

CANADIAN PROSTATE CANCER SUPPORT GROUP

Newmarket, Ontario

Volume 13, Issue 10, June 15th, 2009

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



Dr. Gerard Morton our speaker for the June 18th meeting is a Radiation Oncologist at the Odette Cancer Centre, Sunnybrook Health Sciences in Toronto, where he is Head of the Brachytherapy Program and co-chair of the Genito-Urinary Disease Site Group. He has a major research interest in image guided brachytherapy and is the principal investigator of several ongoing clinical trials of high dose-rate brachytherapy for prostate cancer, with a particular focus on novel fractionation schemes, dose optimization and quality assurance. He will be talking to us about new technology advances that are improving prostate cancer outcomes.

Meeting Date **June 18th, 2009**

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

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

Speaker **Dr. Gerard Morton, Sunnybrook**

Subject: **"How technology advances can be used
to improve patient outcome"**

Canadian Prostate Cancer Support Group,
Newmarket, Ontario. 905-830-0447
a member of the



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.

April Notes...Dr. Robert Bristow, Clinician Scientist, PMH

Subject: Prostate Cancer and Oxygen: "New targets and New Therapies"

Dr. Robert Bristow was our guest speaker for the May 21st meeting. He is a Clinician Scientist at the Princess Margaret Hospital-University Health Network. He is also Associate Professor of Radiation Oncology and Medical Biophysics at the University of Toronto. Dr. Bristow's talk focussed on individualized or personalized treatment as the future for Prostate Cancer care. Here is what he had to say.

There's some really exciting research going on in prostate cancer. I would like to talk about where this research is going in the next five or ten years and what we hope to glean from it. What I really want to leave you with tonight is our concept of individualized or personalized treatment where we will have an ability to actually take from the biopsy a signature of each man and their disease, A unique, genetic signature, from their tumour tissues and normal tissues and start to basically plan a unique therapy based on the genetics for them. That is starting to occur now by first of all having the techniques to go through sequencing the human genome. Now we're starting to sequence the prostate genome. I'm going to focus on one little part of it, which is an active program at Princess Margaret Hospital (PMH), and tell you that although every day breathing in and out is your friend in terms of oxygen, oxygen can be an enemy when it comes to prostate cancer. That's because, in prostate cancer, there are different levels of oxygen and we've found that the lowest levels of oxygen in some patients can predict for a more aggressive cancer. That's the bad news. The good news is, that once we know these sorts of things, as scientists we can come together with new therapies to try to combat that and improve the overall survival of the disease.

Dr. Bristow first went through the basics of what a prostate is, its location and how its cancer is diagnosed. The steps to evaluate this are the Digital Rectal Examination (DRE), the PSA blood test, the Gleason score from a biopsy and the staging to establish the aggressiveness of the cancer. When people come into PMH and are diagnosed, one of the hardest things is to decide how do you actually treat this. Sometimes what happens is that there are equivalent treatments. In other words, there might be two or three treatments that are applicable to the situation based on that PSA, DRE, Gleason score and the doctors then sometimes fire it back to the patient and say, "Well now you get to choose because there's equivalent survival if you use surgery versus radiation therapy." Many patients, understandably, can be upset with that. In other words, the doctors aren't telling you what to do, they're basically telling you that here is the situation, here are the relative side effects, now I'll help you make that decision. That's a different way of doing health care now than it was, say, 10 to 15 years ago, where the doctor took a very paternalistic or maternalistic approach to patients, and just said this is the way it is and this is what you will do. We know now that there are equivalent cure rates with radiation therapy and with surgery for certain stages of the disease. Tell me more about your life style. Tell me more in terms of are you still working, are you retired, what's more important to you

in terms of urinary symptoms, or bowel symptoms? This helps us make the decision, with the patient and for the patient, about the best therapy.

The other issue that I think is an important change in the last five to ten years, is that we now recognize that some prostate cancers are indolent. They are not growing. In fact, we used to know this because patients would die from heart attacks or complications due to diabetes and they would have an autopsy. The prostate would be removed, just as a matter of course from the autopsy and prostate cancer would be found in that gland, a Gleason score of six out of ten, a fairly low grade prostate cancer that the men never knew they had. No-one ever did a PSA on them and they died of something else. Since we now know that there are indolent forms of prostate cancer, the role of the clinician is to help to understand which are the cancers that need to be treated and which are the cancers that don't need to be treated. This is a concept we didn't talk about ten years ago. That means that what we're trying to do is, if we have a diagnosis of cancer, then we would have confidence to tell the patient that it's not an aggressive cancer, we'll follow you like a hawk, very closely, (we call it Active Surveillance) and we will do subsequent biopsies. In a study that was pioneered here in Toronto over ten years, if you took 100 patients who had low risk prostate cancer and tracked them, after ten years basically only 30 of the 100 would go to a type of cancer that needed treatment and 70 might never require treatment at all. But it requires active surveillance of the PSA. We're looking for changes in the PSA and we also do biopsies in year one and year three and five and seven, to be absolutely confident that we're giving the right information to the patient.

Going back to this individualized treatment, what are the differences or the genetic changes in a patient who has the exact same Gleason score, the same PSA but is going to be one of the 30 patients over ten years that will have an aggressive cancer that needs to be treated, versus the 70% of patients that don't need to be treated for prostate cancer. That's a different concept than what we thought of before. So some of these patients with low risk prostate cancer, which is defined as PSAs of less than ten, a Gleason score of six or less and what we call a T1 or T2 tumour, might be candidates for active surveillance.

Then we have this aggressive disease, which is prone to spreading throughout the body. In terms of active disease, we either to treat it with surgery or some form of radiation treatment. In surgery we used to always do what's called an open prostatectomy, with an incision from the belly-button down to the pubic bone and the prostate would be removed

by opening up that area. Now, we're getting into the so-called robotic or laparoscopic surgery. In the USA for example, if you go in for surgery, you are enticed to go in for robotic surgery. I just want to caution you that, when you look at all the studies that have been done so far in Europe and North America, it's still early days to know whether it's a better operation in terms of giving less chance of getting positive margins or leaving anything behind after surgery and also whether there are less side effects. A lot of hospitals have bought the robots but they need about 200 cases a year to really make good use of it. If you have a surgeon who has done a thousand open prostatectomies the classic way versus a surgeon who has only done about 20 of the robots, go open prostatectomy with the guy who has done a thousand—despite the literature, despite the web sites. Radiation therapy has also changed quite a bit. Brachytherapy has become more popular, mostly with low risk cancer. For intermediate prostate cancer, we use external beam radiation therapy, which is a high energy X-ray. This has been improved to include a CT scanner, which shows if the organ is moving and allows the radiation beam to target it better. This means that we can give a higher dose radiation directly to the prostate and spare the surrounding tissue.

Then we go to the more aggressive form of therapy, such as hormone or chemo therapy, this is where the disease has spread elsewhere. We used to say that if you become resistant to hormone therapy, basically the only thing left is chemo therapy. This is usually given when the prostate cancer has spread to the bone. Let me tell you what's coming down the pipe line. If you had bone cancer, which is resistant to hormone therapy, on average there would be a two year survival at that point, not great odds. It's an incurable disease at that point. The reason hormone therapy works or doesn't work is that the cancer cells are either responding to the male hormone in the body or not responding. If they're responding and if we block them with the therapy then we actually block the production of testosterone in the body and the action of testosterone and the cancer cells starve and they die and the PSA goes down. Sometimes the PSA goes back up because the cells outsmart the system and no longer become responsive to the blocked hormones. What we found is that the cancer cells get smart and start producing the hormone themselves. So, despite shutting down everything with an injection locally, the cancer cells start to produce an environment for hormones and start to feed on that themselves. Someone has developed a new drug called *Aperademone?*, from the United Kingdom, 70% of men who had failed their hormone therapy, were now responsive to this new drug that blocked the cancer cells from making their own hormones. That is now in Phase 3, or the highest clinical trial, and we should have the answer next year. We expect that it's going to be a positive trial and a new hope for men who otherwise had hormone independent cancer and would have no options but chemotherapy. This is a new drug that, based on research, will change the way that patients are treated if they have more

aggressive hormone resistant disease. This is one of the exciting new results in addition to the understanding that some patients may not have to have their cancer treated. These two things will make a difference in the next five years.

What are the current standard of treatments and how do we select patients to have brachytherapy, active surveillance or a combination of hormone therapy and radiation? We take into account the three factors: what the organ feels like on the DRE, the PSA and the Gleason score out of ten. A Gleason score of 4, 5 or 6 out of ten is thought to be fairly low risk, not very active; 8, 9 or 10 out of 10 is an aggressive cancer under the microscope and can be aggressive locally or could have the potential of having the ability to spread. A Gleason 7 score is right in between but it probably should be treated, so we don't do active surveillance on patients with a Gleason score of 7 or more. A PSA of less than 10 we tend to put in the category of low risk. Patients who are at higher risk for spread of the disease have a PSA of 20. We now have so many treatment options currently being used for the various levels of risk in prostate cancer, how is a man or his family to decide between all of these? Now, in addition to a DRE, a PSA, a biopsy for a Gleason score, we have a genetic test. Just imagine the finger nail of your little finger, we currently have techniques where we can place probes for 10,000 genes in the body on a slide the size of that finger nail. We can take a sample from a prostate tumour and we can look at the expression of genes by basically laying them onto the slides and within two to three days we can have an answer about 10,000 genes in that sample as to what is what is up and what is down. We are currently doing that in many men and actually asking the question, "Can we see a signature that says they are in a low risk or intermediate risk or high risk and whether or not they would respond to HIFU, Cryo or radiotherapy?" So we can give much better information to the patients when they are selecting their treatments. In general, there are lots of treatments and the idea of personalized medicine over the next decade is that we will know more about your signature and we will be able to give you better advise as to what is the best therapy for you.

Some of those promising factors are the genes, including the low oxygen or hypoxia, and even research dealing with cancer stem cells. Usually we think about embryo stem cells but I am talking about cancer stem cells, which regrow the tumour. We now have a signature for those as well and we're collaborating with a lab in the United Kingdom to better understand which are these stem cells. We think these are the cells that regrow the tumour and we should be able to focus even more on those cells. Out of 100 cells, there could be only ten that could regrow the tumour. So, I think it's a new era in terms of prostate cancer research. In the 1970s it was basically a seek and destroy and in the 21st century we are much better able to target the prostate with precision for better radiotherapy; robotic surgery will pan out to better than the previous open surgery; and also biologic precision where we can target the biology of the patient and control the dis-

ease. For example, in disease which is currently incurable, where the disease spreads to the body, instead convert that to where the disease maybe isn't cured but just stays stable. We feel that personalized medicine will reduce side effects and stabilize previously incurable cancers. We think that for non-aggressive disease, we should be non-aggressive; and for aggressive disease we should be aggressive but we need more information about how to treat the patients.

What we're looking at in the future is individual oncology or individual treatment. If we have a hundred men come through the door with similar Gleason score 7s and PSA between 10 and 20, imagine if we take biopsies from all these people and distil down their cells into individual chromosomes and come up with a biomarker or predictor of response, there are different types of things you could predict with that information. You'd like to predict whether or not a tumour is going to respond to local treatment or not. So what sort of biomarkers or factors might give rise to that information? We could start to make some decisions about whether or not the factors were present in the tumour. There are mutations in what's called the androgen receptor which shows the relative sensivity of cells to hormone therapy — that would be useful information to indicate which patients may be resistant to hormone therapy due to high toxicity. We could also look at secondary cancers. We usually don't think about that. For example younger patients may ask for radiation therapy but I have to consider whether the treatment that can cure their prostate cancer could cause a cancer with the radiation treatment to their normal tissues. These are the types of questions we're asking now, which is very different from the types of questions we asked ten years ago, because we understand there's something special and unique about each patient. This type of personalized medicine is about taking this type of information from individual patients and utilizing it to determine whether therapy is required, what type of therapy and if it's going to be effective and, if you have two effective therapies, which one is going to give the least side effects?

In the mid 1990s when we started to sequence the entire Human Genome, in other words to look at all the genome coding and all the chromosomes, it cost 1 million dollars for one patient. Today, it's \$20,000 and we think in three years it will be \$3,000 to sequence the entire genome. Our technology has improved that much. The problem is that we'll have all this information and somehow we need to put it all together to come up with the signature. It is an embarrassment of riches. We now need to know how to use it. The point is that we are going to be able to do it. This concept of personalized medicine and genetic signature, while I say it's only a decade away, it's because I know that in three years it's only going to cost \$3,000 a patient and then, maybe two years after that, \$1,000. From this we can see which pathways are abnormal in a given man, then we need to develop drugs that will treat them and these two things are coming forward presently. I am sure that we will find out about prostate cancer by

going through the library of the genetic code for individual men. Some of my colleagues and myself are seeking funding on July 1st to start sequencing the entire prostate cancer genome. We are going to do that, hopefully, in collaboration with the Canadian Government. It's going to cost about \$20 million and were going to do it in collaboration with Germany and Australia and try to do this once and for all and find out which are the active cancers and which are the indolent cancers and what's the signature. Who are the patients who will do well with radiotherapy or those who won't do well; what's their signature? Who are the patients who are destined to have disease that has spread and patients who have all their disease local? Because the patients who are destined to have their disease spread will need to have a therapy that will deal with the spreading of the cancer, as well as the local therapy. Right now, we kind of guess on the basis on the PSA and the rectal exam but if we could have a genetic signature, it will change the way we do things. So, having individual treatments improves the over-all outcome for all patients.

We deal with the genetics of cancer and each cancer cell will have it's own signature but then it's about how those cancer cells actually talk to each other when they're in a solid tumour. Think about it this way, there are a lot of times scientists will do their experiments on tissue culture on tissue plates but it doesn't actually represent how well cells work with each other and how aggressive they are when they are in a solid tumour. Because cells don't live in an incubator where they have 20% oxygen that we're all breathing right now. They live under conditions in which it's 5%, 1%, sometimes it's zero per cent oxygen. Why? Because in normal tissues there are these nice blood vessels that look like nice little road maps, that the oxygen gets to all the cells in these tissues equally, whether it's your muscle, your liver, your brain. When we're breathing, all the tissues are functioning but, if you have a stroke, for example, or a heart attack, that's an acute change in oxygen level and, all of a sudden, the cells don't work any longer, so that's what happens when you have problems with a heart attack. In a tumour, it's a very different type of blood vessel network. As the cancer cells grow and divide away from the blood vessel, the oxygen level is getting lower and lower because they're getting further away from the source of the oxygen. What it means is that there are some cancer cells that live in relatively high oxygen areas and then there are other cancer cells that live in very low oxygen levels. When we started to lower the oxygen levels of some tissue levels, they became more aggressive, they started to mutate and have some funny changes in their chromosomes and, if we injected them into animal models, they spread through the body much more quickly. So we asked ourself, if that was true in a patient, maybe low oxygen levels in a patient's tumour, and if we could possibly take the oxygen levels in a patient's tumour, would that start to give us information of who had an aggressive cancer or not? It might also give us information about who would respond to radiotherapy, che-

motherapy or not because we would also know that low oxygen levels were predicting resistance to radiation or resistance to chemotherapy.

I hope I've given you a flavour of some new things that are on the horizon, based on stuff that we started ten years ago and we're finding out about today. It's a very different scenario than thinking that things are always going to be the same and nothing is ever happening in prostate cancer research. Some examples of what is happening today are:

1.) the concept of indolent versus active cancers and starting to not overtreat patients once we're confident that they can be just watched carefully. That's a different way of doing things. Imagine you have prostate cancer and you don't have to think of radiation or surgery.

2.) Then on the opposite spectrum, for the most aggressive form of independent hormone therapy resistant dis-

ease, there'll be a new drug out in the next one to two years that the patient can take for that and that can stave off or prolong survival for another five or six years beyond what is currently available now.

3.) The third thing I started to give you a bit of a taste of, is this concept of personalized medicine. That there are secrets in everybody's prostate tumour, those biopsies that we take. It's up to the scientists to unlock these secrets and then come up with new therapies, which hopefully will have very little side effects, that we can offer patients, so we individualize the treatment to you rather than thinking of you as a group of 100 or a thousand patients and just giving you an average treatment for an average piece of information. We want to give you a specific treatment for a specific piece of information that we think is overall going to increase your cure rate and decrease your side effects.

a lighter moment

from Thomas Cook Holidays (a British Travel Agent) - a few of the guest complaints during the season.

“We booked an excursion to a water park but no-one told us we had to bring our swimming costumes and towels.”

A tourist at a top African game lodge overlooking a waterhole, who spotted a visibly aroused elephant, complained that the sight of this rampant beast ruined his honeymoon by making him feel “inadequate”.

A woman threatened to call police after claiming that she'd been locked in by staff. When in fact, she had mistaken the “do not disturb” sign on the back of the door as a warning to remain in the room.

A guest at a Novotel in Australia complained his soup was too thick and strong. He was inadvertently slurping the gravy at the time.

“Topless sunbathing on the beach should be banned. The holiday was ruined as my husband spent all day looking at other women.”

“We bought ‘Ray-Ban’ sunglasses for five Euros (£3.50 or \$7.00) from a street trader, only to find out they were fake.”

“No-one told us there would be fish in the sea. The children were startled.”

“My fiance and I booked a twin-bedded room but we were placed in a double-bedded room. We now hold you responsible for the fact that I find myself pregnant. This would not have happened if you had put us in the room that we booked.”

Speakers for our Future 2009 meetings.

Mark these dates on your calendar

June 18th Dr. Gerard Morton, Sunnybrook
How technology advances can improve patient outcome

September 17th Dr. Tom Morton (to be announced)

October 15th Dr. Doug Moseley, Southlake (to be announced)

November 19th Tanya Giaquinto, Sunnybrook
Diet and Cancer . . . Continuing info on nutrition.

December 17th Christmas Party

Derek Lawrence is Retiring



Derek Lawrence has informed us of the unthinkable. He is retiring from his many jobs on the executive of our support group at the end of this month. Derek as you know is our founder and the man that helps keep us on track both financially with his fund raising talents and his abilities in booking the many excellent speakers we have each month. He has also provided us with most of the material we see each month on our supply tables.

Here are a few of Derek's contributions to our group over his 14 years of service.

- * A thirteen part series of half hour programs on Rogers T.V. from discovery of prostate cancer to palliative care.
- * A supply of tapes of these programs was sent to all support groups across Canada, and to hospitals and libraries across Ontario.
- * A four part series of Live Forums held in Madsens, Newmarket
- * A "Conquering the Fear" Tape demonstrating the different techniques available for treating prostate cancer. These were also made available for all the other Support Groups in Canada.
- * He also mass produced an audio tape of Dr. Laurence Glotz's book " Prostate Cancer" a guide for patients.

Derek has assured us that he will be available at the meetings or any other time to help new members learn about how to deal with their cancers.

Come to the meeting and join with us as we thank Derek for his years of work on our behalf.

June is Election Time

It's June already and this is our last meeting before we break for the Summer months. It's also the meeting where we hold a election and invite other members to help on the executive committee. What we like to suggest is that anyone willing to come on to the team could start as a "member at large". This would only entail attending a monthly meeting at the cancer society office in the day time: helping with the newsletter mailing and giving some of your fresh ideas to the group. As a member at large by helping here, you would free up some time for some of the other directors so that they could take on some of the many duties left by Derek on his retirement.

The winner of the 50/50 draw on May 21st was Ruth Green and she won \$36.00