Manitoba Prostate Cancer SUPPORT GROUP

Newsletter

Vol. 301 1,300 copies printed/e-mailed **September 2016**

Key themes: from the AUA meeting in San Diego, May 6-10, 2016.

=> The effect of the United States Preventive Services Task Force's grade "D" recommendation against PSA-based screening for prostate cancer has been a decrease in screening since 2012 independent of race, a decrease in referrals for an elevated PSA level, higher PSA levels at the time of referral, fewer prostate biopsies but more positive prostate biopsies, and a higher proportion of cancers with Gleason score greater-than-or-equal-to 8 and metastatic disease.

=> Other series describe fewer prostatectomies performed, and of those being performed, there is a greater proportion being performed for Gleason score greater-than-or-equal-to 8 cancer as well as pathologic T3 disease and extraprostatic extension.

=> An evaluation of data from the European Randomised Study of Screening for Prostate Cancer found that 81% to 89% of the changes in prostate cancer mortality could be explained by a stage shift (cancers being detected at an earlier stage) rather than differences in treatment.

=> Use of the Prostate Health Index and multiparametric magnetic resonance imaging (MRI) in combination has better diagnostic performance than either alone in detecting clinically significant prostate cancer.

=> A multicenter validation study of a molecular urine test revealed that the HOXC6-DLX1 score model improved the accuracy of the detection of clinically significant prostate cancer over serum PSA alone.

(Continued on page 2)

Medical Advisors

Paul Daeninck M.D.
Medical Oncologist

Darrel Drachenberg
M.D. Urologist

Graham Glezerson
M.D. Urologist

Ross MacMahon
M.D. Urologist

John Milner
M.D. Urologist

Jeff Sisler M.D.
Family Practitioner

Thanks!

Next meeting: September 15, 2016

Dr. Darrel Drachenberg, Urologist
Dr. Mark Kristjanson, Family Physician

Topic: General overview of prostate cancer & treatments

Location: Caboto Centre
1055 Wilkes Avenue

Time: 7:00 – 9:00

Dr. Darrel Drachenberg

Dr. Mark Kristjanson

SHARING IS CARING SHARING IS CARING

The Manitoba Prostate Cancer Support Group does not recommend treatment modalities, medications, or physicians.

MPCSG – active since 1992.

Thought of The Day

If I agreed with you ..... we'd both be wrong!

(Continued from page 1)

=> A comparison of MRI-ultrasound (US) fusion biopsy to cognitive registration and traditional sextant biopsy found that the fusion technology improved the biopsy detection rate and pathologic grading.

=> A randomized trial comparing MRI-transrectal ultrasound-guided fusion biopsy to standard biopsy found an improvement in the detection of clinically significant prostate cancer with fusion technology, and if the MRI was negative, only insignificant prostate cancers were missed.

=> In a cost analysis model, cost was 25% less in a hypothetical cohort of 100 men with PSA elevation who undergo prostate MRI with MRI-US fusion biopsy, if indicated, compared with an initial TRUS-guided biopsy. A follow-up study (2006-2013) of an analysis of complications after TRUS-guided biopsy found that the hospitalization rate has remained stable at 4.1% and the overall mortality rate of 0.08% did not change throughout the study. The number of TRUS biopsies performed fell abruptly by 30.6% in 2013.

=> A pre-biopsy checklist found that infection-related hospitalization rate was 0.70% and the most common risk factor associated with infection-related hospitalization following prostate biopsy was prior antibiotic use (31.8%).

=> A higher biochemical cancer recurrence rate was found with delayed versus immediate radical prostatectomy (RP) in active surveillance-eligible patients who required RP.

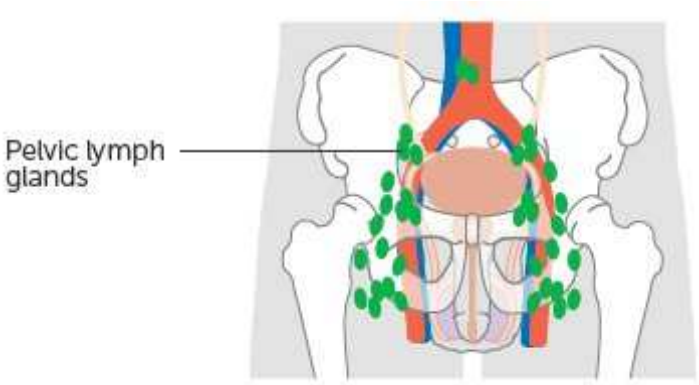
=> Patients with low-risk prostate cancer who enter AS have higher grade disease at RP but similar pathologic outcomes to those who undergo initial RP.

=> A multi-institutional analysis of patients with T3N0 prostate cancer revealed no difference in 10-year metastasis-free survival between adjuvant and salvage radiation therapy.

=> Post-prostatectomy radiation can be avoided in men with low clinical genomic risk.

=> Adjuvant radiation shows an incremental cost of $17,206 and is associated with fewer quality-adjusted life-years compared with salvage radiation (3.7 vs. 4.4 years).

=> Ninety-six percent of patients with positive lymph nodes were correctly staged with extended pelvic lymph node dissection.



=> Super-extended pelvic lymph node dissection may have a detrimental effect on functional outcomes (ie, continence and erectile function) compared with extended pelvic lymph node dissection. Super-extended pelvic lymph node dissection increased the rate of overall complications, lymphedema, and lymphoceles compared with extended pelvic lymph node dissection.

=> A large multi-institutional database of 10,136 patients treated with RP and extended pelvic lymph node dissection from 1987 to 2014 showed the following trends: an increase in the rate of RP in high-grade disease, improved positive surgical margin rates, improved biochemical recurrence rates, and improved cancer-specific survival.

=> Patients with very high-risk prostate cancer compared with high-risk prostate cancer had more extra-prostatic extension, more seminal vesicle invasion, and a higher rate of biochemical recurrence and metastases at 5 years. Of those who had RP for very high-risk prostate cancer, with 18.6 months of follow-up, 47% had persistent or recurrent PSA and 15% developed metastases. The authors suggested that about one-third of patients may have been cured with surgery alone.

=> There was no difference in health-related quality of life between RP and the combination of radiation therapy and androgen deprivation therapy in men with high-risk prostate cancer.

=> Of 202 men with biochemical recurrence after RP with positive mpMRI and/or choline positron emission tomography, 33% exhibited local-only recurrence and 45% had metastatic-only relapses.

=> A comparison of open versus robotic salvage RP found that the robotic approach had lower lymph node yield with lower blood loss, a lower anastomotic stricture rate, less rectal injury, and similar functional outcomes.

=> In patients who underwent RP and had positive lymph nodes, adding ADT to external beam radiation improved cancer-specific survival and overall survival.

Source: Urology Times – June 2016

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Evidence Supports Earlier Use of Radium-223

The approved indication for radium-223 dichloride (Xofigo) is for patients with castration-resistant prostate cancer (CRPC) who are symptomatic, have bone metastases, and do not have known visceral metastatic disease.

However, asymptomatic patients may also benefit from radium-223, says Fred Saad, MD, principal scientist, full professor, Department of Surgery, chair in Prostate Cancer Research, Université de Montréal.

"If we wait to treat a patient until the symptom of significant pain occurs, we don't get as much of a survival benefit because patients are not able to get all 6 cycles," says Saad. "It is important to start treatment when patients are still in a state that they are able to take a full 6 cycles."

This concept was recently evaluated in the international early access program (EAP), which compared radium-223 with placebo in 696 patients with CRPC with symptomatic or asymptomatic bone metastases.

In the study, led by Saad, 21% of patients reported no pain, 52% reported mild-to-moderate pain, and 27% reported severe pain. Eighty-eight percent of patients had an ECOG performance status of 0 to 1. Fifty-eight percent of patients were able to receive all 6 radium-223 injections.

Some of the patients in the study were also treated with concomitant therapy: 22% with abiraterone acetate (Zytiga), 20% with denosumab (Xgeva), 18% with bisphosphonates, and 4% with enzalutamide (Xtandi).

The study found that significantly longer overall survival (OS) was observed in patients who had a good ECOG performance status and no pain. OS also appeared to be better in those treated concomitantly with denosumab or abiraterone and radium-223.

In an interview with OncLive, Saad discusses the results of the EAP study and how it will shape future studies examining radium-223.

OncLive: What were the biggest findings from the EAP?
Saad: The international EAP involved countries from around the world using radium-223 in a real-world setting. We had the opportunity to study almost 700 patients who were part of this study. We wanted to examine different parameters in patients who were metastatic and castration-resistant. We allowed patients to start radium-223 even if they didn't have pain coming into the study.

What we realized by looking at patients with pain, without pain, and with mild-to-moderate pain, was that their survival rates were all different. Patients who came in with less pain had significantly improved survival compared with patients with pain.

This led us to believe that patients who start radium-223 earlier in their disease are able to tolerate more cycles, which leads to better outcomes. Patients who come in with very good performance status live longer than those with less good performance status. The study also gave us the opportunity to investigate concomitant therapy. Patients who came in with radium-223 and abiraterone acetate concomitantly appeared to live significantly longer than those who received radium-223 alone.

We also saw a similar result with denosumab; patients who received concomitant denosumab with radium-223 lived longer versus those who received radium-223 alone. That is very intriguing, and it confirms the importance of the prospective phase III international randomized study that we are doing right now with abiraterone with or without radium-223.

At this point, are there any negative effects associated with administering radium-223 to patients earlier?
We haven't seen any added negative effects. We were very reassured with the international EAP program; it was a real-world setting, and we saw no additional adverse events with radium-223 compared with nearly every other therapy we have for this disease.

Age is not a restriction and no other factors were really restrictive to patients receiving the agent. It is very well tolerated, and that has been our personal experience at our center, as well. Patients seem to tolerate radium-223, regardless of where they are in the spectrum. Therefore, the important thing is to make sure we treat them when they have a 6-month window, so that they get the full treatment and benefit.

What are the most significant benefits from radium-223?
In the phase III study, we saw a 30% reduction in the risk of death. In that setting, the patients who were not able to get the full 6 cycles seemed to have less of a benefit. Since this is a bone-targeted therapy, progression-free survival is not a good reflection of activity.

Alkaline phosphatase seems to be a much better marker of where activity is occurring, as well as response. When patients get a decrease in alkaline phosphatase, their survival is significantly better than those few patients who don't get a reduction in alkaline phosphatase. That is what we recommend regarding follow-up of these patients getting radium-223.

What is on the horizon for radium-223?
We need to confirm the added benefit of combining radium-223 with other therapies, such as abiraterone or enzalutamide. There is also a phase II study looking at the safety of combining it with chemotherapy. That looks very promising for now, although it is still not recommended out of clinical trials. There is no worry about giving this agent post-chemotherapy or vice versa. As of now, these sequences seem very safe, both in our experience and in clinical trials.

Source: www.global.onclive.com

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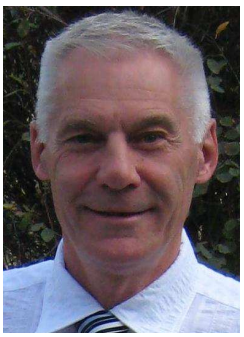
Brian Sprott Retires…



Brian joined the Support Group in 2006 - prior to his treatment for prostate cancer. He was mentored by then Chairperson, Norm Oman, and it wasn't long after his prostatectomy that Norm encouraged him to facilitate the general meetings. And it just went from there…….soon to become the Chairperson of the Manitoba Prostate Cancer Support Group.

During the early days of his involvement, the Support Group was short on funding so Brian set about making contact with various companies and soon we were in the "black" again. He met regularly with these representatives – informing them of our activities and how we were giving them recognition.

Over the years,

=> He attended 4 national Prostate Cancer Canada conferences and 1 regional conference and has continued to remain in touch with a number of Support Groups across Canada;

=> As Chair, he contacted speakers for our general meetings – forming a relationship and keeping in touch with them often;

=> Brian organized all the advertisements for the *Metro* and *Free Press* newspapers;

=> Every year he helped organize the September Awareness Evening at the Caboto Centre;

=> He facilitated almost all of the general meetings and made friends with many members;

=> Brian contributed in other ways, such as, getting business cards, name tags, maintaining our website, responding to our answering machine, keeping in touch with most of the new members, assisting in writing our 20 year history newsletter, keeping binders of records, and the list goes on……..

Literally, there was nothing that he couldn't do… or… wouldn't do to make the Support Group a better experience for those diagnosed with prostate cancer.

The last word goes to him ……

"The primary reason for my involvement has been the people. The individuals and groups that I've had the pleasure, privilege and good fortune to share time with have been a highlight. Thank you all for your support, assistance, encouragement, suggestions, understanding, and cooperation. I've learned so much. Thank you all".

June Sprott, Editor

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Darlene and Kirby Hay are Retiring

Darlene and Kirby have decided to retire from the Manitoba Prostate Cancer Support Group Board.

Kirby has spent 10 years on the Board and contributed in a variety of ways. One of Kirby's special interests was in the education of the newly diagnosed. To that end, he assembled prostate cancer Information Kits that were handed out to those just starting their cancer journey and also to a number of urologists. He made certain that literature was available at our general meetings. Kirby attended and organized health fairs – giving verbal and prostate cancer information to others. He was always willing to share his story in the hope that it would assist others.

Darlene spent 8 years on our Support Group Board. She could always be called upon to assist us with her vast computer skills. She was our Membership chair for many years and, as such, maintained the data base of all our members. She had 100's of names and addresses – and was in constant contact with our printer and our sorting and mailing company to make sure that the right number of newsletters were printed and that each one had the correct postal address.

When we began to email newsletters, it was Darlene who put all the names and email addresses into the data base and made the newsletter appear on your screen each month.

It's impossible to cover the many ways that Darlene and Kirby have contributed over the years. What was most valuable was the way that they would "jump in" and always lend a helping hand. We want to recognize their years of work and say a special "Thank-You". Enjoy your retirement as you travel to Arizona each winter!

June Sprott, Editor

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Note from the Editor

This note will inform you that I am retiring.

I have been the chair of the Manitoba Prostate Cancer Support Group newsletter for most of the 9 years that I have been on the Board …. (in addition to other things, I also spent many years as the secretary) …. it is now time for me to move on to other things.

I want to thank all the readers and also thank those of you that have commented on some of the articles - telling me that a certain one applied to your situation and was helpful. I always appreciated your feedback and tried to make improvements.

My wish for all the readers is that you will have superb health and a long life. I hope our paths will cross again in the future.

Cheers,
June Sprott, Editor

p.s. You can see me every Friday at the Winnipeg airport volunteering as a Goldwing Ambassador.

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Introducing …… The New Newsletter Editor

Pete Szekely from
Bottom Line Computer Services

He really doesn't need much introduction as you have actually come in contact with him every time you read our newsletter. Take a look at the bottom of the last page of your newsletters. Pete has been working hard to format and design every single newsletter since it began in 1998. I send him all the information and he puts it together, inserts pictures and incredible design to make it a first class newsletter. It has been his expertise and commitment to our Support Group that has put this newsletter in your mailbox for 18 years. His computer skills and knowledge are phenomenal but …… now he is going to do much more than that.

Pete will be supplying all the articles, formatting the layout and producing the information that you read in the newsletter. I have every confidence that it will be even greater than before. So, please welcome him into our Support Group family and continue reading and learning about prostate cancer.

June Sprott, Editor

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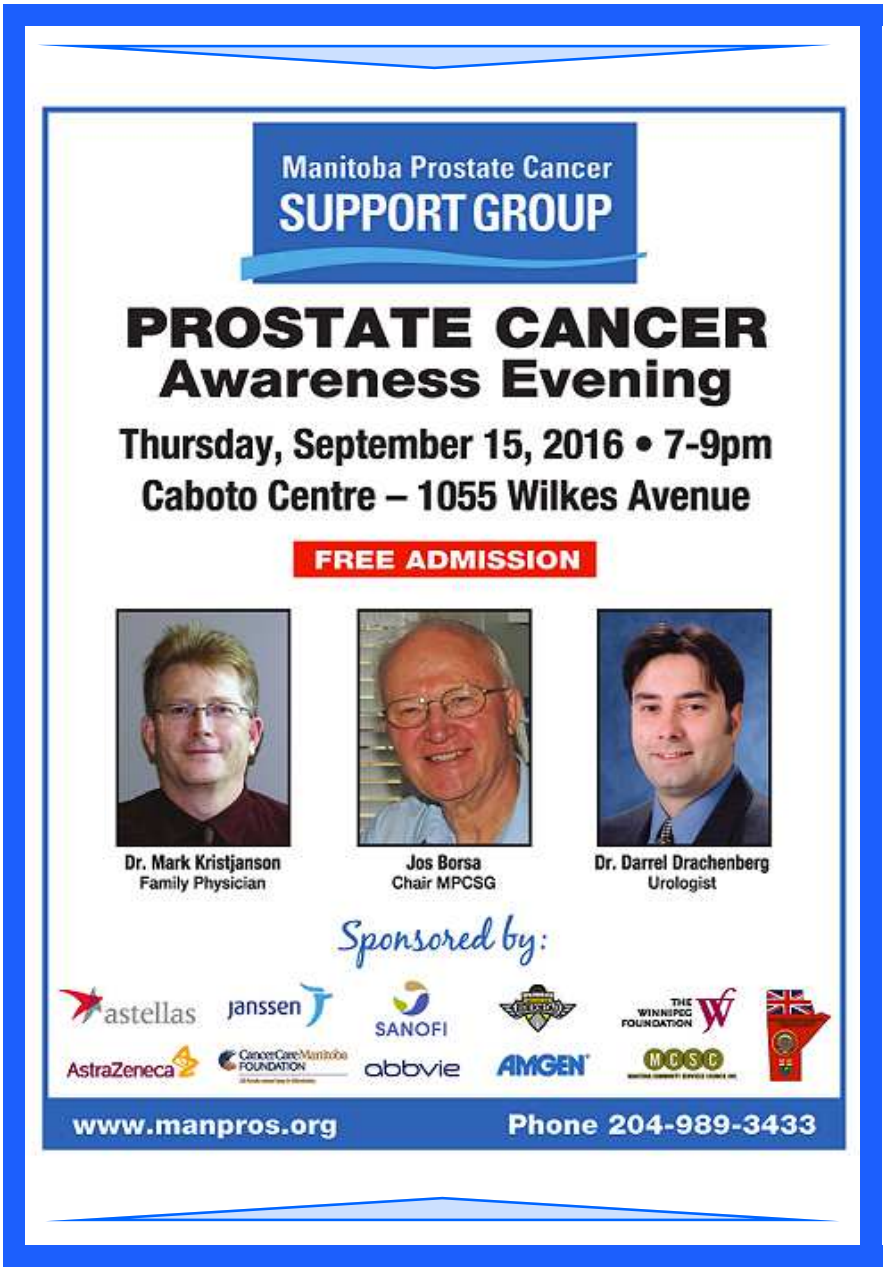
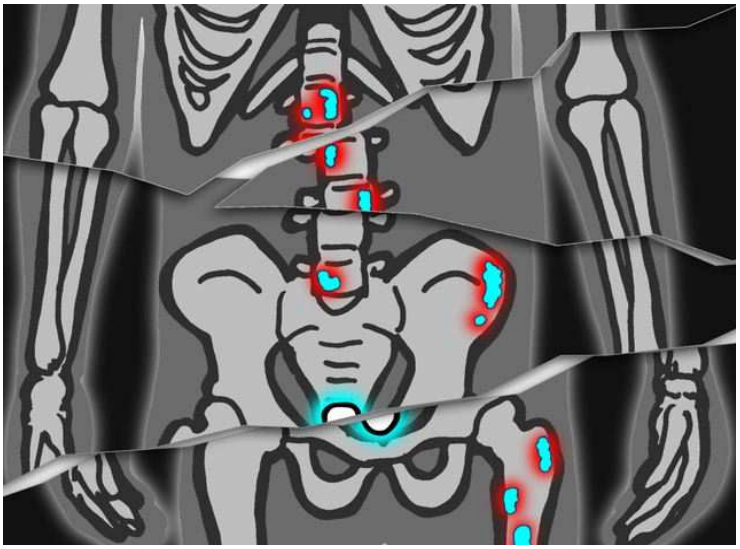


Bisphosphonate Therapy for bone metastases

Prostate cancer is a malignant disease that affects men's reproductive system. The disease occurs when the cells in the prostate start to grow out of control, affecting both the reproductive and urinary systems. The prostate is a gland found in men's bodies, bellow the bladder, near the rectum and around the urethra. It is responsible for the production of a fluid that is expelled with the sperm during ejaculation and that makes the semen more liquid.

The symptoms of prostate cancer include urinary problems like a slow or weak urinary stream or the need to urinate more often, especially at night, blood in the urine, erectile dysfunction, pain in the hips, back (spine), chest (ribs), or other areas from cancer spread to bones, and weakness or numbness in the legs or feet, or even loss of bladder or bowel control from cancer pressing on the spinal cord. There are numerous options of treatment, depending on each situation.



Bisphosphonate Therapy for Patients with Prostate Cancer

Bone is the most common site for prostate cancer metastases. Bone metastases occur in 80% of men with advanced prostate cancer. Bone metastases result in substantial morbidity, including pain, spinal cord compression, and pathologic fractures. While the standard course of treatment in these cases is hormonal therapy, in 70 to 80% of the cases, it ends up becoming ineffective. Bisphosphonate therapy is particularly indicated for these cases.

Bisphosphonates refers to a group of drugs that work by slowing down a group of bone cells known as osteoclasts, which are usually responsible for breaking down the hard mineral structure of bones to help keep them healthy. However, they may become overactive when prostate cancer spreads to the bones. Two bisphosphonate drugs used for treatment are; (1) zoledronic acid (Zometa) - which is administered intravenously, and (2) denosumab (Xgeva) – an injectable targeted drug that binds to a protein called 'receptor for RANKL.' This protein is found on osteoclasts, and binding of denosumab inhibits destruction of bone by osteoclasts. Denosumab thus prevents increase in size and number of metastatic bone lesions. It also delays the onset of bone metastases. Neither Zometa or Xgeva prolongs overall survival.

Bisphosphonates are known to help ease pain and high calcium levels caused by metastasized cancer to the bones, as well as to slow the growth of the metastases and help delay or prevent fractures. In addition, it may also be used to strengthen the bones in men being treated with hormone therapy.

Benefits and Risks of Bisphosphonate Therapy in Prostate Cancer

"Bisphosphonates act predominantly by inhibiting bone-resorbing osteoclasts that are associated with the formation of osteolytic bone lesions. Prostate cancer is associated with osteoblastic (not osteoclastic) bone lesions that result in the deposition of calcium in new bone. The rationale for the use of bisphosphonates in the treatment of prostate cancer is that biochemical and histomorphometric studies have indicated that osteolysis may also be present in prostate cancer bone metastases," added the investigators, who revealed that bisphosphonates decrease the level of pain experienced and reduce the risk of skeletal events like pathologic fractures, hypercalcemia, and the need for radiotherapy or surgery.

However, there are also potential side effects from the bisphosphonates therapy which may include flu-like symptoms and bone or joint pain. Patients with poor kidney function may also experience kidney problems. A rare but very serious side effect of bisphosphonates is osteonecrosis of the jaw (ONJ), which consists on the loss of blood supply to part of the jaw bones and its consequential death.

Source: *Prostate Cancer News Today.*

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Active Surveillance – study shows 3% of men may have metastases.

Treatment such as surgery and radiation for localized prostate cancer may cause significant side effects. Active surveillance (AS) is increasingly accepted as an option for treating patients with clinically insignificant disease to maintain their quality of life. Despite close monitoring, about 3% of patients on AS had metastasis by a median of seven years after diagnosis. This risk increased to 10% in patients with Gleason score (GS) 7, according to new research published in the *Journal of Urology*.

Prostate specific antigen (PSA) screening has enhanced the early diagnosis and treatment of prostate cancer. Currently approximately 40% of newly diagnosed patients are found to have low risk prostate cancer, characterized as GS 6 or less with PSA 10 ng/ml or less. Active surveillance is an approach to manage low and low-intermediate risk prostate cancer, which is designed to reduce harm from over diagnosis and overtreatment.

Investigators at the Sunnybrook Health Sciences Centre, **University of Toronto** initiated a prospective cohort study in 1995 to assess the risk factors for metastases in patients on active surveillance. "This is a detailed analysis of 30 patients initially treated with surveillance for what was thought to be favorable disease, but which eventually progressed to metastatic disease," explained Laurence Klotz, MD, FRCS (C), Professor of Surgery at the University of Toronto. "We previously reported on five such patients. The current report represents a considerably larger group with longer follow-up, which presented an opportunity for risk analysis."

Of the 980 patients analyzed, 211 (21%) were classified as intermediate risk, 109 (11%) had baseline PSA greater than 10 ng/ml and 133 (13%) had GS 7 disease. The investigators analyzed the clinical and pathological correlates of surveillance in patients who eventually experienced metastasis. The median follow-up was 6.3 years.

The researchers confirmed that AS appears safe in patients at low risk and in select patients at intermediate risk, particularly those with GS 6 and PSA greater than 10 ng/ml.

Metastasis developed in 3% (30 of 980) of patients. Of the 980 patients, 211 were classified at intermediate risk. Fifteen died of prostate cancer and four died of another cause while 11 were living with metastases at the close of the study. Metastases developed in bone in 18 patients (60%) and in lymph nodes in 13 (43%). The risk of metastasis increased to ten percent (13 of 133) in patients with GS 7 disease.

Patients with elements of Gleason pattern 4 on diagnostic biopsy were at increased risk for eventual metastasis when treated with an initial conservative approach. "The presence of Gleason pattern 4 on diagnostic biopsy conferred a threefold to fourfold increased risk of metastatic disease," noted Dr. Klotz. "Such patients should be offered surveillance with caution. Further evaluation with MRI and/ or genetic biomarkers should be strongly encouraged if surveillance is elected as an option in these patients."

"The researchers may be overly optimistic about the safety of surveillance, particularly in patients with Gleason 7 disease," commented Michael O. Koch, MD, Chairman of the Department of Urology at Indiana University School of Medicine. "Since median follow-up was only 6.3 years, the number of patients with Gleason 7 disease in whom metastases develop will grow even further. As of now active surveillance would appear to be ill-advised in this group of patients."

"The reported rate of 3% is a best case scenario and it is likely that many more men have metastatic disease," observed Joel B. Nelson, MD, Professor and Chairman of the Department of Urology at the University of Pittsburgh Medical Center. "Active surveillance is obviously safe in men who do not progress. The task now is to avoid misclassification of disease as indolent when it is not and detect progression before it is too late."

Source: "Metastatic Prostate Cancer in Men Initially Managed with Active Surveillance," by Laurence Klotz - **(Toronto)** et al. The *Journal of Urology*, May 2016.

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Memorials

Robert (Barclay) Oliphant, Sept. 6, 2015

Brian Hammond (71), Jan. 5, 2016 - mCRPC

Peter Shaw, Jan. 28, 2016

Mike Talgoy (63), April19, 2016 - mCRPC

Paul Toonstra (72), April 23, 2016

Tom Roberts (62), May 15, 2016 - mCRPC

The beauty
of days gone by …
Is the memory
that lives on forever.

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2016 MEETINGS

The September meeting will be held at the Caboto Centre at 1055 Wilkes Avenue
Sept. 15 Prostate Cancer Awareness Evening
Presenters: Dr. D. Drachenberg
& Dr. M. Kristjanson
Topic: General overview of prostate cancer & treatments

Oct. 20 Dr. Timothy Hiebert, Internist/Geriatrician
Topic: WRHA Palliative Care Program
Nov. 17 Party Time with musician Kirk Leavesley
Pizza, Cookies, Coffee and Conversation
Dec. No Meeting. No Newsletter.

All meetings (except September) will be held at our new location: **Cindy Klassen Recreation Complex at 999 Sargent Avenue**
All meetings are 7 – 9 pm. *Everyone Welcome*

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