

Therapy of Prostate Cancer

Read the various pamphlets, in particular "[Treatment Choices for Men with Early Stage Prostate Cancer](#)" (NCI). Below is some additional information about the various treatments of prostate cancer, and also about the variables that indicate its seriousness, in particular staging, PSA, and Gleason Score. Underlined words in the electronic version link to abstracts and articles.

Prelude

1. One learns, from '[Cancer Facts and Figures 2007](#)' of the American Cancer Society that the estimated *new cases* and the estimated *deaths* in 2007 are 37,170 and 33,370 for pancreatic cancer, 213,380 and 160,390 for lung cancer, and 218,890 and 27,050 for prostate cancer, respectively. Look at those numbers, look at them again, and recognize that not all cancers are the same. The odds of dieing from prostate cancer are about one of eight for the *average* patient: much better than that for most patients but worse for those with adverse staging (T3/T4), PSA (>20), or Gleason Score (≥ 8).

2. The urologist used his or her finger to '**stage**' your cancer as follows: **T1**: cancer not felt with DRE: Digital Rectal Examination; **T2**: cancer felt with DRE, but still confined to the prostate, and **T3 & T4**: cancer is felt to be outside the prostate. Expect your urologist prescribing a **bone scan** if you have a T3 or T4 cancer, or a high PSA (larger than 10), or if your PSA is less than 10 but your GS is 8 or more. A bone scan may show whether the cancer has escaped the prostate and is in the bones (typically the back bone or the ribs): **metastatic prostate cancer**.

3. A **2nd opinion** of the Gleason score is advisable — insurance or Medicare will usually cover the cost— for all men diagnosed with prostate cancer but in particular for those with a GS of 7 or less. It will be based on the re-examination of the biopsy cores by an *expert pathologist* specialized in prostate cancer. Pathologists for a 2nd opinion include David [Bostwick](#) (VA) [800] 214-6628; Jon [Epstein](#) (Hopkins) [410] 955-5043 or 410-955-2162, and Jon [Oppenheimer](#) (TN) [888] 868-7522)

4. Is it necessary to **make a decision quickly** – within weeks? Additional PSAs may help to determine your sense of urgency. A rapidly increasing PSA –e.g., in one month from 4.5 to 4.8 or from 11.0 to 12.0-- is worrisome, as is a high Gleason (8 or more). However, several [studies](#) * [*](#) found that it doesn't make a difference, for *men with a PSA less than 10 and a GS (Gleason score) of 6*, whether they **wait up to one year** before making a decision what to do.

*A man diagnosed with prostate cancer may consider **local therapy** (treating the cancer in the prostate) such as radical prostatectomy (RP) or brachytherapy (brachy or 'seeds'), **active surveillance** (also known as **watchful waiting, WW**), or **hormonal therapy** (androgen deprivation therapy or ADT). About all men diagnosed with prostate cancer take medications (either prescribed or **OTC**: over the counter) that belong to the realm of **alternative or complimentary therapy**.*

The members of PCNG encourage newly diagnosed men to inform themselves about all options. A choice is also a reflection of the personality of the patient, and this explains why two patients with the same diagnosis might choose different therapies.

5. **Local or Radical) Therapies** –Newly diagnosed patients quickly discover that there is not a single therapy for prostate cancer considered optimal by *all* physicians. They have their favorites! Radical Prostatectomy (**RP**) is preferred by urologists, and External Beam Radiation Therapy (**EBRT**) or Brachytherapy (**BT, brachy or 'seeds'**) by radiation therapists. Local therapy is an attractive solution: one gets rid of the cancer and most men will be 'cured'. But the question should be asked, as the odds of dieing of prostate cancer are relatively slim, "*Was this local therapy necessary?*" The answer is "*We don't know*". We don't know because large clinical trials have not yet been done. A small trial* comparing RP with WW indicated that prostate cancer mortality for those with a Gleason Score of 8-10 was less for men

with RP than for men on WW. However, *all men with a GS 6 had the same life expectancy, irrespective whether they had RP or WW*. A statistical study* of men diagnosed with prostate cancer does not support aggressive treatment of localized low-grade cancer. Men on WW would have less impotence and incontinence than men who had local therapy, but they would carry the considerable psychological burden that their cancer is still in them.

6. **Local Therapy and Health Related Quality of Life (HRQOL)** The following are [quotations](#) from an article on HRQOL after RP, EBRT or BT: "**HRQOL...does not differ based on therapy choice...**; BT and EBRT patients alike endured a significant decline in urinary incontinence HRQOL during the 4-year interval between our initial (2.6 years after therapy) and current assessments (6.2 years after therapy);... overall sexual HRQOL deteriorated for the EBRT cohort; ... bowel dysfunction, including diarrhea, painful bowel movements, and rectal bleeding, significantly more prevalent after radiation therapy (BT or EBRT) versus radical prostatectomy, improved between initial and current assessments;... sexual HRQOL for the RP and BT cohorts did not change, but declined in the EBRT cohort;... disease-specific HRQOL remains generally stable between 2 and 6 years of follow-up after RP".

7. **Recurrence after Local Therapy**. In a cohort of 2091 men, all operated by Dr. Walsh at Johns Hopkins University, 16% had recurrence after 5 years, 28% after 10 years, and [39% after 15 years](#). The recurrence percentages after BT or EBRT appear similar to those after RP, but only in men with similar age, PSA, and Gleason score. Radiation ("salvage" EBRT) or hormonal therapy (or a combination of the two) is given after recurrence if the PSA is increasing rapidly (*i.e.*, if the **PSADT** -PSA Doubling Time- is short). Young men (<50 years) have [less recurrence](#) after RP than older men.

8. **Watchful Waiting (WW), Active Surveillance (AS), Deferred Treatment** "[Good risk prostate cancer](#): patients with a Gleason score of 6 or less, PSA <10–15, and T1c–T2a, now constitutes 50% of newly diagnosed prostate cancer. For most of these patients, the disease is indolent and slow growing. There is substantial evidence that it does not pose a threat during the lifetime of most patients. The challenge is to identify those patients who are not likely to experience significant progression while offering radical therapy to those who are at risk". "Many men are found to have minuscule amounts of cancer—smaller than 0.2 cubic centimeters, about the size of a pinpoint, 10% or less of the biopsy cores—, captured by sheer chance".

For a man in his forties or fifties, a very small tumor might be significant, but in men who are in their sixties or older, **Watchful Waiting, Expectant Management** (term used at Hopkins Univ.) or **Active Surveillance** may well be a rational approach. Instead of treatment '**Observation**' is chosen. [Criteria](#) include a Stage **T1c** cancer (cancer detected because of an elevated PSA); free PSA > 15%; Gleason score 6 or lower; cancer in only 1 or 2 cores, and in less than 50% of each core. Patients in observation can be actively involved in battling their cancer. They eat less fat, more vegetables, and more fruit and fish They take over the counter medications such as vitamin E, lycopene, and selenium. They lose weight and have their PSA monitored regularly.

9. **WW or AS** is not necessarily permanent. For example, local therapy may be advised when the PSA begins to increase rapidly. The rate of increase is expressed as the **PSA doubling time (PSADT)**.. In a [study](#) with 231 patients on active surveillance the median PSADT was 7 years. When the PSADT became less than 3 years the men were advised to have local therapy. *WW or AS led to **Deferred Treatment**.*

10. Androgen Deprivation Therapy (ADT) is for patients diagnosed with a **positive bone scan**, *i.e.*, the cancer has spread into the bone, and for men who had a **recurrence** of the cancer after local therapy, but only for those with a rapidly increasing PSA, *i.e.*, a short PSADT. ADT is also used as an **adjuvant therapy** (in addition to a local therapy such as RP or brachy) for those with **high-risk prostate cancer**: T3 or T4, Gleason scores of 8-10, a PSA >20, or a cancer that has spread to the lymph nodes. Other men choose ADT because they are not willing to undergo a local treatment, or because they want to delay local therapy, in particular radiation therapy. This choice has become more popular since the introduction of **Intermittent ADT (IADT)**: periods with therapy are followed by periods without LHRH and/or AA, but often with [Avodart](#) or [Proscar](#). The major advantage of IADT is that the negative effects of ADT are [reversible](#). IADT may be [effective](#) in men with a GS of 6.

11. ADT is also known as **Hormonal Therapy**. Prostate cancer needs, at least initially, testosterone (an androgen) to grow. The cancer can be deprived from the androgen by

a) *stopping production of testosterone* with a **LHRH** medicine (Zoladex or Lupron) or by **estrogen patches**. LHRH weakens the skeleton's bones (**osteoporosis**) and medications against bone loss are necessary: calcium + Vitamin D, and a **bisphosphonate** such as Fosamax or Actonel. Estrogen patches are less expensive than LHRH and do not cause [bone loss](#). They also protect against the risk of [thrombosis](#).

b) *blocking the action of testosterone* with anti-androgen (AA) medications: **Eulexin**, **Casodex** or **Nilandron**. An AA protein, similar to testosterone, fits in the androgen receptor (**AR**), the messenger between a testosterone molecule and the cancer cell. The AA protein is sufficiently different from testosterone that no instructions from the AR will be forwarded to the cancer cell, or

c) *removing the source of the testosterone* with an **Orchiectomy** (removal of the testicles). This is inexpensive as compared with LHRH or AA medicines, but not easily accepted psychologically. a) & b) can be combined, and is then known as **ADT2**. The term **ADT3** is used when the production of another androgen (dihydrotestosterone or DHT) is blocked with either Proscar or Avodart.

12. ADT and Health Related Quality of Life (HRQOL). ADT can cause hot flashes, loss of libido, loss of potency, bone loss (osteoporosis), and increase of breasts (gynaecomastia). ADT is a last choice for surgeons and radiation oncologists but a major therapy for oncologists and a patient may have to visit an oncologist to learn more about this therapy. ADT's side effects are treatable except loss of libido and impotency which are, however, temporary with intermittent ADT.

13. 2nd-line hormonal therapy & chemotherapy. In many men hormonal therapy will last 'forever'; in other men

the prostate cancer becomes sensitive to very small amounts of testosterone or learns to grow without androgens: **androgen independent prostate cancer** or **AIPC**. **2nd-line hormonal therapy** or [secondary hormonal therapy](#) introduces various hormonal manipulations, including withdrawal of an anti-androgen (AA) medication such as Casodex: the PSA goes down in some patients after the AA has been withdrawn. Medicines that were not yet used can also be given, including ketoconazole (Nizoral), aminoglutethimide (Cytadren), nilutamide (Nilandron) or estrogen patches. The PSA might stay down for many months or even years. If the PSA starts rising again and can not be brought down, the prostate cancer has become '**hormone-refractory**'. **Chemotherapy** is the last solution but it will not extend life for more than a few months for most patients, although there will be exceptions as there are always with this disease. Chemo is also given as a **palliative** medicine, against pain. Docetaxel (Taxotere) is the most effective of the various chemotherapeutic agents, and it is even more successful when combined with [thalidomide](#), [calcitriol](#), [carboplatin](#), or an immunotherapeutic [vaccine](#).

14. Alternative or Complementary Therapy.

About all men diagnosed with prostate cancer take one or more of the various alternative medicines, and because this does not exclude an 'official therapy', the term **complementary therapy** is better than alternative therapy. Many patients in our support group take various over-the-counter (**OTC**) medicines, including vitamin E, lycopene, and selenium. Studies have shown that there was less prostate cancer in men taking [vitamin E](#) (in smokers; not necessarily in non-smokers); smaller cancers in those who took [lycopene](#)*, and [selenium](#) reduced prostate cancer incidence, but only in those who had a low selenium baseline. [Green tea](#) appears to prevent prostate cancer* and may be beneficial for those with the disease. [Soy](#) and [dietary supplements](#) can slow the PSA doubling time (PSADT). Other OTC medicines include **curcumin**, **quercetin**, and **EPA & DHA** (fish oil). Medicines normally not associated with prostate cancer include [calcitriol](#), **statin** drugs (e.g., Lipitor), and NSAIDs such as **Celebrex** and **Sulindac**. These drugs which must be prescribed by a physician have an impact on prostate cells *in vitro* (petri dish) and *in vivo* (rats and mice), but are without clinical trials demonstrating an effect on prostate cancer in men. They are taken because hope springs eternally.

15. Life style changes -in addition to medicines- such as dieting, exercise and stress reduction ([Ornish](#)) may improve the HRQL significantly in 12 months. Men diagnosed with prostate cancer die in about equal numbers of heart disease and prostate cancer, and life style changes do have an impact on heart mortality rates. If something won't help for prostate cancer, it may help for heart disease!

What to Do?

Men diagnosed with prostate cancer will have many questions: Local Therapy? Which local Therapy? Watchful Waiting (Aggressive Surveillance)? Deferred Local Therapy? Hormonal Therapy? What type of HT? Which physician? One could argue that the disease management strategy for men diagnosed with low-risk prostate cancer: T1c, PSA <10, and GS 6, can be on more solid grounds if the diagnosis is followed by at least a few months of WW, AS or DT (Watchful Waiting, etc.). These men can learn more about prostate cancer in that time period, and make better decisions.

PCNG encourages all newly diagnosed prostate cancer patients to become knowledgeable about their disease by learning the basics, asking questions, and finding answers by reading the literature, and using the Internet. They'll find themselves also more at ease in their communication with physicians.

Share your feelings with your partner, and come to the PCNG meetings – we won't give advice but share our experiences, and you can learn from that.. Stress and depression are common after diagnosis, but we think that selfempowerment through knowledge can be an excellent remedy. We wish you the best!

PCNG: Prostate Cancer Support Group of Greater Cincinnati. Meetings are at the Wellness Community, 4918 Cooper Road, Cincinnati (OH), the second and last Wednesday of each month.

See <http://www.pcngcincinnati.org/> for more information, including an electronic version of this document, with clickable links.

2/16/2007 - comments: kees.dejong@uc.edu