

Nine Decisions Before Electing RADIATION THERAPY After Radical Prostatectomy

Who might it help? When should it be done?

Understand the risks of side-effects

By Nathan Roundy

The words “the surgeon may not have gotten it all”, or “your PSA is rising” strike fear into the heart of a man who had his cancerous prostate surgically removed. About 15% of low risk men, and up to 80% of high risk men will have rising PSA at some time after prostatectomy, indicating a cancer recurrence⁽¹⁾.

Radiation Therapy Can Help – Radiation after prostatectomy can induce ‘remission’, meaning there is no sign of PSA rising, or any other sign of cancer recurrence. Quality of life is better for men whose PSA does not rise. They have less anxiety, and can avoid additional cancer therapy such as hormone blockade or chemotherapy. Stephenson⁽²⁾ reported 32% of men were free of PSA progression at six years after radiation, and Catalona⁽³⁾ reported 25% PSA free at ten years. Two clinical trials^(4,5) show a survival advantage.

Radiation Can Hurt – If some men can achieve long term remission with radiation therapy after prostatectomy, why not just give every man radiation? The ionizing radiation that kills cancer cells can also damage or kill non-cancer cells including nerves and blood vessels. Before about 1990, radiation technology was not able to precisely focus the radiation on the tumor and men suffered a lot of severe side-effects. Relatively low dose had to be used, and most men did not achieve a long-term remission.

Many advances in the technology now allow precise aiming of narrower beams, allowing higher dose for better control, and causing fewer side-effects. Using today’s most advanced radiation machines in the hands of an expert radiation oncologist, most men report few serious long-term side-effects. But, even today, some have urinary, potency, and bowel side effects that reduce quality of life, or (very rarely) can be life threatening. For example in the SWOG 8794 clinical trial reported by Thompson⁽⁴⁾, 17.8% of men ended up with urethral stricture where scar tissue blocks the urethra and men cannot urinate. That requires medical intervention and can be chronic. 6.5% of the men developed total urinary incontinence which greatly reduces quality of life. Many men report reduced ability to get an erection and some become impotent. The severity of potential side-effects is graded one through five and is detailed in Table 1 at the end of this article.

“Using today’s most advanced radiation machines in the hands of an expert radiation oncologist, most men report few serious long-term side-effects.”

Many men already have urinary and potency problems as a result of prostatectomy, and radiation can make the side-effects worse.

Some might be better served without radiation. For example, a man 75 years old, with some heart issues and diabetes, who has slow growing cancer with PSA doubling time of 1.5 years, might decide to avoid the lost time, expense, and quality of life risks of radiation. His slow growing cancer might never affect his quality of life, and if it ever does become a problem later on, hormone therapy might give a long remission as well.

On the other hand, a younger, 60 year old man in good health, with fast, 6 month PSA doubling time and high Gleason Score 4+5=9, is at high risk of progression and may choose radiation.

Five New Research Papers Provide Better Guidelines – The many details to consider before choosing radiation will only be summarized here. The five papers outlined below provide much of the background for this article. To get a more complete understanding of the issues, the reader is encouraged to download them for free, but the long internet addresses are difficult to enter. Readers can go to the PCRI web site and download the electronic copy of this issue at <http://www.pcri.org>. Click on the Insights and choose the May 2010 issue. Inside the issue, click on the underlined, blue hyperlinks to download the papers.

Stephenson - 2007⁽²⁾ – A landmark paper that presents the statistics of men who got salvage radiotherapy, stratified by their risk factors. Overall, 32% of men treated with radiation were still cancer free six years later. However certain men were more likely to benefit from radiation than others. For example, 41% of high risk men, with a fast PSA doubling time of less than ten months and high Gleason Score 8, 9, or 10, were free of PSA progression at six years, but only if they started radiation when PSA was ≤ 0.50 ng/ml and they had positive surgical margins (cancer left behind after the surgery). A Nomogram, an easy-to-use statistical tool for estimating who might achieve long remission, is presented in the paper and also available for free at the Memorial Sloan Kettering



Cancer Center web site here <http://www.mskcc.org/mskcc/html/10088.cfm>. Download free here: <http://jco.ascopubs.org/cgi/reprint/25/15/2035>

Trock 2008⁽⁵⁾ This paper showed that with a median follow-up of six years after radiation, salvage radiotherapy alone was associated with a significant 3-fold increase in prostate cancer-specific survival relative to those who received no salvage treatment. Only men with the following characteristics had a survival benefit:

- Achieved undetectable PSA after prostatectomy
- Had fast, six month PSA doubling time
- Radiation was started within two years after PSA started rising
- A PSA less than 2.0 ng/ml at start of radiation

Download this article free here: <http://jama.ama-assn.org/cgi/reprint/299/23/2760>

Thompson 2009⁽⁴⁾ – This paper showed a survival advantage for adjuvant (early) radiation given about 90 days after prostatectomy in men with positive margins. Men were randomized for immediate, adjuvant radiation or observation. After twelve years of follow-up, slightly less than 10% of men benefited with longer survival. Download free here: <http://download.journals.elsevierhealth.com/pdfs/journals/0022-5347/PIIS0022534708030590.pdf>

Nielsen, Trock, Walsh 2010⁽⁶⁾ – *This paper discusses the pros and cons of the latest research about the adjuvant / salvage radiation decision. Table 2 points out that some men with positive margins disease after prostatectomy will not have PSA rise for ten (Continued on page 10)*

years even if they do no additional therapy. They point out that if adjuvant radiation is given to all men, many are exposed to side-effects unnecessarily. They also point to research (unrandomized) that indicates salvage radiation has about the same long-term remission rate as adjuvant radiation, as long as the salvage radiation is started at a very low PSA level.

“The Stephenson article (the first article listed above) comments on this issue as well, suggesting that the optimum PSA threshold for early salvage RT should be less than 0.4 ng/mL.

Download the Nielsen, Trock, Walsh article free: <http://www.jnccn.org/content/8/2/228.full.pdf+html>

Choo⁽⁷⁾ – 2010 Presents a complete review of these issues and challenges and does a good job explaining the current research. There is also a good discussion showing that adding hormone deprivation therapy to salvage therapy may improve outcomes. Download free: <http://cancerresearchandtreatment.org/Synapse/Data/PDFData/0036CRT/crt-42-1.pdf>

A surprising result of this latest research is that the group of men who are more likely to progress after radiation are the very same men with the most to gain from radiation. Reflecting this, the most recent update of the NCCN Clinical Practice Guidelines in Oncology⁽⁸⁾: Prostate Cancer states:

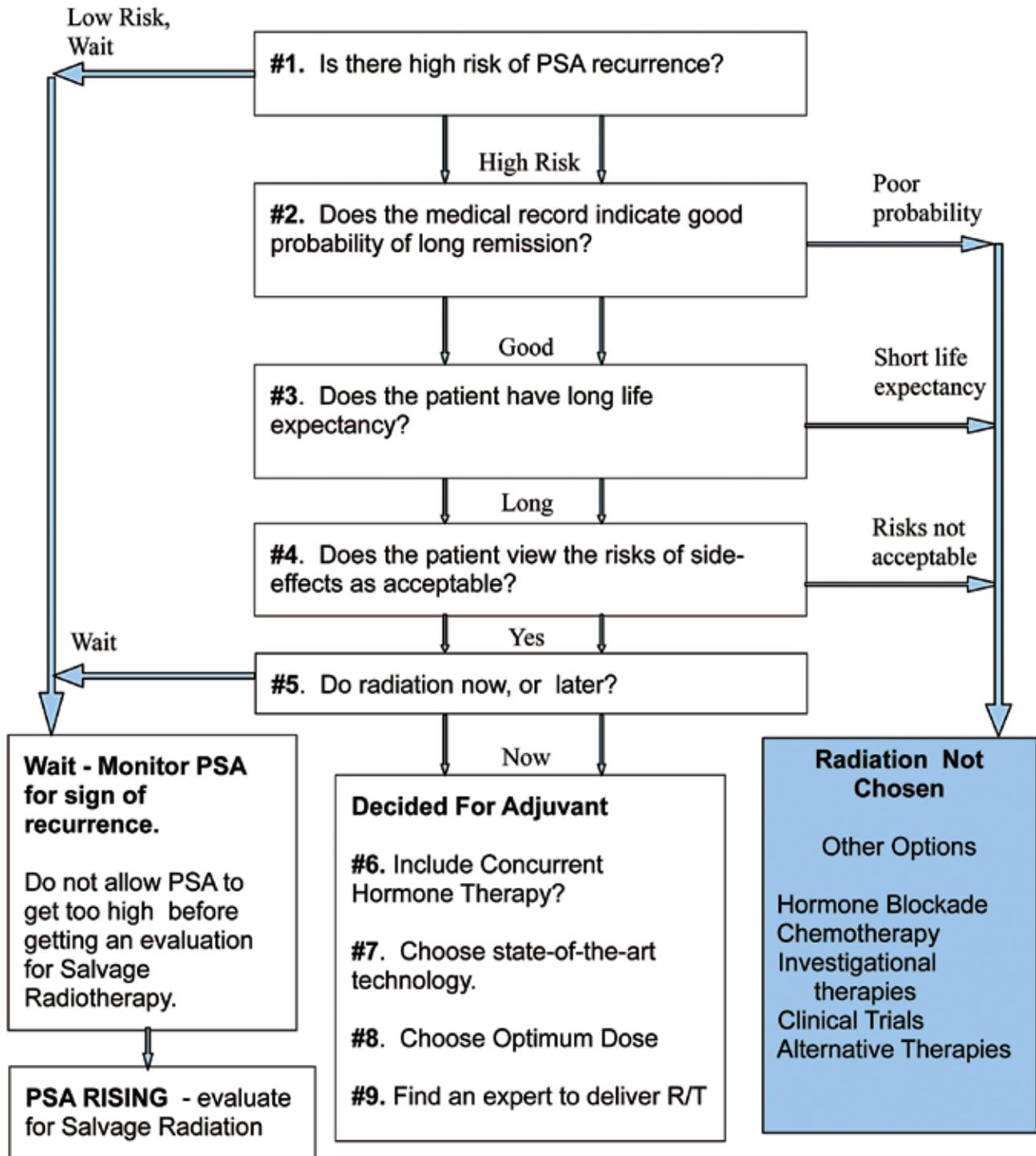
“New evidence supports offering adjuvant/salvage RT in all men with adverse pathologic features or detectable PSA”

Download free: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp

IMMEDIATELY AFTER PROSTATECTOMY, A MAN HAS THREE CHOICES TO MAKE		
SALVAGE RADIOTHERAPY	ADJUVANT RADIOTHERAPY	NO RADIOTHERAPY
<p><i>Salvage (delayed) Radiation</i> is performed at a later time, usually after PSA rises above a minimum threshold, traditionally 0.2 ng/ml. This option may be best when:</p> <ul style="list-style-type: none"> • There is low risk of recurrence • The fear of side-effects from radiation outweigh the concern that delaying radiation could lead to shorter survival • Short life expectancy. 	<p><i>Adjuvant (early) Radiation</i> is performed as soon as the surgery wounds heal, usually about 90 days after surgery when:</p> <ul style="list-style-type: none"> • Pathology indicates high risk of recurrence • PSA low but not undetectable • Medical records indicate a good chance of long remission with radiation • The risk to quality of life is acceptable • PSA is undetectable but the man wants to avoid the risk the cancer progression due to waiting for PSA rise. 	<p>Choose no radiation when;</p> <ul style="list-style-type: none"> • High PSA post surgery, or other factors indicate likely occult, (hidden) distant metastasis • Side-effects risk outweighs the potential benefits • Older or poor health • Slow PSA doubling time • Prefer the risks of side effects from hormone therapy to the risks from radiation.

The goal of this article is to help men understand the trade-offs and to make informed choices. A nine-step decision tree is presented to guide men through the process.

NINE DECISIONS BEFORE DOING EARLY, ADJUVANT RADIATION THERAPY AFTER PROSTATECTOMY



(Continued on page 12)

Understand Your Risk Factors – You cannot make good, informed choices about potential prostate cancer therapy without first understanding your risk factors. And the risk factors cannot be understood without first collecting, reading, and understanding copies of your medical records. Ask your doctor, or contact help@pcri.org if you need assistance understanding your medical record.

COLLECT COPIES OF ALL MEDICAL RECORDS

- PSA History - Make a log with dates of all your PSA tests.
- Surgical Pathology Report that identifies risk factors such as Positive Margin, Extra-Prostatic Extension, Seminal Vesicle Involvement and High Gleason Score.
- Surgeon’s Surgery Report – Describes the operation in detail.
- Written Radiology Report - Describes risk factors and findings.
- Digital Copies of Scans. - Future radiologists will want to compare any new scans with old scans.

DECISION #1 – IS THERE RISK OF RECURRENCE?

First, if there is low risk of recurrence, no radiation is indicated at this time. Salvage is still available if PSA rises.

Immediately after surgery, the prostate and possibly other tissues such as lymph nodes are sent to the pathologist for evaluation. Figure 4 is a Kaplan-Meier plot that illustrates how relapse rates go up when the cancer is more advanced. To understand the plot, 100% are free of progression at time zero. 85% of LN+ men relapse by ten years.

PROGRESSION FREE SURVIVAL

Organ Confined (OC) – no cancer was found outside the prostate capsule.

Extra Prostatic Extension (EPE or ECE) – Tumor cells were found in the tissue outside the prostate.

Positive Surgical Margins (SM or PM) – there are live cancer cells at the inked margin of the removed prostate.

Seminal Vesicle Invasion (SVI) – The cancer was found in one or both of the seminal vesicles.

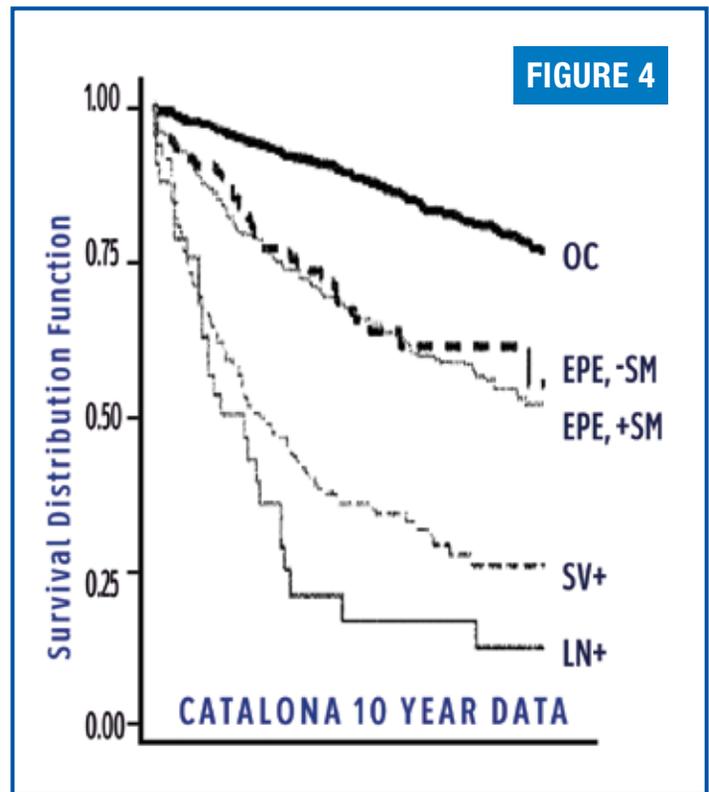
Lymph Node(s) Positive (LN+) - The cancer has invaded the lymphatic system.

Other risk factors for recurrence include:

High Gleason Score, 8, 9, 10 The surgical pathology Gleason Score is often higher than the biopsy because more tissue is available for inspection.

PSA Detectable with ultra-sensitive test 45 days after surgery means there may be cancer left at surgery.

High PSA prior to surgery



The Han Table uses the at-surgery PSA, surgical Gleason Score, and pathological stage to predict the likelihood of recurrence after prostatectomy. Fill in the Han Table at the Johns Hopkins Hospital web site <http://urology.jhu.edu/prostate/hanTables.php>

DECISION #2 – DOES THE MEDICAL RECORD INDICATE GOOD PROBABILITY OF LONG REMISSION WITH ADJUVANT RADIATION?

To make this decision, you need to understand the concept of a Micrometastasis. Prostate cancer cells can break off and ‘leak’ into the lymphatic or blood system and circulate around the body. This can happen relatively early in the disease, and is much more likely to happen when the man has high Gleason Score 8, 9, or 10. It is believed most of these circulating cells die, but sometimes they become lodged in a lymph node, a bone, or somewhere else, and begin to multiply. That is called a micro-metastasis, and it is the mechanism that, years later, eventually leads to prostate cancer progression.

TIP: A man with distant micrometastasis will not be cured by radiation therapy after prostatectomy. Use clues from the medical record to fill in nomograms to estimate if a long remission might be possible.

Micrometastases are too small to be detected with bone or CT scan. We have to depend on PSA and on the clues from the medical record risk factors to estimate if radiation therapy after prostatectomy is worth the side-effects risk. If radiation is unlikely to result in a long remission, perhaps it would be better to evaluate other options such as hormone blockade or investigational therapies.

Indications that reduce the chance of long remission from Adjuvant radiation include:

- **No Positive Surgical Margin – Stephenson data showed that men who did not have a positive margin were less likely to have long remissions from radiation.**
- **PSA Never Goes Undetectable within 45 days after prostatectomy – PSA may be coming from a distant micrometastasis that cannot be killed with radiation.**
- **PSA Rising Quickly, A Short Doubling Time – Ironically, the men with a fast doubling time are less likely to have long remission. However, because their disease is potentially more life-threatening, when the radiation treatment is successful, their survival is improved.**

- **Gleason Score Of 8, 9, or 10 – High Gleason Score cancers are more likely to be associated with micrometastasis**
- **Seminal Vesicle Involvement** is more likely to associated with micro metastasis
- **PSA Has Risen Too High** before radiation.

DECISION #3 – DOES THE PATIENT HAVE LONG LIFE EXPECTANCY?

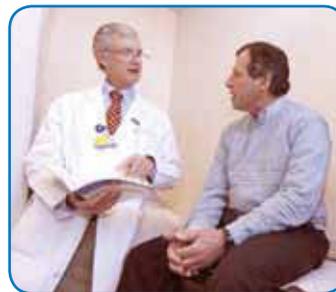
Prostate cancer is often slow growing and may require more than ten years to severely affect quality of life. An older man with health issues such as heart disease may prefer to avoid radiation. This would be especially true for men with lower risk such as Gleason 3+4 disease, or longer PSA doubling times. If the cancer later becomes a problem, hormone deprivation therapy is always an option.

DECISION #4 – DOES THE PATIENT VIEW THE RISK OF SIDE-EFFECTS AS UNACCEPTABLE?

Modern radiation has become far less dangerous. However, as noted above, impotence, incontinence and radiation proctitis can still occur. Since quality of life is such an important consideration, only the patient himself can decide if the risks are acceptable.

DECISION #5 – EVEN THOUGH RADIATION THERAPY IS CHOSEN – DO IT NOW OR LATER?

Some studies like that of Thompson have shown that men who get adjuvant radiation have a lower risk of metastasis and are less likely to undergo hormone therapy. But, in many of those studies, men who got salvage radiotherapy waited until PSA was relatively high. The latest research seems to show that starting **salvage radiation early, before the PSA rises above a low threshold, appears to have about the same long term rate of remission. As early as 2002, Slawin⁽⁹⁾ pointed out that there was no apparent difference in outcome between adjuvant and salvage radiotherapy, as long as salvage was initiated early and there was adequate** (Continued on page 14)



radiation dose. Nielsen⁽⁶⁾ said, referring to trials comparing adjuvant with salvage radiation,

“Since these trials were designed, experts have come to understand that the results of salvage RT are very sensitive to the timing of therapy, with the greatest benefit seen in patients initiating salvage RT at early PSA rise after surgery. In the context of this evolving understanding of salvage RT, the trials do not show that adjuvant RT is superior when delivered in accordance with the best-available evidence.”

Delaying radiation until PSA rises to 2 ng/ml, or waiting 2 years after PSA first rises, greatly reduces the chance of a long remission⁽⁵⁾.

The big advantage of waiting for PSA to rise to a low threshold and then initiate salvage radiation, is that many men will avoid ever having any radiation because they are destined to never have PSA rise. They avoid the lost time, high cost, and treatment-related side-effects of *adjuvant radiation*.

DECISION #6 – ADJUVANT RADIATION THERAPY IS DECIDED – SHOULD HORMONE THERAPY BE INCLUDED?

No large, randomized clinical trials have examined adding hormone therapy, also called Androgen Deprivation Therapy, to adjuvant or salvage radiation. Choo⁽⁷⁾ reported on several small studies that showed benefit, including his own about 75 men who were treated with two years ADT after salvage radiation. After median follow-up of 6.4 years, freedom from PSA relapse was 91.5% at 5 years and 78.6% at 7 years. That is one of the highest success rates reported.

DECISION #7 – CHOOSE A PROVIDER WITH STATE-OF-THE-ART EQUIPMENT

The latest technology allows precise aiming of radiation beams at the prostate bed treatment area, while minimizing dose to the bladder and rectum in order to minimize side-effects. The latest technology is - IMRT which stands for Intensity Modulated Radiation Therapy,

Newer technology such as Cyberknife and Proton Beam radiotherapy are being evaluated. Less clinical data is available to evaluate the safety and efficacy of these techniques. There are clinical trials recruiting for Cyberknife⁽¹⁰⁾ and for Proton Beam⁽¹¹⁾.

DECISION #8 – CHOOSE THE RADIATION DOSE

The 1999 American Society for Therapeutic Radiology and Oncology guidelines recommend a dose of 64 gray or slightly higher.

Higher dose has been shown to improve outcome. The trade off is increased risk of side-effects vs. improving the chance of long remission. It appears the dose response curve is not linear⁽¹²⁾, meaning increasing dose by 1% may result in better than 1% improved remission. Modern technology and techniques provide the opportunity to increase the dose in/around the prostate bed while minimizing dose to sensitive tissue such as the bowel.

King and Spiotto⁽¹³⁾ compared the outcomes of 38 patients treated with 60 Gy to the outcomes of 84 patients treated with 70 Gy. They found a significantly higher 5-year biochemical control rate of 25% to 58% with the higher dose of 70 Gy.

An important consideration for discussion with the radiologist is whether or not to include whole pelvis radiation. For men at high risk of progression, modern equipment and treatment planning allow radiation of the pelvic lymph nodes with far greater safety compared to older radiation technology.



DECISION #9 – FIND AN EXPERT DOCTOR TO ADMINISTER RADIATION

Planning the treatment and executing the therapy is complex. Find a radiation oncologist who continues to research and learn the latest techniques and who ideally has experience doing hundreds of adjuvant/salvage prostate radiation procedures.

SALVAGE RADIATION DECISIONS

The salvage decisions are almost the same as the adjuvant except the man has confirmed rising PSA above a threshold, and time has passed since the man evaluated the adjuvant decision. Stephenson demonstrated that starting radiation at low PSA is more effective.

Stephenson Salvage Data – Better Survival Starting With Lower PSA – 6 year data				
PSA at start of radiation	<= 0.5 ng/ml	.51 to 1.0 ng/ml	1.01 to 1.50 ng/ml	>1.51 ng/ml
Percent progression free	48%	40%	28%	18%

The Stephenson nomogram is printed in the referenced paper, or you can go to the Memorial Sloan Kettering Cancer Center web site to fill in an electronic nomogram to estimate your risk. <http://www.mskcc.org/mskcc/html/10088.cfm>

After evaluation with the Stephenson nomogram, proceed to adjuvant decisions #2, #3, #4, #6, #7, #8, and #9.

Conclusions:

Quality of life issues are the paramount concern. The risk of side-effects has declined substantially with better technology.

A surprising result of the latest research is men at high risk may be the ones most likely to have survival benefit. Besides survival, an important quality of life benefit for men in remission is avoiding of additional therapy such as androgen deprivation therapy. While many men experience some urinary, potency, and bowel side effects, most do not report excessive long term problems.

Because of the many, subtle considerations, men are encouraged to develop an expert medical team that might include a medical oncologist, who specializes in prostate cancer, for an overall view including the role of hormone therapy, a radiation oncologist with access to the latest equipment, and a urologist who can advise about dealing with side-effects.

By carefully evaluating the risks of side-effects and weighing them against the chances of long remission, a man can make a well-informed choice whether or not to proceed to adjuvant or salvage radiation therapy after prostatectomy.

Table 1. Radiation Side Effects By Grade

Note that while many men get Grade 1 or Grade 2 side-effects, they often subside with time. Few men get Grade 3 side-effects, but those affect quality of life. Very few men get Grade 4 side-effects, but they can be life threatening. [Source: http://www.rtog.org/members/protocols/0232/a4.html](http://www.rtog.org/members/protocols/0232/a4.html) (Continued on page 16)

TABLE 1. ADJUVANT RADIATION SIDE EFFECTS BY GRADE				
SOURCE	GRADE 1	GRADE 2	GRADE 3	GRADE 4
GENITO-URINARY	Frequency of urination or nocturia twice pretreatment habit/ dysuria, urgency not requiring medication	Frequency of urination or nocturia which is less frequent than every hour. Dysuria, urgency, bladder spasm requiring local anesthetic (e.g., Pyridium)	Frequency with urgency and nocturia hourly or more frequently/ dysuria, pelvis pain or bladder spasm requiring regular, frequent narcotic/gross hematuria with/ without clot passage	Hematuria requiring transfusion/ acute bladder obstruction not secondary to clot passage, ulceration or necrosis
SMALL/LARGE INTESTINE	Mild diarrhea; Mild cramping; Bowel movement 5 times daily Slight rectal discharge or bleeding	Moderate diarrhea and colic; Bowel movement >5 times daily; Excessive rectal mucus or intermittent bleeding	Obstruction or bleeding, requiring surgery	Necrosis/Perforation Fistula

* Nocturia means having to get up at night to empty bladder. * Dysuria means painful urination * bladder spasm is very painful and prolonged cramping of the bladder muscles * Hematuria is passing blood in the urine that in extreme cases can cause blockage due to clots or anemia due to lost blood * necrosis is dead tissue * Perforation fistula means a hole develops due to dead or weakened tissue, for example between the the rectum and bowel cavity.
 There is a slight risk (1/200) the radiation will cause other cancer to the bladder or colon at some later date^(14,15).

RESOURCES

1. [CANCER PROGRESSION AND SURVIVAL RATES FOLLOWING ANATOMICAL RADICAL RETROPUBIC PROSTATECTOMY IN 3,478 CONSECUTIVE PATIENTS: LONG-TERM RESULTS](#)
KIMBERLY A. ROEHL, MISOP HAN, CHRISTIAN G. RAMOS, JO ANN V. ANTENOR AND WILLIAM J. CATALONA THE JOURNAL OF UROLOGY® 0022-5347/04/1723-0910/0 Vol. 172, 910–914, September 2004
2. Stephenson - [Predicting the outcome of salvage radiation therapy for recurrent prostate cancer after radical prostatectomy.](#)
Stephenson AJ, Scardino PT, Kattan MW, Pisansky TM, Slawin KM, Klein EA, Anscher MS, Michalski JM, Sandler HM, Lin DW, Forman JD, Zelefsky MJ, Kestin LL, Roehrborn CG, Catton CN, DeWeese TL, Liauw SL, Valicenti RK, Kuban DA, Pollack A.
3. J Clin Oncol. 2007 May 20;25(15):2035-41. Erratum in: J Clin Oncol. 2007 Sep 10;25(26):4153.
Catalona - [SALVAGE RADIATION THERAPY FOR PROSTATE SPECIFIC ANTIGEN PROGRESSION FOLLOWING RADICAL PROSTATECTOMY: 10-YEAR OUTCOME ESTIMATES](#)
JOSEPH F. PAZONA, MISOP HAN, SHEILA A. HAWKINS, KIMBERLY A. ROEHL, WILLIAM J. CATALONA The Journal of Urology October 2005 (Vol. 174, Issue 4, Part 1, Pages 1282-1286)
4. Thompson IM - [Adjuvant radiotherapy for pathological T3N0M0 prostate cancer significantly reduces risk of metastases and improves survival: long-term followup of a randomized clinical trial.](#)
Thompson IM, Tangen CM, Paradelo J, Lucia MS, Miller G, Troyer D, Messing E, Forman J, Chin J, Swanson G, Canby-Hagino E, Crawford ED. J Urol. 2009 Mar;181(3):956-62. Epub 2009 Jan 23.
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Trock BJ, Han M, Freedland SJ, Humphreys EB, DeWeese TL, Partin AW, Walsh PC. JAMA. 2008 Jun 18;299(23):2760-9.
6. Nielsen - [Salvage or Adjuvant Radiation Therapy: Counseling Patients on the Benefits](#)
Matthew E. Nielsen, MD;a Bruce J. Trock, PhD;b and Patrick C. Walsh, MD
Journal of the National Comprehensive Cancer Network | Volume 8 Number 2 | February 2010
7. Choo, Richard - **Salvage Radiotherapy for Patients with PSA Relapse Following Radical Prostatectomy: Issues and Challenges** - Department of Radiation Oncology, Mayo Clinic, Rochester, MN, USA Cancer Res Treat. 2010;42(1):1-11 DOI 10.4143/crt.2010.42.1.1 <http://cancerresearchandtreatment.org/Synapse/Data/PDFData/0036CRT/crt-42-1.pdf>
8. Mohler J, Amling CL, Bahnson RR, et al. NCCN clinical practice guidelines in oncology: prostate cancer. Version 2, 2009. Available at: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.
9. Slawin - [Radiation Therapy After Radical Prostatectomy: Why Patience Is a Virtue! The Case for Salvage Radiation Therapy](#) Kevin M Slawin, MD Scott Department of Urology and The Baylor Prostate Center, Baylor College of Medicine, Houston, TX Rev Urol. 2002 Spring; 4(2): 90–94. PMID: PMC1475979

10. CyberKnife Radiosurgery for Locally Recurrent Prostate CA
 Verified by CyberKnife Centers of San Diego, February 2009
 First Received: February 25, 2009 Last Updated: February 26, 2009 [History of Changes](#)

Sponsor:	CyberKnife Centers of San Diego
Information provided by:	CyberKnife Centers of San Diego
ClinicalTrials.gov Identifier:	NCT00851916

11. (Proton) Postoperative or Salvage Radiotherapy (RT) for Node Negative Prostate Cancer Following Radical Prostatectomy (PR06)
 Verified by University of Florida, October 2009
 First Received: August 28, 2009 Last Updated: October 29, 2009 [History of Changes](#)

Sponsor:	University of Florida
Information provided by:	University of Florida
ClinicalTrials.gov Identifier:	NCT00969111

12. King CR, Kapp DS. Radiotherapy after prostatectomy: is the evidence for dose escalation out there? Department of Radiation Oncology, Stanford University School of Medicine, Stanford, CA 94305, USA. crking@stanford.edu [Int J Radiat Oncol Biol Phys.](#) 2008 Jun 1;71(2):346-50. Epub 2008 Jan 30.
13. [King CR](#), [Spiotto MT](#). Improved outcomes with higher doses for salvage radiotherapy after prostatectomy. Department of Radiation Oncology, Division of Urologic Oncology, Stanford University School of Medicine, Stanford, CA 94305, USA. crking@stanford.edu [Int J Radiat Oncol Biol Phys.](#) 2008 May 1;71(1):23-7. Epub 2008 Jan 22.
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15. Brenner DJ, Curtis RE, Hall EJ, et al. Second malignancies in prostate carcinoma patients after radiotherapy compared with surgery. *Cancer* 2000;88:398–406.



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- What questions do you have?

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