-85-31 — randomizing patients with locally advanced prostate cancer to external beam radiotherapy alone versus radiotherapy plus immediate hormonal therapy — demonstrated a disease-specific survival advantage for patients who received immediate hormonal therapy.
   a. True
   b. False

8. A meta-analysis of RTOG Phase III trials showed the benefit of neoadjuvant androgen blockade for localized prostate cancer is greater for patients at intermediate- than high-risk.
   a. True
   b. False

9. In an exploratory subgroup analysis of the EPC trial, those patients with localized disease treated with bicalutamide in addition to watchful waiting showed a trend towards decreased survival.
   a. True
   b. False

10. Multiple studies have shown that men treated with long-term hormone therapy for prostate cancer have an increased rate of osteoporosis:
    a. True
    b. False

Post-test Answer Key: 1b, 2a, 3d, 4d, 5b, 6a, 7a, 8a, 9a, 10a

Evaluation Form: Prostate Cancer Update, Issue 6, 2003

Research To Practice respects and appreciates your opinions. To assist us in evaluating the effectiveness of this activity and to make recommendations for future educational offerings, please complete this evaluation form. A certificate of completion is issued upon receipt of your completed evaluation form.

Please answer the following questions by circling the appropriate rating:

5 = *Outstanding* 4 = *Good* 3 = *Satisfactory* 2 = *Fair* 1 = *Poor*

GLOBAL LEARNING OBJECTIVES

Upon completion of this activity, participants should be able to:

- Critically evaluate the clinical implications of emerging clinical trial data in prostate cancer treatment 5 4 3 2 1
- Inform patients about the specific risks and benefits of local and systemic therapies 5 4 3 2 1
- Provide individualized counseling to patients regarding the choice and timing of endocrine therapy 5 4 3 2 1
- Offer patients information regarding their prognosis with and without various therapeutic options 5 4 3 2 1

SPECIFIC LEARNING OBJECTIVES FOR ISSUE 6

Upon completion of this activity, participants should be able to:

- Consider the use of neoadjuvant and adjuvant hormone manipulation in addition to radiation therapy in the management of patients with locally advanced prostate cancer 5 4 3 2 1
- Discuss recent and ongoing clinical trials of brachytherapy in the management of patients with prostate cancer 5 4 3 2 1
- Describe the results of the Early Prostate Cancer trial and the implications for clinical practice 5 4 3 2 1
- Counsel patients with prostate cancer about the morbidities associated with brachytherapy 5 4 3 2 1

EFFECTIVENESS OF THE INDIVIDUAL FACULTY MEMBERS

Faculty	Knowledge of Subject Matter	Effectiveness as an Educator
Gregory S Merrick, MD	5 4 3 2 1	5 4 3 2 1
Judd W Moul, MD, FACS	5 4 3 2 1	5 4 3 2 1
Colleen A Lawton, MD, FACR	5 4 3 2 1	5 4 3 2 1

OVERALL EFFECTIVENESS OF THE ACTIVITY

Objectives were related to overall purpose/goal(s) of activity 5 4 3 2 1
Related to my practice needs 5 4 3 2 1
Will influence how I practice 5 4 3 2 1
Will help me improve patient care 5 4 3 2 1
Stimulated my intellectual curiosity 5 4 3 2 1
Overall quality of material 5 4 3 2 1
Overall, the activity met my expectations 5 4 3 2 1
Avoided commercial bias or influence 5 4 3 2 1

Evaluation Form: Prostate Cancer Update, Issue 6, 2003

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___Yes ___No

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_____

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What other faculty would you like to hear interviewed in future educational programs?

_____

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