CANADIAN PROSTATE CANCER SUPPORT GROUP

Newmarket, Ontario **Volume 12, Issue 8, April 15th, 2008**

**A support group that provides understanding,
hope and information to prostate cancer patients and their families**

Our speaker for the April 17th meeting is Dr. Durhane Wong-Rieger. She is President and CEO of the Institute for Optimizing Health Outcomes. She is also president of the Canadian Organization for Rare Disorders and founder and head of Consumer Advocare Network, a national network to provide a common voice for patient organizations. Internationally, she serves as a Board Member of the International Alliance of Patient Organizations. She is a licensed T-Trainer with the Stanford-based Living A Healthy Life with Chronic Conditions. Dr. Wong-Rieger has also served on numerous health policy advisory committees and panels, including Project Coordinator for the Policy Dialogues for the Romanow Commission on the Future of Healthcare in Canada and consultant to the Ontario Premier's Advisory Board on Organ Donation. As president of the Canadian Hemophilia Society, she advocated on behalf of consumers infected through Canada's tainted blood system. She was the consumer representative on the federal/provincial/territorial committee to establish an independent blood agency and was named to the Board of Directors as well as the National Blood Safety Council.

Meeting Date: **April 17th, 2008**

Place: **Newmarket Seniors Meeting Place**
474 Davis Drive, Newmarket

Time: **7:00 to 9:00 pm**

Speaker: **Durhane Wong-Rieger, PHD**

Subject: **Living A Healthy Life with Chronic Conditions.**

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a member of the

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Canadian Prostate Cancer Network

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The Newmarket Prostate Cancer Support Group does not recommend products, treatment modalities, medications, or physicians. All information is, however, freely shared.

March speaker notes Dr. Juanita Crook, Princess Margaret Hospital

Subject: "Brachytherapy and your Quality of Life"

Many of you who have been diagnosed with prostate cancer will remember that, when you were first diagnosed, it was very confusing because there were a lot of options to consider and you were trying to get yourself to understand all these things, all very rapidly. Sometimes watchful waiting or active surveillance is appropriate. So, you've found out that you have cancer but then they may be telling you that you don't need to do anything about it. That in itself is pretty confusing. Most people find out their diagnosis from a urologist, so probably one of the first options you hear about is surgery. Then there's radiation therapy. There's seeds, or brachytherapy, which is what we'll be focussing on mainly tonight. Cryotherapy, which means freezing the malignant tumour in order to get rid of it. Some men have hormones for all or part of their treatment, so when are those used? HIFU is the most recent treatment to be available to men in Canada. It stands for High Intensity Focussed Ultrasound, so should people be looking for that? Should they be offering to pay $20,000 in order to have it? And then in your health magazines you read about the effects of diet and vitamins and everything like that. And you're supposed to digest all this very rapidly and come to some sort of a decision about what to do about your prostate cancer. It's not easy.

What we're going to talk about is, first of all, to try to simplify things a bit by dividing prostate cancers into three basic groups called risk groups. All physicians, oncologists, urologists, everyone uses risk groups now in order to make decisions on what is best for whom and what the appropriate choices are. Then I'm going to present some long term results for Brachytherapy, because this has now been available since the late 1980s and we have published results for up to 15 years: how we select men for brachytherapy; what quality of life is like after brachytherapy; a little bit of how we do it because that's kind of neat and interesting; and then some frequently asked questions.

So risk groups tell us not only how we can expect someone to do, whether you've got a good tumour that you can take your time on or a bad tumour that's aggressive, which is going to be a more immediate threat to your life but also what tests need to be done in order to complete the work up and know what we're dealing with and how to approach the treatment. The risk groups for prostate cancer are: basically favourable, intermediate and high risk. They are based on three things which everybody has and everybody should know their values for: the T-stage, which stands for the stage of the tumour; the Gleason score, which is a number between two and ten, assigned to your biopsy by the pathologist when you are first diagnosed; and a PSA or blood test, which is usually the first thing that triggers the investigations and raises the alarm signals.

T-stage comes from T1 to T4. T1 means you can't see the tumour on ultra sound or feel it on the Digital Rectal Exam (DRE). T2 means there's a nodule, "A" is small, "B" is bigger. T3 means that the nodule is extending outside the prostate and T4 means that it's extending into other organs. So obviously T4 is one that's quite advanced. As I mentioned, Gleason scores go between two and 10. The lower numbers are less aggressive tumours, slower growing, less of an ability to spread, less of an immediate threat to your life and, as you move up the scale, they are more aggressive, faster growing and more of an ability to spread. So we consider any Gleason scores of six or under to be favourable, seven is intermediate and eight, nine and ten are the bad ones. The vast majority of the good cancers we see are Gleason 6. I can honestly say we never see Gleason 2, 3 or 4s, 5s are rare and so the vast majority of the good cancers are Gleason 6. PSA doesn't take too much explaining, that's just your blood test. So, for the favourable risk cancers, you're talking about either a tumour that you can't feel at all or is a small nodule, a Gleason of six or less and a PSA blood test of less than 10. For this group, you can take your time, you can explore your options. Sometimes no treatment is appropriate. You don't need a whole bunch of tests to see if it's gone elsewhere because that's not likely to have happened, so you don't need bone scans and CAT scans and stuff like that. The intermediate group, which is somewhere between favourable and bad, is a bigger nodule or a Gleason 7 or a PSA between 10 and 20. Any one of those features kicks you out of the favourable group and into the intermediate group. Finally, high risk is a T3, which is one that's extending outside of the prostate locally or the high aggressive Gleason scores between 8 and 10 or a PSA at diagnosis of over 20. So those are our basic three categories which help you to combine those three factors and simplify things so you know whether you've got something that's good or more serious. For all three of these groups, if you're treating with radiation, the amount of radiation you give, the dose, is very important.

There was some work from the Fox Chase Cancer Centre some years ago and what they found was that when they looked at men who got a dose lower than 74 Gy to over 74 Gy they found that for each of these groups, the favourable ones, the intermediate and the high risk, they all did better if they got the higher dose. There is more evidence that shows that dose is important. In a randomized trial by Allan Pollack at M D Anderson, done when we were finding out about dose in 2002, he randomly selected men to get either 70 Gy, or 78 Gy, and the ones that got the higher dose had a higher chance

of being cured by the radiation than the ones who got the lower dose. So that was really solid evidence that dose is important if you are going to have radiation. Well, how do we get this higher dose in? There's different ways of doing it and for the favourable prostate cancers, the best way of getting that dose in is brachytherapy or seed implant and I'll explain why. The dose that we generally give with brachytherapy is a very high dose. We were just talking about 74 Gy, 70 Gy, 78 Gy, the dose with brachytherapy is 145 Gy, it's almost double. If you have intermediate risk tumours, we can use a combination of external beam and a seed implant. We can use a type of external radiation, called IMRT or Intensity Modulated Radiation for which we usually give the 78 Gy, dose, which is the more effective one, or you can use external beam plus a different kind of brachytherapy, a temporary implant called HDR, or High Dose Rate brachytherapy, which is generally given as three separate applications of an intense shot with needles into the prostate. For the more aggressive tumours, you can either use IMRT to 78 Gy, or the IMRT plus the seeds. So we use different combinations of treatment in order to deliver that dose, to give people the best chance of cure.

Well, why do we have to use different kinds of treatment? Because, for favourable prostate cancer you don't need to cover very widely around the prostate. A margin around it of 2, 3, 4 millimeters is going to be plenty and the best way to do that is with the intensely focussed radiation of a seed implant. If you have an intermediate cancer, you may want to cover more widely around there. That 3 mm isn't going to be enough and you might need 7 or 10 mm to make sure that you've got any potential extra capsular, extra prostatic spread of the cancer and to that you'd either use external radiation alone, given as IMRT, or the combination of external and seeds. Because once you've put in the external radiation you can draw that margin out and get a better coverage around the prostate. For the high risk prostate cancers, we're now looking at the whole pelvic area as the treatment target as what's at risk for prostate cancer and what needs to be treated. The prostate itself is small but what we have to include is the lymph node drainage patterns, so you have to treat the whole pelvis as well as the prostate. So that's why different types of radiation are appropriate for the different risk groups.

So now, turning to the seeds. There are basically two types of radiation seeds that are used. Iodine 125 or Palladium 103. These are just two different isotopes. They're very similar. They both have very low energy, which is measured in Kilo electron volts. Remember from your physics in high school, kilo means 1,000 so this is 28,000 electron volts, whereas the photons that we use with external beam are measured in mega volts. So you're talking about millions of electron volts. So these are a low energy source of radiation and because of that there's very limited tissue penetration. It doesn't go very far. You put in a seed and it only treats a little bit around that seed. That's why we don't put in one or two or six seeds, we put in an average of 100, so that a conglomerate of seeds together will create an isodose shape that covers the prostate. This low energy allows us to give a very high intraprostatic dose because the energy doesn't go very far, so where you have a cluster of seeds, it's giving a very high dose but then it falls off very quickly so the dose to the adjacent organs is very low. Therefore the radiation damage to the adjacent organs is much less than with other forms of radiation treatment. There's some good evidence that this type of radiation using a seed implant, delivers the highest effective dose to the prostate, as well, even though it's such a gentle form of radiation that's going in so slowly over a six month period. The seed radiation will drop your PSA level lower. Barbi Pickett from UCLA did a study where she looked at medium PSAs with men treated with a seed implant and dropped to levels of 0.2, whereas with external beam the medium PSA was just slightly under one. So you're getting a lower PSA reading but what was more important is she looked at something called Magnetic Resonance Spectroscopy. This is like an MR scan but with fancy tweaking so that they can read the metabolic spectra of the metabolites within the cancer cells. She found that with external radiation only 20% of the prostates she examined showed this complete atrophy, where all the cancer cells were completely obleted by the treatment. Whereas, with the seeds, 86% of the prostates had this complete black metabolic atrophy, which is a good sign that the treatment is very effective.

So, what about some clinical outcomes for brachytherapy? There is a series reported by Lou Potters from New York of 12 year results. He actually reported on a series of about 1100 men but 480 of them had the favourable risk prostate cancer and at 12 years after treatment, 91% of them were free of any evidence of recurrence, by chemical standards, meaning using the PSA to show that they were free of cancer, 91% of them were. About a fifth of these men had some hormone therapy with the seed implant and only 2% had a combination with external radiation. But what Potters found when he did the analysis, was that adding hormones or external radiation didn't make any difference. They all did equally well and they showed disease free curves in both the favourable risk, the intermediate risk and the high risk patients, so brachytherapy was working well for all these. Another series from Peter Grimm in Seattle is really interesting because these 125 men were the first in the United States to be treated by a permanent seed implant. They received their brachytherapy back between 1988 and 1990. Not all of them were favourable risk, but the majority of them were and, with ten year follow-up, 81% of them had PSAs less than 0.2, which was an excellent result, especially considering that, in those days, they were just developing the technique. They weren't even sure how to do it properly but they had this idea of putting all these seeds into the prostate and it was a remarkably effective approach. Only 3% of the men had a recurrence in the prostate. Anyone who did have a failure was diagnosed in

the first eight years and beyond that there was no reoccurring. So the results up to ten years and longer are well maintained. These studies indicated that men who made it to six or seven years with no recurrence, were out of the woods. John Blascoe who is the grandfather of modern brachytherapy and who worked with Peter Grimm, showed that after 15 years for this same group of patients, 84% were cured of prostate cancer from these very early days of brachytherapy, with a median PSA of 0.1. Greg Merrick has reported on a slightly smaller group of about 650 men and reported 8 years of disease free for 98%. Why is this higher? Is he better? Well, no but this is more recent and the technique has improved. Between 1988 and 1995 people learned a lot about how to put seeds into a prostate properly and he's getting very good disease free rates with a median PSA rate in these men after treatment of less than 0.1. Again, like Lou Potters reported in the first paper, adding hormones and external radiation to this kind of treatment for the favourable prostate cancer did not improve results. It's working for all three groups but its better obviously for the favourable group. A paper from Michael Zelefsky for Sloane Kettering in New York reported seven year results for 1100 men that had both favourable and intermediate risk prostate cancer. 400 of them had brachytherapy and 700 had IMRT external radiation. Their PSA recurrence free rates at seven years were 98% for brachytherapy, 88% for IMRT. Both of these are very good although the brachytherapy had a little bit of an edge and again adding hormones didn't make any difference to either group. The brachytherapy patients had a little bit more bothersome urinary troubles afterwards, compared to the external radiation one.

Urologists sometimes worry that this is O.K. for older guys but young men really need surgery. Greg Merrick has reported on over 100 men who were all under age 55 when they chose to have brachytherapy and their 8 year disease free rates are 96%. So these young men are having just as good a result as the older men and the median PSA for those men who are free of any recurrence is 0.05. So, it's not something that's age specific and it's certainly something that younger men should also consider when they are trying to make up their mind about what to do for their prostate cancer.

What about quality of life post implant? After your treatment for prostate cancer, your quality of life is obviously extremely important and these are considerations. Men want to know that they are going to be able to carry on with their normal lifestyle after treatment and that life doesn't end after treatment for prostate cancer. The symptoms that men worry about are mainly urinary symptoms, sexual symptoms and bowel symptoms because these are the three things that are all crammed into that area around the prostate.

So we'll deal first with the urinary outcome after brachytherapy. When you use these seeds, especially the Iodine 125 seeds, the dose of radiation is given over a 6 month period, so you have to expect some urinary symptoms for three to six months while the prostate is under treatment. If you were coming into the hospital every day and lying under a big machine and having radiation, you'd kind of expect to feel some upset and irritation but when your implant was three months ago and you're still having to pee more often than usual, you start to wonder "Why is this happening?" Well, it's because you're still on treatment. 24 hours a day, 7 days a week, the seeds are still working. But, the quality of life for these guys is usually pretty much back to normal by about three months. We do symptoms scores which are a little more accurate reflection of what they are going through in terms of urinary symptoms and those are usually back towards baseline by six months and certainly by 12 months and we give medication to help the return of the function to normal. The risk of needing a catheter over all, if you look through various published papers, is generally about 15%, most men 85% won't need one at all. For a third of these men who do need a catheter, it's a trivial thing for maybe less than a week. For another third, it will be somewhere between a week and a month and for the other third it can be a longer term of over a month. We've become pretty good at figuring out who is likely to need a catheter and so the ones that are over a month I rarely see any more because we weed these out ahead of time and say that because of this, this and this I don't think you're going to be happy after the brachytherapy, so you should look at other options. About 1% of men will have a narrowing of the urethra that might need some dilatation. That's called a stricture. The symptoms scores that I mentioned are maintained out at five years and even eight years at pretty much the baseline.

Irritation in the rectum, which can be a big thing after external radiation, is seen in a mild form in 3% and moderate in less than 1%. Because the seeds are so focussed on the prostate and it doesn't have that tissue penetration to involve the rectum and things, you don't see a lot of complications with that. The symptoms score that I have alluded to a few times is called the International Prostate Symptoms Score, (IPSS) and it's just seven questions that ask you about your subjective of feeling of being empty after you've passed your urine; whether you have to pee after a two hour interval, whether the stream flows continuously or is interrupted, whether you have to push or strain to start it, weak stream, difficulty postponing and the number of times you're up at night. So you get a number out of 35 and that's something that we follow to make sure that you're progressing back to normal.

In terms of sexual function, the men that I have treated at Princess Margaret Hospital, about 85% of them were potent prior to having their procedure (about 16% were using some help from some medication but that's O.K.). One thing I warn people is that the amount of fluid in the ejaculate is going to be quite markedly reduced after radiation of the prostate, so 70% of men will notice that there is less fluid and occasionally it will be absent. Medication in what we call the PDE5 class, and that's the class of drugs that includes Viagra,

Cialis and Levitra is very helpful after treatment in preserving erections and in maintaining good erectile function. Potency rates are generally reported around 80 - 85%. There is also a questionnaire for sexual potency which indicated that erectile function was quite well preserved after brachytherapy. Another thing that was important is that there was no deterioration in the score over time. One of the beliefs out there is that radiation's fine because your potency will be good right afterwards but, by three or four years, it's gone. We didn't find that, because the scores for men in their first year were the same as for men that were more than three years out. So it seemed to be very well preserved and I think the reason that this has changed is not that people had the wrong impression before. Potency is preserved better but the reason is because of these drugs. Because what radiation can do is it will gradually narrow blood vessels that are within that radiation field. If blood vessels supplying the penis for erection become narrower, then the erection is not going to be as good. What these drugs do is dilate the blood vessels, so if you take them on a regular basis as soon as it's getting narrower, you dilate it and after you dilate it several times, it stops getting narrow. So what I've encouraged men to do is to use these drugs on a regular basis for several weeks, several months and quite often, after a while, they feel they don't need them any more and things are working quite satisfactorily.

What are your chances of maintaining the potency? Important predictors of maintaining potency after brachytherapy include: whether or not you smoke, because smoking is a huge insult to your blood vessels everywhere in your body and, if you're a smoker, your chances of maintaining your erectile function into your older age is very low; high blood pressure that's untreated, if it's been treated that's O.K.; diabetes is another factor which is often very harmful to potency. So, if you're not diabetic, if you don't have high blood pressure and you don't smoke, you've got a very good chance of maintaining erectile function. The other thing that's important, of course, is age. A study out of New York showed that if men were in their 50s when they had their implant, 92% of them maintained potency after treatment. If they were in their 60s it was about 65% and even in their 70s almost 60% maintained potency but obviously there's an age related decline, which happens for everyone anyway.

To sum up on the quality of life part of this, after brachytherapy, certainly there's less incontinence, less impotence than surgery, it has less bowel injury and impotence than external radiation but it's true that it does have more irritative urinary symptoms than either surgery or external beam especially for that first six months period. Some practical advantages from your point of view, you don't have to stay in hospital, it's a one day procedure and you return rapidly to normal activities. Half the men I treat are in their 50s and they'll be back at work the following week. I tell them you just have to have a job where you can get to the washroom when you need to because you're going to have to pee more often but you're not going to be in any other way disabled. Technical advantages, from my point of view, it eliminates a lot of the issues of lining up radiation beams. Any of you who've gone through external radiation realize the great lengths that your doctors and the radiation therapist go to make sure things are lined up exactly every day by putting little fiducial markers in your prostate and taking films and everything. So you don't have that because once the seeds are in place your prostate can shift around wherever it wants and the seeds are always going to be in the right place doing their job.

So how do we decide if someone is suitable for brachytherapy? Well, there are guidelines in Ontario which limit the use to men with favourable risk prostate cancer. So no nodule, or small nodule, a Gleason 6, a PSA under 10. It's advised that you don't do it if someone has had a previous TURP and they also advise it more for men with prostate under 50cc. These are just guidelines and the part about the previous TURP and the prostate volume are not firm guidelines. The part about the staging is pretty firm. The majority, probably two thirds to 70% of men, when they are first diagnosed, will actually fit into these considerations. My own criteria are the same for the stage but I'll go up to 60cc, even up to 70cc provided the guy's got a big bony frame and can pee well, so they really have to have more than just adequate voiding function, they have to have excellent voiding function if I'm going to implant a prostate over 50cc. Preferably no prior resectioning of the centre portion of the prostate because that can cause problems. The voiding study that I use for an assessment at the initial consultation is just having you pee into a little flow meter.

Dr. Crook then took us through a slide presentation showing the procedures they follow in implanting radiation seeds. She then opened it up to questions by the following comments.

Now let's look at some frequently asked questions. Why does prostate size matter? How big is too big? What if you have had a TURP, is it going to be possible to have brachytherapy? What is seed migration, where do they go, when, do I have to worry about this? Am I radioactive? What's the risk to my children and my grandchildren?

First of all on prostate size. There's no absolute cut-off. It depends on the relationship of the prostate to the pubic arch because, when we're doing the implant, if the prostate is partly behind the pubic arch, and we have to go under the pubic arch to get into the prostate, then you could be banging into the bone and you are not going to be able to put the needles where you want. So when does this become an issue? Well it depends on your bony frame and your skeletal size. In a small boned, very slim hipped man, you may get some interference even with a prostate of 40cc, while in a large boned, tall individual Eastern European type, 65cc-70cc is fine. You can sort of tweak things when they're marginal so that you can still do it. If someone has a prostate that's too big and they really,

really want brachytherapy, we can shrink the prostate by giving some hormone therapy first, which will shrink it down by 20, 30, 40%. However, hormones have a price attached to them and I don't mean a price in dollars, I mean a price in terms of side effects, such as sexual function and things like that. So I don't generally do this. If someone's prostate is too big I just send them in a different direction. The other thing is that we've found out that if you have someone with a really big prostate and you shrink it down with hormones, you tend to shrink the outside part and not the inside part. So these men tend to have a higher risk of urinary difficulties afterwards and a higher risk of needing a catheter.

What about the prior resection of the prostate? What they do with this is they take out the central portion of the prostate because it's obstructing the urinary flow. If that hole is too big relative to the rest of the prostate, there's not enough prostate left to put the seeds into. Initially it was thought that this was going to cause more problems with brachytherapy, with incontinence and strictures and stuff like that but we found out that a small resection of the prostate, done prior to the procedure, with enough time left for things to heal up, will not impact on someone's quality of life and urinary symptoms afterward.

What about seed migration? This refers to a seed that travels through the blood stream to the lungs. It doesn't refer to seeds that might be lost in urine or lost in the ejaculate, both of which can happen occasionally but only ones that travel through the blood stream. How do seeds get into the blood stream from the prostate? The prostate is surrounded by some very big thick veins and anyone who's had a radical prostatectomy and had to bank blood before hand in case they needed a transfusion realizes that it can be a very vascular procedure with a lot of bleeding. These veins are the route for the seeds to travel to the lungs. We distribute the seeds all round the prostate, we have to get the dose right out to the edge and if a seed is two or three millimeters too far, it can work its way into a vein and then it just travel through the veins to the heart and the heart pumps it out to the lungs and it will get caught in the fine capillaries at the edge of the lungs. This occurs in anywhere from 10 to 20% of men, usually only one seed, occasionally two and it's of no consequence. it's not going to cause any scarring or problems in the lung. People have been followed with this now for over 15 years, so it's nothing to worry about.

Radiation safety is a frequent question. The men worry about their wives, the wives worry about their children, then everybody's worried about getting radiation when they don't need it. Iodine 125 has a half life of two months, so that means it takes two months to give half the radiation. In the next two months you get another half, which is a quarter. In the next two months you get half of what's left then, which is an eighth. So it takes about six months to get five sixths, or 87% of the radiation dose. In the first two months, when the radiation is still quite active in the prostate, we recommend that you try to keep a six foot or 2 metres distance from babies, pregnant women or small children but it's not a risk to non-pregnant adults in a work or home environment. This is based on a few studies that were done and reported in the literature. In one study men were given little radiation dosimeters for themselves, for all the household members, and pets and in every room of the house. They collected them all after a six month period and none of them showed a reading higher than you would expect for a natural background for a year. So nobody was getting any kind of worrisome exposure, in fact 97% of the room monitors showed no exposure reading at all. The calculated life time exposure to a spouse from living intimately with her husband after he's had this implant, and that includes sleeping in the same bed, is the equivalent of two flights to Europe, because at 30,000 ft. you're exposed to cosmic radiation.

So, in conclusion, the seed implants are highly effective treatment for early stage prostate cancer. There's over 15 years experience which demonstrates excellent results. My own experience extends out to nine years now. You need proper technique, appropriate selection and then you're going to get great results and very low morbidity. Certainly, there's that period of irritation in the urinary symptoms, which everyone has to go through and I warn people about that. There's the longer period of uncertainty because of the PSA bounce. Surgery's going to give you a quicker result in terms of your PSA and your pathology but you have a different price to pay for that.

Speakers for our 2008 meetings. Mark these dates on your calendar

- **April 17th Durhane Wong-Reiger, Pres. and CEO. Optimizing Health Org.**
- **May 15th Dr. Andrew Mather, PMH. on Depression**
- **June 19th Jerome Green, Urologist, Southlake Cancer Centre**