Report from the Annual Meeting of Radiation Therapists

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Last September, thousands of radiation therapists attended ASTRO, the annual radiation therapy conference. Thousands of scientific studies were presented. Several hundred were on the topic of prostate cancer. After sifting through every abstract about prostate cancer, I judged six to be important enough for comment in this month's issue of Insights: Three are about radiation, two about hormones and one about PSA doubling time.

One of the most compelling scientific reports came from a well-known center of excellence. They used state-of-the-art radiation techniques, and studied a large number of patients. In ***abstract #311***, Dr. Zelefsky from Memorial Sloan Kettering reported the cure rates with very high dose IMRT (86 Gy) compared to the cure rates achieved with IMRT *combined* with a seed implant boost. The study group consisted of 870 men with *Intermediate-Risk* prostate cancer (TEAL). Fifty percent of the group treated with IMRT alone got hormones while only 30% of the IMRT plus seeds group got hormones. The cure rate at seven years was 81% in the men treated with high-dose IMRT and 92% in the men treated with IMRT plus a seed implant boost. There was no difference in late term side effects.

Comment: This is an important report. Despite using the finest, most state-of-the-art IMRT, cure rates for men with *Intermediate-Risk* prostate cancer treated with IMRT alone were clearly inferior to what can be achieved when IMRT is coupled to a seed implant boost.

Another study addresses one of the biggest issues men with newly-diagnosed prostate cancer face, especially younger men—losing sexual potency. However, there are relatively few reports describing the frequency and severity of this problem. In ***abstract #2497*** Dr. Shasha from Beth Israel Medical Center in New York reported the incidence of sexual function being preserved in 68 healthy, nonsmoking, sexually potent men under the age of 60 (median age 56) who were treated with radiation. Prior to radiation none of the men were using Viagra, Cialis or Levitra. Three years after radiation 90% of the men remained potent. Only 10% required medication. An additional 10% use medication for potency enhancement.

Comment: According to this study, the rate of potency preservation in young men treated with radiation is clearly superior to what can be achieved with surgery.

The next study addressed the issue of doing radiation after surgery if the surgical margin is positive. A positive margin (tumor left behind) occurs between in 10% to 50% of the time after surgery. Postoperative radiation can reduce the incidence of future PSA relapse. However, studies have shown that about half of the men who have positive margins will remain cured with no radiation at all. Therefore, some experts have argued that radiation should only be administered to men if their PSA begins to rise, thus sparing half of the men from the potential side effects of radiation. The real question that needs to be answer is, "Will the men who delay radiation until the time of PSA relapse experience a higher rate of subsequent metastases?"

In ***abstract #261*** Dr. Nguyen from Dana-Farber Cancer Institute looked at the combined results of the three largest randomized prospective studies in combination. Over 1700 patients were evaluated. Dr. Nguyen found that there was a 13% higher incidence of metastasis in the men treated at the time of PSA relapse compared to the men who were treated right after surgery. However, because the 13% difference is relatively small, statisticians point out that there is a chance that this small difference is only the result of statistical variation.

Comment: In these studies the group of men treated after a PSA rise didn't get radiation until their lapse PSA was above 1 or 2! We know from other studies that the cure rate would have been much better if the radiation was started before the PSA rose above 0.5. Despite this, the metastases rate of the men who got delayed radiation was only 13% lower than the men who were treated right after surgery when their PSA was still undetectable. These studies strongly suggest that men with positive margins can consider waiting and monitoring closely. Radiation can be started at the first sign of a PSA relapse without facing a greater risk of future metastases.

The number one study of the whole conference addressed a perennial question that has been hanging in the air for years: How long do you continue hormones in men with *Intermediate-Risk* disease (TEAL) who are being treated with radiation?

Dr. Pisansky from the Mayo Clinic headed up a prospective randomized study of over 1500 men with Intermediate-Risk prostate cancer treated with radiation plus 4 months of hormone blockade (arm A) compared to radiation plus 8 months of hormone blockade (Arm B). Prostate cancer mortality after 10 years was 5% in Arm A compared to 4% in Arm B, a difference so small it could easily be due to statistical variation. Relapse rate was 24% in Arm A compared to 23% in Arm B.

Comment: The results of this study, along with the results of previous studies using even longer duration hormone therapy clearly show that maximum benefit from hormones is achieved by 4 months.
Another study addresses the following important question: Should you give hormone therapy at the same time as radiation in men with relapsing disease after surgery (INDIGO).

In ***abstract #1024*** Dr. Jackson from the University of Michigan reported on 680 men who had radiation after surgery along with variable amounts of hormone therapy. More than half received no hormone therapy at all. They found that mortality was 50% lower in men who were administered hormone therapy for 6 months. Mortality was 90% lower if the hormone therapy was continued for 2 years.

Comment: Relapsing prostate cancer after surgery is potentially aggressive. Logic would dictate that longer duration treatment with more effective hormone therapy should improve survival. This study strongly supports using longer-term hormone blockade in men being treated with radiation for relapsed disease.

The last study looked at the rate of PSA rise (PSA doubling time) after treatment and its effect on long-term survival. Previous reports have already determined that PSA doubling time is an important indicator of survival that is second only to the predictive power of PSA *nadir* after hormone therapy. ***Abstract #1016*** reported on the survival rates of men at Memorial Sloan-Kettering Cancer Center who were originally treated with IMRT.

Dr. Zelefsky evaluated the survival rates of 419 men who were relapsing. He and his collaborators looked at prostate cancer specific survival rates depending on whether the PSA doubling time was above or below 6 months. The seven year mortality rate for men with PSA doubling less than 6 months was 40% with a median time to mortality of 8 years. In the men whose doubling time was above 6 months, there was only a 10% risk of mortality and in those 10%, mortality occurred after a median of 16 years.

Comment: The outcome of men with relapsed disease (INDIGO) can vary greatly depending on the response to hormone therapy (PSA nadir) and the rate of PSA rise (PSA doubling time). This study well-illustrates the important differences between the various diseases we term "prostate cancer." □