Participant Information and Consent Form

A Phase II Randomized Pilot Study of Low Dose Rate compared to High Dose Rate Prostate Brachytherapy for Favourable Risk and Low Tier Intermediate Risk Prostate Cancer

BCCA Principal Investigator: Dr Juanita Crook, Centre for the Southern Interior
Telephone: 250 712 3958

Co-investigators at Centre for the Southern Interior (Telephone: 250 712 3900)
Dr François Bachand: Radiation Oncologist
Dr David Kim: Radiation Oncologist
Dr David Petrik: : Radiation Oncologist
Dr Deidre Batchelar : Physicist
Matt Schmid MSc : Physicist
Marie Pierre Milette : Physicist
Cynthia Araujo : Physicist
Michelle Hilts : Physicist

Co-investigators at Kelowna General Hospital
Dr Terry Bainbridge: Pathology
Dr Brenda Farnquist: Radiology

Sponsors: British Columbia Cancer Foundation

For emergencies only: Call the centre nearest you and ask for your study doctor or, if he or she is not available, ask for your usual oncologist or the oncologist on-call

Emergency Contact Number (24 hours / 7 days a week): 250 862 4000

Non-Emergency contact numbers are noted at the end of this document under the section heading "Contact".

1. Invitation:

You are being asked to participate in this study because you have been diagnosed with prostate cancer that is of intermediate risk and you have expressed interest in treatment by brachytherapy, a form of internal radiotherapy.

2. Your Participation is Voluntary

Your participation in this clinical study is entirely voluntary. You may decide not to participate or you may withdraw at any time and your doctors will continue to offer you the best available treatment without any negative consequences to the medical care, education, or other services to which you are entitled or are presently receiving.

You should be aware that there is a difference for both you and your doctor between being a patient and being a research participant. As a patient all medical procedures and treatments are carried out for your benefit only according to standard accepted practice. As a research participant you and your doctor also must take into account the requirements for the research study. These may include procedures and treatments that are not part of standard practice or are not yet proven. This consent form describes the diagnostic and treatment procedures that are being carried out for research purposes. Please review the consent document carefully when deciding whether or not you wish to be part of the research and sign this consent only if you accept being a research participant.

If you wish to participate in this study, you will be asked to sign this form.

Please take time to read the following information carefully and to discuss it with your family, friends, and doctor before you decide.

3. Who is conducting this study?

This study is being conducted by the Prostate Cancer Brachytherapy Group of the BC Cancer Agency Center for the Southern Interior. This group is comprised of Radiation Oncologists and Physicists with special expertise in prostate brachytherapy. In addition, there is collaboration with the departments of radiology and pathology at the Kelowna General Hospital. This study is in part supported by donor funds from the BC Cancer Foundation but is not receiving

funds or sponsorship from any external agency. The company providing the genetic testing is not providing funding for the study.
Neither the BC Cancer Agency nor any of the investigators or staff conducting this study will receive any personal payments for conducting this study.

4. **Background:**

For men who are otherwise suitable for brachytherapy and who have chosen brachytherapy as their preferred treatment option, there are 2 types of brachytherapy available. The standard type of brachytherapy in British Columbia is a permanent seed implant where tiny radioactive seeds containing a radioactive isotope called Iodine-125 are permanently implanted in the prostate, under ultrasound guidance while you are asleep under anaesthesia. Over the next 6 months these seeds deposit a very high and effective dose of radiation into the prostate. This type of brachytherapy has been available in BC for over 15 years. It is highly effective and is considered the standard of care.

An alternative type of brachytherapy is known as “HDR” or “high dose rate”. This is performed in a similar fashion, under anaesthesia and ultrasound guidance but treatment is delivered very rapidly over a 15-20 minute period and no radioactive material is left in the prostate. When this type of brachytherapy is used, it is necessary to do the procedure twice, at 2 separate sessions about 2 weeks apart. Presently in British Columbia, this type of brachytherapy has only been used when combined with 4 weeks of external radiation.

In this randomized feasibility study we will be comparing the 2 types of brachytherapy, when used alone without the addition of external radiation. Studies have indicated that the HDR brachytherapy is effective when used alone to treat your type of prostate cancer but it has not been directly compared to the standard permanent seed implant. Ultimately we want to determine if there are any advantages of one type over the other, specifically in how quickly men recover from their treatment.

As part of this study you will have an advanced imaging study of the prostate done for the purposes of staging the cancer. This test is called a multi parametric MRI

and in the majority of cases allows your doctor to see the tumour within the prostate and determine if it extends beyond the capsule of the prostate. These images will be electronically fused (or overlaid) on the ultrasound images which are used to plan your brachytherapy to ensure that there is optimal dose coverage of the actual cancer.

An optional component of this study involves getting a biopsy of the area of the prostate identified on MRI to see if this differs from what was found on your initial diagnostic biopsies. This would be done while you are asleep for your brachytherapy procedure and would be sent initially to the Kelowna General Hospital Pathology department for examination to confirm that your cancer was accurately sampled, and subsequently the biopsy material would be sent for genetic testing to see if the genetic profile of your cancer has an effect on how you respond to treatment. You may participate in this study comparing the two types of brachytherapy but decline the biopsy part of the study if you wish. There is a separate Consent Form and signature sheet for this part of the study.

60 men will be invited to participate in this initial feasibility phase of the protocol. It is expected that this will take about 18 months to complete. It is hoped that we will be able to expand to a total of 200 after this initial phase is completed.

5. Purpose

A “pilot study” is done to test the study plan and to find out whether enough participants will join a larger study and accept the study procedures. This type of study involves a small number of participants, in this case 60, and so it is not expected to be able to prove safety or effectiveness. These will be monitored but there is already a lot of experience with the safety and effectiveness of the “new” HDR treatment. The results may be used as a guide for a larger study, although there is no guarantee that it will be conducted. Participation in this pilot study does not mean that you would be eligible to participate in a future larger study. Knowledge gained from pilot studies may be used to develop future studies that may benefit others.

This Pilot Study has a randomized Phase II study design. A Phase II study is a study of a new treatment (in this case HDR brachytherapy) which is being compared to a standard treatment (in this case LDR brachytherapy) to confirm its effectiveness, monitor side effects, and collect information to determine whether it should have a larger role in the management of prostate cancer in BC. HDR prostate brachytherapy is relatively new in British Columbia but it is not experimental and is considered standard in other parts of Canada, North America and Europe. The randomized design means that neither you nor your doctor will be able to choose which treatment you receive. The treatment will be selected by a process of randomization equivalent to flipping a coin. You have an equal chance of receiving either the standard LDR brachytherapy or the new HDR brachytherapy procedure.

The main purpose of this study is to evaluate your symptoms and recovery time after brachytherapy for prostate cancer. The 2 different ways of administering brachytherapy are summarized below.

Low dose rate brachytherapy (seed implant)

The standard in British Columbia since 1998 is the permanent implantation of radioactive seeds under anaesthesia. These deliver the required radiation dose over a 6 month period. The standard seed implant requires only a single procedure for seed placement, but 2-6 weeks before the procedure you must undergo a transrectal ultrasound of the prostate to obtain images for planning the implant, and 4 weeks after the implant you must return for imaging studies to confirm adequate seed placement .

High dose rate brachytherapy

The alternate type of brachytherapy is called high dose rate or HDR and involves implanting an array of needles into the prostate while you are asleep under anaesthesia. To deliver treatment, a single seed containing a high amount of radioactivity travels sequentially through each needle delivering the required radiation dose over a 10-15 minute period. The needles are then removed and no radioactivity remains in the body. This type of brachytherapy has been offered in

British Columbia at the Center for the Southern Interior since 2011 but up until now has only been used as a "boost" in combination with external beam radiotherapy. **When HDR brachytherapy is used, 2 procedures under anaesthesia are required, 2 weeks apart, but no planning or follow up imaging studies are required**.

This is a Phase III randomized study. This means that if you consent to participate you do not choose which type of brachytherapy you will receive. Your treatment will be randomly assigned by a process similar to the flip of a coin, so that you have a 50:50 chance with each of the 2 types of brachytherapy.

No patients in this trial will receive either external beam radiation or hormonal therapy in addition to the brachytherapy.

An MRI scan will be offered to all participants in this study to help localize the site of the cancer within the prostate. This will help in planning the radiation and in the dose delivery.

6. Who Can Participate in this Study

You may participate in this study if:

- You fully understand the study and give your informed consent to participate as demonstrated by signing this consent form.
- You have already chosen brachytherapy as the desired form of treatment for your prostate cancer.
- You have either a stage T1 or T2 prostate cancer, that is intermediate (Gleason 7 and/or PSA 10-20 ng/ml, and /or T2B) or favourable (Gleason 6 or less, PSA less than 10 ng/ml, T1c/T2a)
- You are fit for a general or spinal anaesthetic.

7. Who Should Not Participate In This Study?

You should not participate in this if:

- You are not technically suitable for brachytherapy (prostate too big, severe urinary troubles)
- You are unable to have an anaesthetic

- You are on blood thinners which cannot be safely stopped for the brachytherapy procedure
- You are not able to return for the follow-up appointments which are done for this study.
- You are claustrophobic or unable to have an MRI scan.

8. What does the Study Involve?

Both types of brachytherapy are performed in an operating room or procedure room, under general or spinal anaesthesia. During the procedure transrectal ultrasound is used to visualize the prostate so that the needles can be accurately placed according to the radiation plan. The procedure takes 1.5 to 2 hours. It is an out-patient procedure meaning that you are able to return home the same day after a period of monitoring in the Recover Room.

Study Procedures

A: Procedures required for <u>everyone</u> having prostate brachytherapy: BEFORE

- Measurement of serum PSA and testosterone (blood test)
- Measurement of hemoglobin, blood sugar, coagulation test, liver and kidney function in preparation for anaesthesia
- ECG and Chest X-ray
- Trans-rectal ultrasound mapping study to determine prostate size and the required number and arrangement of radioactive seeds or needles
- Prostate MRI to visualize the location of the cancer within the prostate

B: Procedures required for everyone having LDR prostate brachytherapy: AFTER

ONLY for patients having the LDR permanent seed implant:

One month after the seed implant, patients will undergo:

- Chest X-ray
- Pelvic X-ray
- CT scan of prostate

Fax 250.370-8296

399 Royal Avenue
Kelowna, BC, Canada V1Y 5L3
www.bccancer.bc.ca

Tel: 250.712.3900
Toll free: 1.888.563.7773
Fax: 250.712.3911

- MR (Magnetic Resonance) scan of prostate

These tests are done for quality assurance to check the position of the seeds within the prostate. These tests are **NOT** required for patients having HDR brachytherapy because there is no radioactive material left in the prostate. However, the men receiving HDR brachytherapy come back for a second brachytherapy procedure two weeks after the first one.

For all patients in the study:

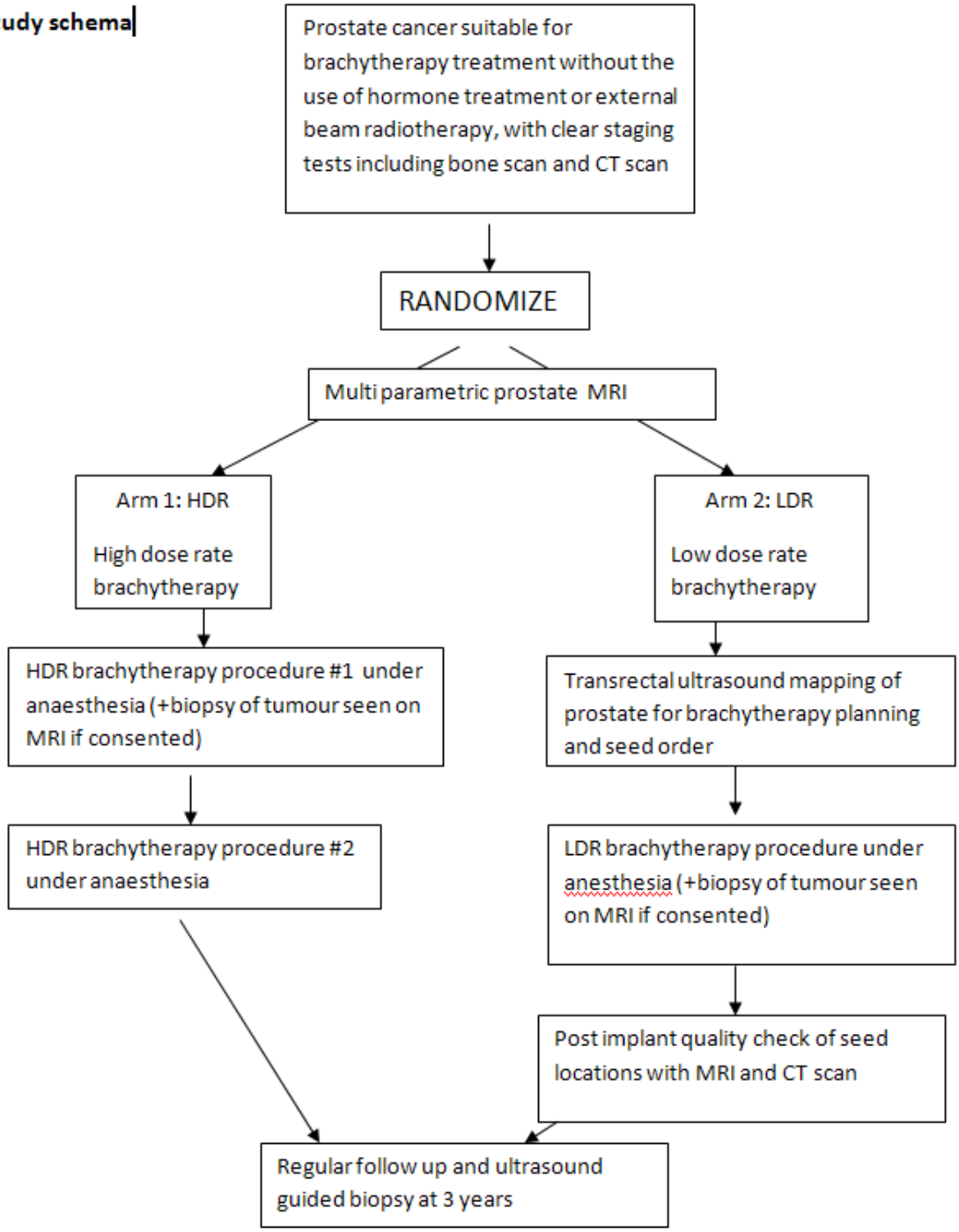
- Periodic clinic visits (the timing may change depending on you and your physician's preferences) . These are generally at 1 month, 3 months and 6 months after the procedure and then every 6 months to 3 years and then annually to 10 years
- Blood work at clinic visits checking your PSA and testosterone levels
- Questionnaires at clinic visits asking you about your urinary, bowel and sexual function
- Ultrasound-guided biopsy of the prostate 3 years after treatment to verify that the treatment has been effective

C: Procedures required that are additional for participants in this study

- Prostate MRI in the past has only been offered to selected intermediate and high risk patients but will be available to all participants in this study.
- Biopsies of the cancerous lesion in the prostate as seen on MRI are not routine and neither is genetic testing of the cancer to determine aggressiveness. If you consent to this **optional part of the protocol,** the biopsies will be performed while you are under anaesthesia, as part of your brachytherapy procedure. The results of the genetic profile will not alter your treatment. There is a separate consent form for the biopsy of the prostate that is done during the brachytherapy procedure .
- Follow up biopsy of the prostate 3-years after treatment to assess whether the cancer is gone

If you have any questions about this study you can contact your study doctor whose phone number is at the end of this document.

Study schema



Fax 250.370-8296

399 Royal Avenue
Kelowna, BC, Canada V1Y 5L3
www.bccancer.bc.ca

Tel: 250.712.3900
Toll free: 1.888.563.7773
Fax: 250.712.3911

9. What are my responsibilities?

Since the primary objective of this study involves a comparison of your quality of life after treatment, filling out the questionnaires at each visit is important. If you are unable to attend a clinic visit at the required time, the questionnaire can be mailed to you and returned by post to your study doctor.

10. What are the possible harms and benefits?

Radiation treatment to the prostate can be associated with changes to bladder, bowel and sexual function. Delivering radiotherapy in the form of brachytherapy minimizes the risk of long term side effects because the radiation is delivered directly into the prostate from the "inside out". Nonetheless, symptoms may occur related to any of these bodily functions. The types of side effects and approximate frequencies are listed below. The goal of this study is to compare the severity, frequency and duration of side effects from these 2 types of brachytherapy treatment.

Early side effects (1st 3 months)
Urinary urgency, frequency and burning: common > 50%
Urinary retention (needing a catheter) < 10%
Blood in the urine (<5%)
Increased frequency of bowel movements: < 20%
Decreased volume of semen: common > 50%

Later side effects (after 3 months)
Urinary urgency, frequency or burning: 20%
Urinary retention < 5%
Blood in urine: < 1%
Increased frequency of bowel movements: <5%
Blood with bowel movements < 5%
Decreased volume of semen: common ~ 100%
Decreased erections: 20%

Reproductive Risks

Because the prostate will be receiving radiation and is located close to the testicles where sperm are produced, you should not father a baby for one year after your brachytherapy treatment. An effective method to avoid pregnancy should be used. If your partner is pregnant you will not be offered participation in this protocol.

Risks of prostate biopsy

You already had an ultrasound guided biopsy of the prostate which determined that you have prostate cancer. The repeat biopsy at the time of the brachytherapy procedure is to establish that the cancerous area that was seen on the MRI shows the same characteristics as the tissue obtained in your original biopsy.
The biopsy scheduled for 3 years after treatment is to make sure that all traces of the cancer are gone.
Biopsies can be associated with pain or discomfort, bleeding and infection. Antibiotics are given before and after the biopsy to minimize the risk of infection and your blood is checked to make sure you don't have an increased risk of bleeding.

11. **What are the potential benefits of participating**?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope the information learned from this study will help other patients in the future.
The advanced imaging with multi parametric MRI may provide additional information about your cancer that can help in designing an optimal brachytherapy plan for you.

The overall results of the study may help to establish HDR brachytherapy as a standard of care in British Columbia which may benefit men with your type of prostate cancer in the future.

The results of the genetic profile of your cancer will not alter your treatment but may help to select more aggressive or less aggressive treatment for other men in the future.

12. **Alternative Treatments**

If you decide not to participate you will continue to be followed at the Cancer Center and offered the best standard of care. You could undergo anti-hormone therapy with LHRH agonist injections +/- anti androgen pills, LDR brachytherapy alone (off-study) or external beam radiotherapy, or you could choose to do nothing at all and just be monitored.

13. **What If new Information Becomes Available That May Affect My Decision to Participate?**

If new information becomes available that could affect your decision to participate, you will be informed of this and given the opportunity to withdraw.

14. What happens if I decide to withdraw from the study?

You may withdraw from this study at any time without giving reasons. If you decide to withdraw you will continue to be followed at the Cancer Center and offered the best standard of care. All information about you collected up to the point of your withdrawal will be retained for analysis in order to protect the integrity of the research, which may benefit future research participants and patients. However, no further information will be collected.

If your participation in this study includes enrolling in any optional studies or long term follow-up, you will be asked whether you wish to withdraw from these as well.

15. ***Can I Be Asked to Leave The Study*?**

If you are unable to comply with the schedule of study visits this will be discussed with you and a decision reached as to whether you wish to stay in the study.

16. **How will my taking part in this study be kept confidential?**

Your confidentiality will be respected. However, research records and health or other source records identifying you may be inspected in the presence of the Investigator or his or her designate by Health Canada, and the UBC BCCA Research Ethics Board for the purpose of monitoring research. No information or

records that disclose your identity will be published without your consent, nor will any information or records that disclose your identity be removed or released without your consent unless required by law.

You will be assigned a unique study number as a subject in this study. Only this number will be used on any research-related information collected about you during the course of this study, so that your identity [i.e. your name or any other information that could identify you] as a subject in this study will be kept confidential. Information that contains your identity will remain only with the Principal Investigator and/or designate. The list that matches your name to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law. Your birth date will also be provided if requested by the sponsor or responsible regulatory agency.

Reports concerning your progress and photocopies of certain portions of your medical record, identified by a study code only, may also be sent to:

UBC BCCA Research Ethics Board, the research ethics committee that oversees the ethical conduct of this study in your centre
Health Canada

Information in these reports may include:

Tests results
Reports of operations
Images from your ultrasound tests
Results of your treatment
Laboratory tests
Reports from your questionnaires
Imaging tests/reports

Your family physician will be notified of your participation in the trial so that your study doctor and your family doctor can provide proper medical care.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to insure that your privacy is respected and also give you the right of access to the information about you that has been provided to the sponsor and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request to your study doctor or the UBC BCCA Research Ethics Board.

17. **What If Something Goes Wrong?**

By signing this form, you do not give up any of your legal rights and you do not release the study doctor, participating institutions, or anyone else from their legal and professional duties. If you become ill or physically injured as a result of participation in this study, medical treatment will be provided at no additional cost to you. The costs of your medical treatment will be paid by your provincial medical plan

In case of a serious medical event, please report to an emergency room and inform them that you are participating in a clinical study and that the following person can then be contacted for further information: Dr._____ at telephone number: _____

18. **What will the study cost me?**

All research-related care and treatment will be provided at no cost to you. You will not be paid for participating in this study. In the event of a research related injury, please speak to your doctor (indicated above) or (after hours) call the BCCA centre nearest you and ask for your study doctor or, if he or she is not available, your usual oncologist or the oncologist on call.

19. **Whom do I contact if I have questions about the study during my participation?**

You understand that if you have any questions or desire further information with respect to this study, or if you experience any adverse effects, you can ask your doctor, who is _____ at 250 712 2000 or the principle investigator of the study who is Dr. Juanita Crook Telephone: 250 712 3958

Or, you can speak to the Head Radiation Oncology Program of the Center for the Southern Interior, BC Cancer Agency. That person can be reached at 250 712 2000 or 250 862 4000

20. Who do I contact if I have any questions or concerns about my rights as a participant?

If you have any concerns about your treatment or rights as a research subject you may contact the Research Subject Information Line at the UBC Office of Research Services at the University of British Columbia at (604)-822-8598 or toll free at 1-877-822-8598, or by email to RSIL@ORS.ubc.ca

21. After the study is finished

After the treatment and follow up period are completed you will continue to be followed as per standard prostate cancer management.

Fax 250.370-8296

399 Royal Avenue
Kelowna, BC, Canada V1Y 5L3
www.bccancer.bc.ca

Tel: 250.712.3900
Toll free: 1.888.563.7773
Fax: 250.712.3911

Subject Consent for Randomization to HDR brachytherapy or LDR seed brachytherapy:

My signature on this consent form means:

- I have read and understood the information in this consent form.
- I have had enough time to think about the information provided.
- I have been able to ask for advice if needed.
- I have been able to ask questions and have had satisfactory responses to my questions.
- I understand that all of the information collected will be kept confidential and that the results will only be used for scientific purposes.
- I understand that my participation in this study is voluntary.
- I understand that I am completely free at any time to refuse to participate or to withdraw from this study at any time, and that this will not change the quality of care that I receive.
- I authorize access to my health records as described in this consent form.
- I understand that I am not waiving any of my legal rights as a result of signing this consent form.
- I understand that there is no guarantee that this study will provide any benefits to me.

I will receive a signed copy of this consent form for my own records.
I consent to participate in this study.

_____	_____	_____
Subject's Signature	Printed name	Date

_____ ____	_____	_____ ____
Signature of Person Obtaining Consent	Printed name	Study Role Date

Fax 250.370-8296

399 Royal Avenue
Kelowna, BC, Canada V1Y 5L3
www.bccancer.bc.ca

Tel: 250.712.3900
Toll free: 1.888.563.7773
Fax: 250.712.3911

If this consent process has been done in a language other than that on this written form, with the assistance of an interpreter/translator, indicate:
Language:_____

Was the subject assisted during the consent process in one of ways listed below?
□ Yes □ No

If yes, please check the relevant box and complete the signature space below:
□ The consent form was read to the subject, and the person signing below attests that the study was accurately explained to, and apparently understood by, the subject (please check if subject is unable to read).
□ The person signing below acted as an interpreter/translator for the subject, during the consent process (please check if an interpreter/translator assisted during the consent process).

_____	_____	_____
Signature of Person Assisting in the Consent Discussion	Printed Name	Date

_____	_____	_____
Investigator Signature	Printed name	Date

My signature above signifies that the study has been reviewed with the study participant by me and/or by my delegated staff. My signature may have been added at a later date, as I may not have been present at the time the participant's signature was obtained.

Fax 250.370-8296

399 Royal Avenue
Kelowna, BC, Canada V1Y 5L3
www.bccancer.bc.ca

Tel: 250.712.3900
Toll free: 1.888.563.7773
Fax: 250.712.3911