BC Cancer Agency
CARE & RESEARCH

Participant Information and Consent Form

Androgen Suppression with Stereotactic Body or External Beam Radiation Therapy (*ASSERT)*

A Phase II randomized trial for intermediate and high risk prostate cancer

Principal Investigators: Dr. Abraham Alexander
BC Cancer Agency, Vancouver Island Center
Phone: 250-519-5575

Dr. Winkle Kwan
BC Cancer Agency, Fraser Valley Center
Phone: 604-930-4085

Co-Investigators: Dr. David Kim
BC Cancer Agency, Center for the South Interior
Phone: 250-712-3958

Dr. Boris Valev
BC Cancer Agency, Center for the North
Phone: 250-645-7335

Dr. Gaurav Bahl
BC Cancer Agency, Abbotsford Center
Phone: 604-851-4742

Sponsors: This study is supported by grants from the CARO Uro-Oncologic Radiation Awards (ACURA) and from AstraZeneca Canada

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.

Vancouver Centre	(604) 877-6000
Vancouver Island Centre	(250) 370-8000
Fraser Valley Centre	(604) 581-2211
Abbotsford Centre	(604) 851-4700
Centre for the Southern Interior	(250) 862-4000
Centre for the North (Prince George)	(250) 645-7300

For non-emergency contact numbers: See sections 19

1. Invitation

You are being invited to take part in this research study because you have prostate cancer and you will receive radiation treatment for the cancer.

2. Your participation is voluntary

Your participation is voluntary. You have the right to refuse to participate in this study. If you decide to participate, you may still choose to withdraw from the study at any time 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 Department of Radiation Oncology at the British Columbia Cancer Agency (BCCA). The study is being supported by grants from the Canadian Association of Radiation Oncologists ACURA Award and from AstraZeneca Canada

4. Background

Prostate cancer is one of the most common cancers in men. Treatment options for prostate cancer may include either surgery or radiotherapy. For participants who choose to be treated with radiotherapy, their disease can be treated with various combinations of implanted radioactive seeds (“Brachytherapy”) and external beam radiation (high energy X-rays) in British

Columbia. Androgen deprivation therapy (ADT or "hormonal treatment") which suppresses male hormone production is frequently added to the radiation for better disease control.

For participants who do not want Brachytherapy, treatment with external beam radiotherapy delivers the radiation in daily "fractions" Monday to Friday. Various "standard" radiation fractions are used in the BC Cancer Agency. They vary from 28 fractions to 35 or 38 fractions. This study compares the standard 28 fraction external beam radiotherapy with a new form of radiation called the *Stereotactic Ablative Radiotherapy (SABR)*.

SABR is a form of external beam radiation delivered with sharper beam margins, made possible by technological advances. As a result, the surrounding organs should receive lower doses of scattered radiation, allowing doctors to finish the radiotherapy in fewer daily fractions. Recent medical literature suggests that the radiotherapy can be delivered in 5 – 7 fractions instead of the usual more than 20 fractions and the success rates and side effects of this new treatment appear to be about the same as the standard radiotherapy delivered in 25 – 40 daily fractions. While SABR is promising, full treatment reports have only been published in about 1,000 patients in the English literature. There are no published results comparing SABR directly with standard longer fractionations.

This current study has two treatment groups:
1. Half of the participants will receive external radiation delivered in the standard 28 daily fractions Monday to Friday (standard arm), and
2. The other half will receive external radiation delivered by SABR over 5 fractions, given approximately once a week (SABR arm).

If you agree to participate in this study, you will be randomly assigned to receive one of these two treatments. You cannot choose which one you will receive. Study participants must be randomly assigned to a treatment group to ensure that the 2 groups are being compared fairly. This ensures that meaningful results will be produced at the end of the study.

5. What is the purpose of the study?

This is a Phase II study. A Phase II study is undertaken after preliminary safety testing on a treatment. It is usually conducted on a small number of individuals (100-300 persons), and its goal is to begin to find out what effect it has on your cancer and to further evaluate its safety.

The current study has two main purposes:
1. It will try to determine what proportion of subjects who are suitable for the study will agree to participate, and
2. It will estimate the side effects of the new radiation technique (SABR) to allow design of a bigger study in the future.

6. Who can participate in this study?

You may be able to participate in this study if*:*

- You are diagnosed with "intermediate" or "high risk" prostate cancer. The risk category of a prostate cancer is dependent on the stage of disease, its PSA level at diagnosis and how aggressive the biopsy tissue appears under the microscope (measured by a score called the "Gleason score"). Your cancer doctor can explain to you in details how this risk classification system works.
- Your cancer shows no signs of spread outside the prostate
- You are of reasonable health with a life expectancy of at least 5 years
- There is no reason for not treating you with androgen deprivation therapy (ADT or hormonal treatment)

7. Who should not participate in this study?

You will not be eligible to participate in this study if:

- There is evidence of cancer spread beyond the prostate
- Your prostate is too large (larger than 90 cc) because a large prostate cannot be well planned with the techniques required for SABR
- You had a history of inflammatory bowel disease. Examples of common inflammatory bowel diseases are Crohn's disease and ulcerative colitis. This is because inflammatory bowel diseases can make one more susceptible to radiation effects. You should check with your cancer doctor if you are not sure.
- You have had radiation treatment to the pelvis
- You have an artificial hip or a metal reconstruction of your hip. This is because metals in an artificial hip make estimation of the radiation dose to the prostate difficult.
- You were diagnosed with other cancers less than five years ago. However, you can still participate if your cancer has not come back for five or more years, or if your cancer was only some relatively slow growing skin cancers such as "basal cell cancer" or "squamous cell cancer" of the skin.

8. What does the study involve?

If you agree to participate in the study, you will receive one of the two radiation treatments listed below. The process for assigning which treatment you will have is random (like flipping a coin) with equal chance of getting either treatment. Neither you nor your doctor can choose which treatment you will get but it will be assigned in a random way by a computer.

1. Standard radiotherapy over 28 daily fractions, given one fraction (one treatment) per day, five days a week, or

2. Stereotactic Ablative Radiotherapy (SABR) over 5 daily fractions, given one fraction (one treatment) per week

The 28 fraction radiotherapy is one of the standard ways of delivering radiation in the B.C. Cancer Agency. Subjects receive one radiotherapy treatment (one fraction) every day Monday to Friday. The total course of treatment will therefore last 5 ½ weeks.

The 5 fraction SABR is new to the B.C. Cancer Agency. Subjects receive one radiotherapy treatment for one day every week. The total course of treatment will last about 5 weeks (but with only one treatment day every week).

All subjects will receive hormonal therapy to suppress their male hormone production. This is because such hormonal treatment has been shown to improve cancer control. Hormonal therapy together with radiation is standard therapy for your stage of disease. The duration of hormonal treatment varies depending on whether you have "intermediate" or "high" risk prostate cancer. Your doctor can provide further information on the duration of hormonal treatment which is not the subject of the current study.

Preparation for radiotherapy in all subjects involves a session called "simulation". Simulation is a process which allows the doctor to plan the radiotherapy. A CT scan will be done during simulation and little tattoo marks will be placed in the lower abdomen and hips to help direct the radiotherapy. While the technical process of radiotherapy planning after simulation is very different between the two arms of treatment, the process as experienced by the subject during simulation is the same. The only difference is that if you are going to receive SABR, three gold seeds (called fiducials) will be inserted into the prostate before simulation so that the targeting of the radiotherapy beams can be more accurate. If you are assigned to receive standard 28 fraction radiation, the gold seeds may or may not be used depending on the preference of your doctor.

All subjects will be required to complete questionnaires prior to radiotherapy, during radiotherapy, and at their follow up appointments. These questionnaires seek to collect information about side effects of treatment and how subjects feel regarding their quality of life. They include the following:
1. The *International Prostate Symptom Score (IPSS)* questionnaire consisting of 8 questions on urinary control
2. The *Expanded Prostate Index Composite (EPIC)* questionnaire consisting of 32 questions on quality of life.

Once radiotherapy treatment starts, subjects will be seen by their doctors at week 5 of the radiation treatment, and after the radiation at 2 weeks, 8 weeks, 6 months, 12 months, 18 months, 24 months then yearly for assessment of cancer control and treatment related side effects. Subjects will be followed for 5 years in this study. Questionnaires will be completed in these follow up appointments. The schema below outlines the study procedures, the tests

involved and the questionnaires needed for each appointment. Your doctor may decide to see you more often if it is regarded necessary to do so depending on your clinical condition.

Schema of clinic visits associated with this study

Assessments & Procedures	**Registration and pre-registration**	**Within 6 weeks before RT start Date**	**During Radiation**	**Follow ups (2 weeks, 8 weeks, every 6 months until 2 years, yearly until year 5)**
Biopsy	**X Within 365 days**			
History/physical	**X Within 60 days**			
PSA/testosterone	**X Within 90 days**		**X Within 1 week Before RT starts**	**X**
CT/Bone scans	**X Within 90 days**			
NCI CTCAEv4 & Modified RTOG/SOMA		**X**	**Week 5**	**X**
IPSS	**X**	**X**	**Week 5**	**X**
EPIC		**X**	**X**	**X**
Doctor's assessment	**X Within 60 days**		**Week 5**	**X**

Research or study related procedures
This paragraph outlines the procedures, tests or clinic appointments you would be asked to have if you are in the study compared to standard radiation treatment outside the study:

1. Gold seed marker (fiducials) placement for directing the radiation is mandatory if you are randomized to the SABR treatment, but optional for the standard 28 fraction treatment. The fiducials allow radiotherapy to be delivered more accurately, and in some centers are considered part of standard procedure for regular radiotherapy of the prostate. They are placed under local anaesthesia in a process similar to doing a biopsy except that no tissue is taken. The procedure can cause temporary local discomfort, some slight bleeding in the urine and carries a small (<5%) risk of infection. They will be left permanently inside the prostate even after the treatment. They are not known to cause any discomfort or pain once they have been successfully placed.

2. Completion of the various questionnaires during follow up appointments. These can take an extra 15-30 minutes each time but can be done while you are waiting to see your doctor. The questionnaires ask you if you have problems in passing urine, having bowel movements or having sexual intercourse. We encourage you to answer all questions but if there are questions you don't feel comfortable about, you do not have to answer them.

9. What are my responsibilities?

If you agree to participate in the study, you will be expected to undergo the treatment assigned by the randomization process. If you are getting SABR treatment, you should accept the use of gold seed marker placement. We also expect that you agree to complete the questionnaires required for the study.

10. What are the possible harms and discomforts?

The 28 fraction radiotherapy in this study is one of the standard ways of delivering the radiation for your cancer and the possible harms of such treatment will be explained to you by your doctor.

The 5 fraction SABR treatment has not been done in British Columbia. While similar treatments have been delivered in other major centers in the world, including some other Canadian centers, published results of this form of radiation in prostate cancer are still limited.

It is possible that SABR radiation for prostate cancer will not be as effective as standard radiation. Potential side effects of SABR treatment are the same as those that can be associated with standard 28 fraction radiation although the chance for you developing these side effects could be either higher or lower than standard treatment. These side effects include:

1. Urinary toxicity
    a. Burning sensation on urination
    b. Weakness of urinary stream
    c. Passing blood along with urine
    d. Inability to pass urine
2. Bowel toxicity
    a. Diarrhoea
    b. Painful bowel movements
    c. Passing blood in stools
    d. Pain or discomfort at the anus
3. Feeling tired during and after radiotherapy
4. Erection problems after radiation

Very serious complications including severe bleeding requiring transfusion, persistent inability in passing urine requiring long term catheter or surgery, and fistula formation (an abnormal passage) between the bladder and bowel can develop but are very rare (< 1%) in published medical literature. However, because worldwide experience in SABR is much more limited than standard treatment given daily over 4 or 5 weeks, doctors are less certain of the frequency of these serious complications. It is also possible that there are side effects of SABR radiation still unknown to the doctors at this time.

The SABR treatment requires placement of gold seed fiducials. This procedure is also done sometimes when standard 28 fraction radiation is used but will be mandatory for the 5 fraction SABR. The procedure is very well established and side effects include transient mild to moderate local pain, some bleeding in the urine for a day or two, and infection of the urine and blood. Infection happens only in < 5% of subjects.

11. What are the potential benefits of participating?

No one knows whether or not you will benefit from this study. There may or may not be direct benefits to you from taking part in this study.

We hope that the information learned from this study can be used in the future to benefit other people with a similar disease.

12. What are the alternatives to the study treatment?

If you choose not to participate in this study or to withdraw at a later date, the following treatment options may be available to you:

- Standard external radiation given over 28 – 38 fractions
- Prostate seed implantation (Brachytherapy) used alone or combined with external radiation
- Surgery (removal of the prostate)

You can discuss these options with your doctor before deciding whether or not to participate in this research project.

13. What if new information becomes available that may affect my decision to participate?

If you choose to enter this study and at a later date a more effective treatment becomes available, it will be discussed with you. You will also be advised of any new information that becomes available that may affect your willingness to remain in this study.

14. What happens if I decide to withdraw my consent to participate?

You may withdraw from this study at any time without giving reasons. If you choose to enter the study and then decide to withdraw at a later time, 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.

You may withdraw from this study at any time without giving reasons. If you choose to enter the study and then decide to withdraw at a later time, you have the right to request the withdrawal of your information collected during the study. This request will be respected to the extent possible. If you would like to request the withdrawal of your data, please let your study doctor know.

15. Can I be asked to leave the study?

If you are not able to follow the requirements of the study or for any other reason, the study doctor may withdraw you from the study and will arrange for your care to continue. On receiving new information about the treatment, your research doctor might consider it to be in your best interests to withdraw you from the study without your consent if they judge that it would be better for your health. If you are asked to leave the study, the reasons for this will be explained to you and you will have the opportunity to ask questions about this decision.

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 by representatives of Health Canada and the BC Cancer Agency Research Ethics Board for the purpose of monitoring the 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 participant in this study. This number will not include any personal information that could identify you (e.g., it will not include your Personal

Health Number, SIN, or your initials, etc.). Only this number will be used on any research-related information collected about you during the course of this study, so that your identity 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 rights to privacy are legally protected by federal and provincial laws that require safeguards to insure that your privacy is respected.

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

17. What happens 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. Winkle Kwan at telephone number 604-930-4085, or Dr. Abraham Alexander at telephone number 250-519-5575.

18. What will the study cost me?

All research-related medical care and treatment and any related tests that you will receive during your participation in this study will be provided at no cost to you.

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

If you have any questions or desire further information about this study before or during participation, or if you experience any adverse effects, you can contact Dr. Winkle Kwan or Dr. Abraham Alexander or their representatives at: 604-930-4085 (Dr. Kwan), 250-519-5575 (Dr. Alexander).

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.

Or, you can speak to the doctors who are the principal investigator, Drs. Winkle Kwan and Abraham Alexander. Their telephone numbers are: 604-930-4085 (Dr. Kwan), 250-519-5575 (Dr. Alexander).

Or, you can speak to the Head of Radiation Therapy Program of the BC Cancer Agency. That person can be reached at 604-877-6193.

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

If you have any concerns or complaints about your rights as a research participant and/or your experiences while participating in this study, contact the Research Participant Complaint Line in the University of British Columbia Office of Research Ethics by e-mail at RSIL@ors.ubc.ca or by phone at 604-822-8598 (Toll Free: 1-877-822-8598).

21. After the study is finished

You may not be able to receive the study treatment after your participation in the study is completed. There are several possible reasons for this, some of which are:

- The treatment may not turn out to be effective or safe.
- The treatment may not be approved for use in Canada.
- Your caregivers may not feel it is the best option for you.
- You may decide it is too expensive and insurance coverage may not be available.
- The treatment, even if approved in Canada, may not be available free of charge.

Participant Consent

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.

_____	_____	_____
Participant's Signature	Printed name	Date

_____	_____	_____	_____
Signature of Person Obtaining Consent	Printed name	Study Role	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.

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 participant assisted during the consent process in one of ways listed below?

☐ Yes ☐ No [Note: For typical situations where the person conducting the consent discussion simply reads the consent with the participant to ensure that informed consent is properly obtained, check "no".]

If yes, please check the relevant box and complete the signature space below:

☐ The consent form was read to the participant, and the person signing below attests that the study was accurately explained to, and apparently understood by, the participant (please check if participant is unable to read).

☐ The person signing below acted as an interpreter/translator for the participant, 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