



Tina Sotis. *The Tropic of Capricorn* ©2001. Oil on canvas, 18" × 28".

Technological advances in external-beam radiation therapy and the developments in equipment and computers allow for safer delivery of higher radiation doses to the prostate.

External-Beam Radiotherapy in the Management of Carcinoma of the Prostate

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Background: *External-beam radiotherapy (EBRT) has been used in the treatment of adenocarcinoma of the prostate gland for more than 30 years. Well-documented clinical series have demonstrated the effectiveness of EBRT in achieving both cause-specific survival and freedom from biochemical (prostate-specific antigen [PSA]) progression.*

Methods: *The indications and expected treatment results for treatment by EBRT in the management of adenocarcinoma of the prostate gland are reviewed. The treatment of early-stage disease definitively by EBRT alone or as complement to radioactive seed implant is emphasized. In the management of locally advanced disease, the use of EBRT with combined androgen ablation is discussed as definitive therapy and also as indicated in the postoperative adjuvant management of surgically identified pathologic stage T3 disease.*

Results: *The relative clinical benefit of EBRT compared with the mostly predictable and well-defined moderate side effects, which are manageable in most instances by conservative measures treatment, is well established. Advances in defining radiation-beam parameters have led to more effective and safer treatment for prostate cancer.*

Conclusions: *EBRT has historically been a mainstay in the management of prostate cancer. It remains a useful and indicated treatment modality in patients with early-stage, locally advanced, and metastatic disease.*

Treatment of Early-Stage Prostate Cancer

Definitive External-Beam Radiotherapy Treatment

Effective external-beam radiotherapy (EBRT) for treatment of prostate adenocarcinoma began with the development of high-energy, or "mega-voltage," delivery systems. Investigators at Stanford University pioneered the development of treatment techniques that allowed

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the use of these early, relatively low-energy treatment units in the treatment of deep pelvic organs such as the prostate gland, thus resulting in one of the largest treatment series in the pre-PSA era.¹ The technology has now evolved to the conventional use of high-energy linear accelerator-generated x-ray therapy or proton particle-beam irradiation, which is now being evaluated at the Massachusetts General Hospital and the Loma Linda University Medical Center. EBRT treatment is evolving toward the use of intensity-modulated radiation beam (IMRT) to “conform” the irradiation fields to the target cancer while minimizing dosage to normal sensitive tissues. Just as modulation and conformality technologies have evolved to optimize treatment delivery, so have the radiation oncologist’s tools to evaluate patients with prostate cancer and to optimize protocols of radiotherapy delivery to increase the potential for local control and cure while minimizing complications to nontarget tissues.

Patient Selection

The first issue requiring definition by oncologists was the selection of patients with prostate adenocarcinoma who might be curable by radiation therapy. Patients with the greatest probability for cure by radiotherapy are those with organ-confined disease or with minimal risk for extracapsular extension and without risk for significant nodal or distant metastatic spread. The patients conventionally regarded as having early-stage prostate cancers were those who, on digital rectal examination, were believed to have clinical stage T1c to T2a primary tumors according to the American Joint Committee on Cancer (AJCC) TNM evaluation criteria.²

The criteria for true early-stage prostate cancers have been further refined by Partin and colleagues³ by combining the prognostic parameters of clinical T stage, PSA level, and Gleason score into a table-based nomogram. These “Partin tables” have increased the prognostic prediction and selection of appropriate and indicated therapy for patients based on predictive measures for potential extracapsular extension, seminal vesicle involvement, nodal metastasis, and distant metastasis. Many radiation oncologists base their treatment planning on these prognostic parameters, specifically with respect to the volume or extent of tissue that would require effective irradiation to achieve cure. This often determines a major decision point in recommending the use of brachytherapy, either alone or in combination with EBRT, as part of the overall plan of treatment.⁴

Radiation Dosage

The second issue of importance in radiation treatment is determining the optimal irradiation dose

required to achieve maximal tumor control probability without exceeding the limits of acceptable risk. This is analogous to the classically described dose-response effect in pharmacology, including the risk for toxic side effects or irreversible complications at high treatment (irradiation) dosages. Dose escalation/optimization to improve clinical outcome is a subject of continual investigation. It has been addressed through multiple irradiation dose delivery techniques using both the traditional end points of absolute and disease-free survival rates and the current standard of treatment success, which is freedom from PSA progression.

Many single-institution and retrospective series have suggested improvements in freedom from biochemical or PSA progression with escalation of treatment doses achieved with improvements in treatment planning and delivery technology.⁵⁻⁹ Two randomized trials demonstrated that improved outcomes can be achieved with modest increases in irradiation dose, but these results occurred in patients diagnosed with intermediate or advanced prostate cancers. A randomized trial performed at the Massachusetts General Hospital utilizing proton-beam irradiation for dose escalation during the “boost” phase of prostate irradiation demonstrated a benefit for patients with Gleason pathology scores of 8-10.¹⁰ This trial was initiated prior to the development of PSA screening and before the significance of elevated PSA levels was recognized. Also, the subject population was limited to patients with advanced AJCC clinical stage T3 prostate tumors. A more recent and potentially technically relevant randomized trial completed at the M. D. Anderson Cancer Center evaluated a conservative 8-Gy dose escalation using conventional photon irradiation delivered with three-dimensional (3-D) conformal planning technology.¹¹ Patients who demonstrated the most significant benefit were those with intermediate or advanced disease as determined by pretreatment PSA values of more than 10 ng/mL. Five-year freedom from progression rates (biochemical and clinical) for patients treated with 70 Gy vs the escalated dose of 78 Gy were 48% and 75%, respectively ($P=.011$). No significant improvement was observed in patients with pretreatment PSA values of <10 ng/mL, with freedom from progression rates of 80% demonstrated for both treatment groups.

Most EBRT treatment plans begin with the use of a four-field box irradiation technique that is optimized to the individual patient’s anatomy and includes the appropriate extent of tissue and target volume as clinically indicated by the prognostic parameters discussed above. Regardless of the decision process on whether the target treatment volumes should include the seminal vesicles, the periprostatic or obturator nodes, or the regional, pelvic, or distant nodes or nodal groups, the

current standard of care utilizes computed tomography (CT) or computer planning technology for delivery of EBRT in the treatment of prostate cancers. As many as 25% of patients may receive inadequate treatment when treatment field designs are based on conventional fluoroscopic planning rather than CT-based planning systems.^{12,13} This process continues to evolve as our understanding of the regions and volumes of tissue most at risk for disease based on prognostic factors of stage, PSA level, and Gleason score continues to improve together with the ability to more accurately image and visualize pelvic anatomy and the potential sites of tumor. Current radiotherapy planning optimizes the conformality of 3-D external-beam treatment delivery to achieve the maximum potential for radiation dose delivery to the target tissue while minimizing the potential for complications to adjacent nontarget tissues. This becomes particularly important as treatment fields are designed to boost radiation to the prostate gland or the primary tumor volume to the maximal deliverable irradiation dose.¹⁴ Several clinical trials^{7,8,15} have suggested improved biochemical or PSA response and control by using highly conformal dose escalation techniques to achieve final prescription doses to the tumor of 80-90 Gy. These doses are greater than the commonly accepted limits of approximately 70 Gy achievable with conventional treatment planning and delivery methods.

Treatment Planning/Delivery

Treatment planning and delivery technology have progressed from simple 2-D or film- and fluoroscopic-based methods through 3-D or CT-scan computerized techniques to the currently evolving IMRT beam delivery technology. With simple 2-D planning or even sophisticated 3-D digital image-based planning, optimal treatment delivery is achieved only through the shaping of the irradiation fields or ports to maximally follow

or conform to the target tissues while avoiding normal tissues. The IMRT delivery system begins with precision targeting of the treatment volumes and critical irradiation dose limiting of sensitive structures. It then utilizes mathematical models and back projection techniques to dynamically modulate or vary the intensity of the treatment beam as small segments of each treatment field or portal irradiate the targeted cancer. Thus, the technology enables the treating oncologist to conform the radiation fields to the target and also to further optimize the conformality of the radiation dose delivery to the target. Again, through the use of 3-D imaging and multiple beam arrangements, the intensity modulation effect is optimized to all dimensions of treatment delivery, especially with respect to delivery of irradiation doses to deep structures while sparing surrounding sensitive tissues. Figs 1-3 demonstrate the progressive improvement in irradiation dose delivery to targeted prostate volumes with simultaneous sparing of surrounding normal tissues, most importantly the rectum, with the evolution of treatment planning and beam delivery technologies from simple 2-D opposed fields through 3-D or "beam's-eye" conformal planning and finally to beam-intensity modulation with IMRT.

Although a large amount of data is available that defines the probable clinical outcomes after EBRT of early-stage (T1-T2) prostate cancers, the majority of long-term data (more than 10-15 years) must be interpreted based on the limited disease-staging capabilities available in the pre-PSA era before the 1990s. Also, while many single-institution series provide data on large numbers of patients treated in a consistent manner over a long time period, the data vary in patient selection, reported end points, and methods of data analysis. Four national multi-institutional data sets have been analyzed with respect to outcomes of local control, disease-specific survival, and long-term survival relative to expectations according to age.¹⁶ The local con-

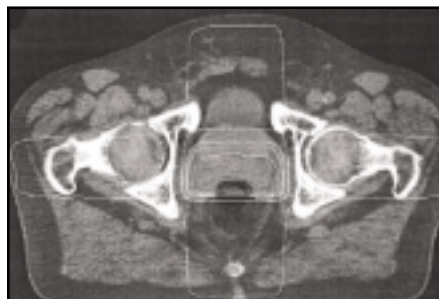


Fig 1. — Isodose distribution pattern for a simple 2-D treatment plan that utilizes the traditional four-field box technique for primary irradiation of the prostate and periprostatic tissues. Note the significant extension of the dose distributions anterior and posterior to the bladder and rectal tissues, respectively, as well as lateral to the hip joints.

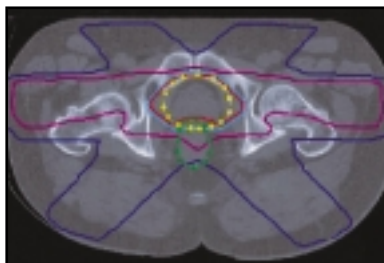


Fig 2. — Typical isodose distribution achieved with conventional 3-D treatment planning techniques utilizing conformal optimization of treatment fields by definition of target and normal tissue structures. This plan illustrates the use of a conformal six-field technique to minimize exposure of the rectum and thus limit the risk for radiation proctitis as a late effect complication.

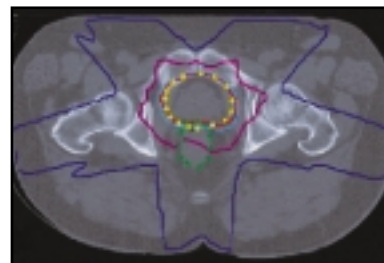


Fig 3. — Example of isodose distribution about the prostate gland achieved by modulating the intensity of the radiation beam (IMRT technique). By optimizing the energy of small sub-segments within each beam in a typical multifield arrangement, the delivery of irradiation energy can be even more specifically localized to the prostate gland with conformal sparing of the rectal tissues.

tol rates, although only clinically evaluable in these series, were high at 90%-96% at 5 years and 85%-95% at 10 years. The overall survival rates for clinical stage T1 prostate cancer were approximately 81%-86% at 5 years, 54%-64% at 10 years, and 40%-46% at 15 years. Absolute survival rates were closely paralleled by the "no evidence of disease" (NED) survival rates of approximately 75% at 5 years, 53% at 10 years, and 39% at 15 years, thus indicating a high probability cure for stage T1 prostate cancer with EBRT. For clinical stage T2 tumors, the absolute survival rates at 5, 10, and 15 years were approximately 75%, 45%, and 22%, respectively, with correspondingly lower NED survival rates of 53%-64%, 27%-34%, and 15%. Also noted for the patients with clinical stage T2 tumors were higher local recurrence rates ranging from approximately 15% at 5 years to 30% at 15 years.

Hanks et al¹⁶ performed a hazard ratio analysis comparing patients treated for prostate cancer by EBRT relative to expected survival for age. Patients treated for clinical stage T1 tumors did not demonstrate any excess mortality relative to expected survival, thus being potentially "cured" of disease to survive to expected longevity. Patients treated for clinical stage T2 prostate cancers experienced an excess mortality rate of approximately 5% at 5 years, which increased to an excess of approximately 20% at 15 years. Single-institution series may provide long-term outcome data on patients treated in a consistent manner, but biases in patient selection and stratification methods and in data

analysis and presentation can be highly variable and need to be recognized. Table 1 presents results from several institutions with published experiences in EBRT of prostate cancer in terms of local control and actuarial survival.¹⁷⁻²¹

The prostate tumor grade or Gleason score and the PSA value at diagnosis significantly influence clinical outcomes, particularly survival. In the pre-PSA era, histologic grade was considered the most significant prognostic factor, responsible for an estimated 20% inferior survival for patients with poorly differentiated T2 prostate cancers compared to patients with moderately to well-differentiated adenocarcinoma.²⁰ This grade effect has also been demonstrated in patients with otherwise favorable prognostic factors of early clinical stage (T1-T2) and initial PSA level less than 15 ng/mL, using freedom from PSA progression as an end point.²² Since PSA testing became widespread beginning in the early 1990s, it has become apparent that the PSA level at diagnosis is a more significant independent prognostic variable than grade^{22,24} and that the posttreatment PSA levels represent the standard for measurement of treatment effectiveness and patient cure.²⁵ Differences range between 10% and 40% for outcomes, based on reports of clinical control vs PSA findings.

Although PSA is a reasonably accurate marker of disease presence and approximate tumor burden, the PSA level combined with other significant variables represents only a prognostic predictor of clinical out-

Table 1. — Local Control and Survival Outcomes for EBRT Treatment of Prostate Cancer at Institutions Reporting 10- and 15-Year Series

| | Institution | Stage | | | | |
|-------------------------------------|------------------------|-------|-----|----|-----|-------|
| | | T1 | T1B | T2 | T2A | T2B-C |
| % Actuarial Local Control at 10 Yrs | Stanford ¹⁷ | 100 | | | | |
| | EVMS ¹⁸ | | 92 | | | |
| | MDA ²¹ | | 100 | 88 | | |
| | MIR ¹⁹ | | 80 | 76 | | |
| | MGH ²⁰ | | 84 | 82 | | |
| % Actuarial Local Control at 15 Yrs | Stanford ¹⁷ | 100 | | | 82 | 71 |
| % Actuarial NED Survival at 10 Yrs | Stanford ¹⁷ | 75 | | 61 | | |
| | EVMS ¹⁸ | | 66 | | 57 | 48 |
| | MDA ²¹ | | 60 | | | |
| | MIR ¹⁹ | | | 85 | | |
| | MGH ²⁰ | | 70 | 56 | | |
| % Actuarial NED Survival at 15 Yrs | Stanford ¹⁷ | 75 | 50 | | | |

EVMS = Eastern Virginia Medical School
MDA = M.D. Anderson Cancer Center
MIR = Mallinckrodt Institute of Radiology
MGH = Massachusetts General Hospital
NED = no evidence of disease

come. Based on the data available with long-term follow-up (15 years and longer), it is evident that although more men than previously realized have died of other causes with prostate cancer present, they did not die due to clinically apparent recurrent cancer. This circumstance represents a significant new dilemma in counseling and management where electing treatment based on a laboratory value may ultimately result in a decrease in quality of life without increasing the potential for longer survival.

EBRT With Brachytherapy

With the development of the PSA test for detecting prostate cancers in the late 1980s and its use as a marker for tumor control and cure in the 1990s, it was realized that rates of absolute “biochemical” cure by EBRT were unacceptably lower than previously expected and that this might be due to inadequate dose delivery to the primary prostate tumor. This realization, combined with advances in radiologic imaging technology, computerized dosimetry planning, and treatment delivery techniques, prompted a reevaluation of interstitial brachytherapy in the treatment of prostate cancers. A resurgence in the use of brachytherapy procedures occurred in the latter half of the 1990s based on data that demonstrated feasibility and safety in delivering irradiation doses of 160 Gy to the prostate gland by permanent seed implants (and equivalent or greater doses by temporary high-dose-rate procedures). Early results reported excellent efficacy based on outcome measures of PSA control.^{4,21,26-33} It has been advocated that brachytherapy techniques represent the optimal method for conformal radiation therapy treatment delivery, based on the high irradiation doses that can be delivered directly to the prostate with a rapid fall-off in exposure to surrounding nontarget tissues. Conformal

dose delivery represents the greatest strength of brachytherapy, but it is also the greatest limitation, as any disease that may extend outside of the implant volume will not receive effective irradiation. This realization led to the development of combined modality treatment protocols whereby EBRT is delivered to the low pelvic periprostatic tissues to eradicate potential microscopic or otherwise clinically undetectable disease, and the brachytherapy implant “boosts” treatment to escalate the maximally achievable dose delivered to the prostate gland and primary tumor.^{21,27,28}

The currently available data for the modern era of prostate brachytherapy are represented by single-institution retrospective reviews that report their results in terms of PSA control outcomes (Table 2).^{4,28-33} Unfortunately, most results are presented in terms of institution-specific criteria for PSA control. Even so, based on knowledge of pretreatment PSA levels, Gleason score, and T stage, most series have achieved effective stratification of patient groups to provide data by which selection of the optimal therapy according to defined prognostic variables can be based. Using these PSA-based outcome results combined with pathologic and prognostic data available from the Johns Hopkins Hospital surgical series,³ several guidelines and conclusions can be derived.

First, it is apparent when treating patients with true early-stage disease and minimal risk for widespread regional or distant metastasis based on initial PSA level, Gleason score, and T stage, equivalent rates of PSA control can be achieved by surgical prostatectomy or radiation. Second, in patients with favorable early-stage prostate cancers (initial PSA level <10 ng/mL and low or average Gleason scores), any additional benefit of EBRT to the periprostatic tissues appears limited and may not

Table 2. — EBRT With Permanent Brachytherapy vs Permanent Brachytherapy Alone: PSA Control Outcomes by Baseline PSA at Diagnosis

| Series/Author | Treatment | Median Follow-up (mo) | Percent of Patients With PSA Control Based on PSA at Diagnosis | | | | |
|-----------------------------|----------------|-----------------------|----------------------------------------------------------------|------------|------------|-------------|-----------|
| | | | 0-4 ng/mL | 0-10 ng/mL | 4-10 ng/mL | 10-20 ng/mL | >20 ng/mL |
| Wallner et al ⁴ | Pd-103 + EBRT | 38 | | 82 | | 85 | 70 |
| Critz et al ²⁸ | I-125 + EBRT | 45 | 98 | | 84 | 55 | 50 |
| Grado et al ²⁹ | I/Pd +/- EBRT | 47 | | 88 | | 72 | 57 |
| Ragde et al ³⁰ | I/Pd + EBRT | 58 | 93 | | 76 | 72 | 64 |
| Ragde et al ³⁰ | I-125 / Pd-103 | 56 | 95 | | 87 | 77 | 65 |
| Wallner et al ³¹ | I-125 | 36 | 100 | | 80 | 45 | 39 |
| Beyer et al ³² | I-125 | 34 | 94 | | 70 | 45 | 32 |
| Stock et al ³³ | I-125 / Pd-103 | 36 | 100 | | 80 | 45 | 39 |

be warranted, given the increased cost and morbidity potentially associated with combined therapy. Finally, in patients with initial PSA values >10 ng/mL, pelvic EBRT appears to offer potential benefit — even more so when initial PSA levels are at 20 ng/mL or higher since the probability of control with brachytherapy may be less than 50%.³¹⁻³³

Treatment of Locally Advanced Prostate Cancer

Rationale and Treatment Techniques for EBRT for Stage T3 or Greater Prostate Cancers

At diagnosis, approximately 10%-15% of prostate cancer cases clinically found on digital rectal examination extend beyond the confines of the prostate capsule (AJCC clinical stage T3-T4),² with no evidence of regional nodal or distant metastatic spread. Fortunately, the widespread use of PSA as a screening tool has increased the detection of prostate cancers even before the first abnormalities are evident on digital rectal examination. EBRT treatment has long been considered the treatment of choice for management of locally advanced prostate cancers since surgical resection would usually result in pathologically positive margins and thus would require adjuvant postoperative radiotherapy to achieve local control and potential cure. The mid to late 1990s saw a strong surgical interest in “downstaging” locally advanced prostate cancers with neoadjuvant antiandrogen and then proceeding with radical prostatectomy. Although androgen ablation produced significant tumor responses and pathologically negative margins were often achieved at resection, PSA recurrence was the norm once androgen ablation therapy was discontinued, indicating the presence of residual tumor.

Both local recurrence and regional/distant metastasis have plagued conventional EBRT treatment of locally advanced prostate cancer. Local recurrence rates at 10-15 years following treatment have ranged between 20% and 60%, depending on the method of detection and reporting.^{17,19,34} Several approaches have been investigated in attempts to improve results in this challenging patient population. The first approach focused on dose escalation techniques to selectively increase the irradiation dose to the prostate gland while not exceeding the normal tissue tolerance limits of critical adjacent structures. The radiotherapeutic techniques of 3-D conformal radiotherapy planning (3DCRT), particle proton (or other heavy particle) beam radiotherapy, interstitial prostate brachytherapy boosting, and IMRT represent this direct approach to achieving increased efficacy. As discussed above

Table 3. — Survival Rates (10- and 15-Yr) for Locally Advanced Stage T3 and T4 Prostate Cancer in National and Single Institutional Studies

| Study/Institution | Clinical T Stage | Survival % | |
|--------------------------------|------------------|------------|------------|
| | | 10 Year | 15 Year |
| Patterns of Care ¹⁶ | T3 - T4 | 33 | 23 |
| RTOG 75-06 ¹⁶ | T3 - T4 | 38 | No results |
| Mallinckrodt ¹⁹ | T3 | 38 | No results |
| Stanford ³⁵ | T3 | 35 | 18 |
| Stanford ³⁵ | T4 | 15 | 15 |
| M.D. Anderson ³⁶ | T3 | 45 | 31 |

with respect to the surgical treatment of advanced prostate cancers, the use of adjuvant androgen ablation therapy in combination with EBRT has been investigated to achieve both increased local-regional control of the tumors and possible sterilization of more distant micrometastatic deposits. This approach represents an attempt at radiosensitization of the prostate cancer by activation of the mechanism of biologic apoptosis, thus reducing overall tumor burden, and also by simple reduction of the prostate tumor size or bulk, thus potentially facilitating the utility of conformal radiotherapy treatment techniques.

Results of Conventional EBRT Treatment

Results for EBRT treatment of locally advanced AJCC stage T3 and T4 prostate cancer expressed in clinical terms of overall survival at 10 and 15 years are available from two national studies and also from reports of several academic institution with extensive long-term experiences. The Patterns of Care studies compiled by Hanks et al¹⁶ represent a national experience review that is comparable to that of individual institutions. The Radiation Therapy Oncology Group (RTOG) Protocol 75-06 evaluated the use of extended pelvic radiotherapy for stage T3 and T4 tumors in more than 500 patients in a prospective protocol.¹³ The results in these series consistently demonstrate the probabilities for survival of advanced stage T3 prostate cancer to be approximately 35% to 45% at 10 years (Table 3).^{16,19,35,36}

Few long-term data are available that define control of advanced-stage prostate cancers with respect to PSA control. The Massachusetts General Hospital reported results for 10-year biochemical disease-free survival rates of 10%-33% for T3 and T4 tumors, depending on substage and grade.³⁷ This corresponds to an 11% biochemical disease-free survival rate for T3 and T4 cancers reported by the Eastern Virginia Medical School based on PSA analysis of serum routinely banked during follow-up of their patient series.²⁴

Studies of dose escalation using 3DCRT technology have been initiated at multiple institutions. Initial reports provide considerable technical data and demonstrate early feasibility and safety results with the risk of severe acute toxicity contained within acceptable levels. Dose limits for the tolerance of normal tissues are now becoming available, although methods of analysis and reporting vary among institutions. There is still disagreement as to whether a predictable dose-response curve exists for the development of acute toxicity for all regional tissues.^{7,8} Early results from the M.D. Anderson Cancer Center indicate that using 3DCRT techniques to escalate prostate gland treatment doses to 74-78 Gy achieves a higher rate of biochemical disease-free survival compared to earlier results achieved with conventional techniques and doses of 72 Gy or less.⁵ Although initial results appear promising for the application of 3DCRT in the treatment of locally advanced prostate cancers, late toxicity and complication data are not yet available. Therefore, treatment of the prostate gland and pelvic region with EBRT at doses greater than 74 Gy is recommended only within the structure of a prospective clinical trial.

Androgen Ablation Therapy With EBRT for Clinically Advanced Prostate Cancers

The clinical benefit of androgen ablation therapy on advanced prostate cancer has been recognized since the 1960s. Early studies by the RTOG in the 1970s and early 1980s evaluated the use of antiandrogen therapies concurrent with radiotherapy treatment, but a survival benefit was not demonstrated due to the cardiovascular toxicity associated with the agents available at that time — estrogen and diethylstilbestrol. When the luteinizing hormone-releasing hormone (LHRH) agonist agents became available, a series of trials were initiated that have demonstrated significant survival advantage for combining androgen ablation and EBRT in patients with locally advanced prostate cancers and/or high Gleason score.

The RTOG Protocol 85-31 randomized patients to receive EBRT with goserelin acetate beginning at the conclusion of radiotherapy and continuing indefinitely vs radiotherapy alone with goserelin therapy at relapse.³⁸ Patients who received initial androgen ablation therapy demonstrated higher rates of local control (84% vs 71%), distant metastasis-free survival (83% vs 70%), disease-free survival (60% vs 40%), and PSA relapse-free survival (53% vs 20%). No overall survival advantage was seen on analysis of the whole series, but on subset stratification, an absolute survival advantage was noted for patients with Gleason score 8-10 prostate cancers (66% vs 55%).

A second RTOG trial, Protocol 86-10, evaluated the use of goserelin acetate and flutamide given 2 months before and during radiotherapy vs EBRT alone to doses of 65-70 Gy.³⁹ The results again showed improvement in local control (84% vs 71%), distant metastasis-free survival (68% vs 57%), progression-free survival (29 vs 20%), and distant metastasis occurrence (35% vs 46%). Again, no overall survival advantage was seen for the full study group.

A final trial reporting early 5-year data demonstrated a survival advantage with adjuvant antiandrogen therapy. The European Organization for Research and Treatment of Cancer (EORTC) randomized patients to receive either EBRT alone to 70 Gy or EBRT plus concurrent goserelin acetate that continued for 3 years following radiotherapy.⁴⁰ During the first 4 weeks of radiotherapy and goserelin treatment, patients in this combined treatment group also received cyproterone acetate as a direct androgen-blocking agent. With a median follow-up of 45 months and with 27% of patients still receiving postradiotherapy goserelin treatment, improvement in overall 5-year survival rate of 79% for adjuvant hormone therapy vs 67% for radiotherapy alone was reported. The 5-year disease-free survival rate for the patients who received concurrent hormone therapy was 85% vs 48% for the patients receiving radiotherapy alone.

Conclusions

EBRT is an effective therapeutic modality in the treatment of adenocarcinoma of the prostate gland, regardless of the methods used to assess clinical outcomes — either by survival or by biochemical measures of PSA levels. Continued improvements in both 3-D conformal planning and delivery technology combined with enhanced imaging ability will allow increased accuracy and specificity in EBRT treatment. Even as new or refined treatment modalities such as brachytherapy evolve in parallel, subgroups of patients with prostate cancer remain who, by stage, grade, or PSA level, would be best managed by incorporating EBRT as a component of the overall treatment plan. Finally, for patients diagnosed with locally advanced stage T3 or T4 prostate cancers, either at initial presentation or on pathologic review after prostatectomy, optimal EBRT combined with hormonal manipulation will be important in achieving long-term survival or cure.

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