Supplementary

Appendix 1

Case Report Form (CRF)

Screening Visit

Patient study code: _____
Gender: male/female
Year of birth: _____
Date of visit (DD/MM/YYYY): _____

Eligibility Criteria
Inclusion Criteria

Yes	No	
□	□	Patient age >18, resectable pulmonary metastases without a more effective systemic therapy option (regardless of type of primary malignancy, excluding hematologic malignancies) with the primary malignancy already having been treated without evidence of local recurrence
□	□	Patient having single-organ metastasis to lung only (with the exception of colorectal CA with synchronous hepatic metastasis)
□	□	Tumors <5cm
□	□	Patient with no evidence of nodal disease on pre-treatment CT scan
□	□	Patient having adequate pulmonary function to tolerate lung resection (post-operative predictive FEV1≥40%).

Exclusion Criteria

Yes	No	
□	□	Patient having comorbidities not amenable to surgery
□	□	Patient with uncontrolled primary malignancy
□	□	Patient with hematologic malignancies (leukemia or lymphoma)
□	□	Patient having more than 5 tumors in one lung
□	□	Patient with prior history of thoracic radiation

Informed Consent

Yes	No	
□	□	The patient does meet the inclusion criteria
□	□	A signed informed consent form has been obtained

Informed Consent Signature Date (DD / MM / YYYY) : _____

https://dx.doi.org/10.21037/tcr-22-232

Baseline Visit

Patient study code: _____
Date of visit (DD / MM / YYYY): _____

Radiology:

CT chest _____ (DD / MM / YYYY)	□ No evidence of disease progression □ Evidence of disease progression. Please specify: _____

Circulating tumour cells

Date of blood work collected _____ (DD / MM / YYYY)	Results:

Primary Cancer

□	Soft tissue sarcoma	□	Melanoma	□	Gastric cancer
□	Colorectal cancer	□	Head and neck cancer Specify:	□	Other:
□	Renal cell carcinoma	□	Osteosarcoma		
□	Germ cell cancer	□	Breast cancer		
□	Gynecologic cancer Specify:	□	Hepatocellular cancer		

Date of resection of primary cancer (DD / MM / YYYY):
Final pathology of primary cancer: T _____ N _____ Margin: clear / positive

Pulmonary Metastases

Number of Nodules

□	Right upper lobe_____	□	Right middle lobe _____	□	Right lower lobe _____
□	Left upper lobe _____	□	Left lower lobe _____		

Biopsy performed?
□ No
□ Yes Location of nodule: _____ Date of biopsy: _____ Pathology: _____

https://dx.doi.org/10.21037/tcr-22-232

Medical History

Significant Medical History? □ Yes □ No	
System	Comments
Ear, Nose, Or Throat	
Ophthalmologic	
Cardiovascular	□ CHF Class. I □ II □ III □ IV □ □ Angina Class. I □ II □ III □ IV □ □ MI □ CABG □ Coronary Artery Disease □ Hypertension □ Hypercholesterolemia □ Other:
Respiratory	□ COPD Class. I □ II □ III □ IV □ Other: FEV 1: DLCO:
Gastrointestinal	
Neurological	
Genitourinary	
Musculoskeletal	□ Osteoarthritis □ Other:
Endocrine	□ Diabetes Insulin dependant Yes □ No □ □ Other:
Dermatologic	
Blood disorders	
Lymph Nodes	
Mental	
Pre-op Chemo/Radiation	Pre-op chemo Yes □ No □ Pre-op rad. Yes □ No □ Body site:
Other:	

Smoking Status		Smoking history
Never Smoked	Patient quit smoking? Yes □ No □	
Past Smoker		
Current Smoker	How long ago did patient quit smoking?	
No Information	# of □ years □ months □ days	# Pack years

CHF, Angina, and COPD Classification. Symptoms only with: Class I: severe or strenuous activity. Class II: moderate activity. Class III: light activity. Class IV: at rest

https://dx.doi.org/10.21037/tcr-22-232

Baseline

Patient study code: _____
Date of visit (DD / MM / YYYY): _____

Study Information:

Date of surgical resection (DD / MM / YYYY)	
Date of discharge (DD / MM / YYYY)	
Date Trial intervention commencement (DD / MM / YYYY)	
Research Coordinator Signature:	

Stereotactic Body Radiation Therapy (SBRT)

Patient undergoes SBRT delivered according to a risk-adjusted dose fractionation contingent on tumor size and location.

Study Information:

Date of SBRT (DD / MM / YYYY)	
Date of discharge (DD / MM / YYYY)	
Tumor characteristics	Size Location
Doses of Trial intervention (DD / MM / YYYY)	Dose other
Research Coordinator Signature:	

Post-Radiation Follow-up Clinic Visit (Re-evaluation post SBRT)

Patient study code: _____
Date of visit (DD / MM / YYYY): _____

A) Radiology:

CT chest _____ (DD / MM / YYYY)	□ No evidence of disease progression □ Evidence of disease progression. Please specify: _____

B) Circulating tumour cells

Date of blood work collected _____ (DD / MM / YYYY)	Results:

C) Surgical Resection

Proceed with surgical resection? □ Yes □ No. Please specify reason: _____

https://dx.doi.org/10.21037/tcr-22-232

Operation/Clinical Stage (Pre-Surgery)

Patient study code: _____
Date of operative procedure (DD / MM / YYYY): _____
Surgeon: □ Y. Shargall □ C. Finley □ W. Hanna □ J. Agzarian

Incision:
□ Open
□ MIS
□ VATS converted to open

If open:
□ Thoracotomy:
□ right □ left
□ post-lateral □ antero-lateral □ axillary
□ Sternotomy
□ Rib resection _____ (rib #)

If MIS:
□ right □ left
# of ports: _____

Lung resection:
□ Lobectomy: □ RUL □ RML □ RLL □ LUL □ LLL
□ Pneumonectomy: □ right □ left
□ Segmental resection _____ (segment #)
□ Wedge: □ RUL □ RML □ RLL □ LUL □ LLL _____ (# of wedges)

Lymph node stations: _____

https://dx.doi.org/10.21037/tcr-22-232

First Post-operative Follow-up Clinic Visit (6 week follow up)

Patient study code: _____
Date of visit (DD / MM / YYYY): _____

A) Pathologic Report (Complete pathologic response - pCR):

□ Soft tissue sarcoma	□ Melanoma	□ Gastric cancer
□ Colorectal cancer	□ Head and neck cancer Specify:	□ Other:
□ Renal cell carcinoma	□ Osteosarcoma	
□ Germ cell cancer	□ Breast cancer	
□ Gynecologic cancer Specify:	□ Hepatocellular cancer	
Margin: clear / positive		

B) Radiology:

CXR - Post-op _____ (DD / MM / YYYY)	□ Normal □ Abnormal. Please specify: _____

C) Circulating tumour cells

Date of blood work collected _____ (DD / MM / YYYY)	Results:

D) Adjuvant Therapy:

Is this patient on chemotherapy or radiation? □ Yes □ No If yes, please fill out the chemotherapy/radiation Case Report Form

E) Overall Assessment:

□ No evidence of recurrence & clinically well □ No evidence of recurrence. Problem identified : □ Intervention to problem identified: □ Recurrence □ Other:

Follow up Plan	□ 3 months □ 6 months □ 12 months □ PRN

https://dx.doi.org/10.21037/tcr-22-232

Late Follow-up Clinic Visit (Routine follow up for 3 years)

Patient study code: _____
Date of visit (DD / MM / YYYY): _____

A) Radiology:

CXR - Post-op _____ (DD / MM / YYYY)	□ Normal □ Abnormal _____ (details)
CT chest (if performed) _____ (DD / MM / YYYY)	□ No evidence of recurrence or complication □ Evidence of recurrence. Please specify: _____

B) Adjuvant Therapy:

Is this patient on chemotherapy or radiation? □ Yes No If yes, please fill out the chemotherapy/radiation Case Report Form

C) Overall Assessment:

□ No evidence of recurrence & clinically well □ No evidence of recurrence. Problem identified : □ Intervention to problem identified: □ Recurrence □ Other:	
Follow up Plan	□ 3 months □ 6 months □ 12 months □ PRN

https://dx.doi.org/10.21037/tcr-22-232

Concomitant Medications

Patient study code: ___________________

Is the patient taken any concomitant medications? If Yes, please provide details below	□ Yes □ No

Medication	Indication	Other Information
		Started medication at: □ Baseline Other:_________________ Discontinued this medication? □ Yes
		Started medication at: □ Baseline Other:_________________ Discontinued this medication? □ Yes
		Started medication at: □ Baseline Other:_________________ Discontinued this medication? □ Yes
		Started medication at: □ Baseline Other:_________________ Discontinued this medication? □ Yes
		Started medication at: □ Baseline Other:_________________ Discontinued this medication? □ Yes
		Started medication at: □ Baseline Other:_________________ Discontinued this medication? □ Yes
		Started medication at: □ Baseline Other:_________________ Discontinued this medication? □ Yes
		Started medication at: □ Baseline Other:_________________ Discontinued this medication? □ Yes

https://dx.doi.org/10.21037/tcr-22-232

Adverse Events

Patient study code: ___________________

Adverse Event *	Severity **	Attribution ***	Date Started (DD/MM/YYYY)	Date Ended (DD/MM/YYYY)	Patient Outcome
		□ Surgery □ Chemotherapy □ Radiation □ Other:		□ Ongoing	□ Remains in study □ Withdrawn from study □ Lost to follow-up □ Death
		□ Surgery □ Chemotherapy □ Radiation □ Other:		□ Ongoing	□ Remains in study □ Withdrawn from study □ Lost to follow-up □ Death
		□ Surgery □ Chemotherapy □ Radiation □ Other:		□ Ongoing	□ Remains in study □ Withdrawn from study □ Lost to follow-up □ Death
		□ Surgery □ Chemotherapy □ Radiation □ Other:		□ Ongoing	□ Remains in study □ Withdrawn from study □ Lost to follow-up □ Death

* Adverse Event: Event not considered an SAE, but an event that was identified through patient reports (diaries, interviews). Examples might include fragmented sleep, appetite issues etc.
** Severity: Please use the Common Terminology Criteria of Adverse Events (CTCAE) V.5 to assign grading
***Attribution Description: 1. Unrelated 2. Unlikely 3. Possible 4. Probable 5. Definite

https://dx.doi.org/10.21037/tcr-22-232

Serious Adverse Events

Patient study code: _____

*** If an SAE has occurred please report to your local REB and notify the coordinating center within 48 hours of the identification of the event. Please see the AMPLCaRe Procedures Manual for more instruction, or call the coordinating center. ***

Serious Adverse Event*	Severity **	Attribution ***	Date Started (DD/MM/YYYY)	Date Ended (DD/MM/YYYY)	Date Reported (DD/MM/YYYY)	Patient Outcome
		□ Surgery □ Chemotherapy □ Radiation □ Other:		□ Ongoing		□ Remains in study □ Withdrawn from study □ Lost to follow-up □ Death

I am aware of this serious adverse event, and have verified the details above: _____
Site Principle Investigator Date

* Serious Adverse Event: Death; life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect. Please see AMPLCaRe Procedures Manual for more instruction, or call the coordinating center.
** Severity: Please use the Common Terminology Criteria of Adverse Events (CTCAE) V.5 to assign grading
***Attribution Description: 1. Unrelated 2. Unlikely 3. Possible 4. Probable 5. Definite

https://dx.doi.org/10.21037/tcr-22-232

Documentation Record Log

Patient study code: _____

Date of visit (DD / MM / YYYY): _____

Tests to be completed from baseline to follow up appointments:

Baseline/pre-RT Week- 0	Post RT Follow-up Week -6	1st Pre-op Follow-up Week 8-12	3-month Follow-up	6-month Follow-up	9-month Follow-up	12-month Follow-up	18-month Follow-up	24-month Follow-up	30-month Follow-up	36-month Follow-up
□ CT chest □ CTC	□ CT chest □ CTC	□ Chest x-ray □ CTC	□ CT chest	□ CT chest	□ CT chest	□ CT chest	□ CT chest	□ CT chest	□ CT chest	□ CT chest

*Please include the results of these tests on the Case Report Forms.

CRFs to be completed by Research Coordinator:

Baseline Date:	Post RT Follow-up Date:	Operatory/ Clinical Stage Date	1st Post-op Follow-up Date:	3-month Follow-up Date:	6-month Follow-up Date:	9-month Follow-up Date:
□ Screening visit □ Medical history □ Study info □ Medication log	□ Post RT form	□ Operation form	□ 1st FU form	□ Late FU form	□ Late FU form	□ Late FU form

12-month Follow-up Date:	18-month Follow-up Date:	24-month Follow-up Date:	30-month Follow-up Date:	36-month Follow-up Date:	End of Study Date:
□ Screening visit □ Medical history □ Study info □ Medication log	□ Post RT form	□ Operation form	□ 1st FU form	□ Late FU form	□ End of Study form

* At any stage, please be sure to fill out an AE/SAE form if needed.

** If patient withdraws please fill out the 'End of Study' report

End of Study

Patient study code: _____

Year of birth: _____

Date (DD / MM / YYYY): _____

Date of final follow up: (DD / MM / YYYY)	
Reason to End Study:	□ Normal Completion □ Recurrence, patient decides to stop study drug □ Serious Adverse Event □ Death □ Patient withdrawal, reason: _____ □ Lost to follow up □ Principal Investigator Decision, Specify: _____ □ Other: _____
Comments:	

https://dx.doi.org/10.21037/tcr-22-232

Adjuvant Chemotherapy/Radiation

Patient study code: _____

Cycles of Chemotherapy:

Drug(s)	Dose(s)	Date Started (DD / MM / YYYY)	Date ended (DD / MM / YYYY)	Adverse Events
				Y □ N □
				Y □ N □
				Y □ N □
				Y □ N □
				Y □ N □
				Y □ N □

Courses of Radiation:

Daily Dose	Total Dose	Date Started (DD / MM / YYYY)	Date ended (DD / MM / YYYY)	Adverse Events
				Y □ N □
				Y □ N □
				Y □ N □
				Y □ N □
				Y □ N □
				Y □ N □

https://dx.doi.org/10.21037/tcr-22-232

Appendix 2

Consent Form

Study Information and Informed Consent Form
Post SBRT Pulmonary Metastasectomy (PSPM) Trial

Post SBRT Pulmonary Metastasectomy: Evaluating the effects of SBRT on pulmonary metastasis using post-surgical histologic evaluation.

Study ID: SJHH_PSPM 7925

Lead Investigator:	Dr. John Agzarian, BHSc, MD, MSc Division of Thoracic Surgery St. Joseph's Healthcare Hamilton T2105-50 Charlton Ave E. Hamilton ON Tel: 905-522-1155 x 32701
Co-Investigators:	Dr. Anand Swaminath, MD, MSc (*Radiation Oncology*), Dr. Christine Fahim, PhD, MSc (*HRM & Implementation Science*), Dr. Asghar Naqvi, MD (*Anatomic Pathology*), Dr. Yaron Shargall, MD (*Thoracic Surgery*), Dr. Christian Finley, MD, MPH (*Thoracic Surgery*), Dr. Wael Hanna, MD, MBA (*Thoracic Surgery*)
Research Coordinator	Housne Begum, MSc, PhD Division of Thoracic Surgery T2105-50 Charlton Ave E. Hamilton ON Tel: 905-522-1155 x 35338 Email: begumh@mcmaster.ca
Funding Source	MSA Grant, JHCCF Grant, Firestone

Emergency Contact Number (24 hours/7 days a week): 905-870-2647 (pager)
Non-Emergency contact numbers are at the end of this document under Contacts.

You are being invited to take part in a study called Post SBRT Pulmonary Metastasectomy (PSPM) Trial, because you are a patient will having surgery to remove metastatic lung nodules. Participating in this study is optional, and will not affect your any usual treatment.

In order to decide whether or not you want to be a part of this research study, you should understand what is involved and the potential risks and benefits. This form gives detailed information about the research study. Please take your time to fully understand what comprises participation. After you have read this form, you will be asked to sign it if you wish to participate.

Introduction
The role of SBRT as a treatment for small-volume tumors in the lung is well established, but the effectiveness of tumor eradication has yet to be determined. Surgery and stereotactic body radiation therapy (SBRT) are both acceptable treatment options for the local management of lung tumors where the cancer has originated elsewhere in the body. This trial will assess whether the addition of SBRT to surgery offeres better tumor control, and whether it decreases recurrence of the cancer. This is a collaborative effort between the divisions of Thoracic Surgery and Radiation Oncology to evaluate the effects of dual treatment of pulmonary metastasis amenable to curative resection with upfront SBRT followed by surgical resection.
Study recruitment and analysis will be conducted at St. Joseph Healthcare Hamilton and the Juravinski Cancer Center. The Primary Outcome will be measured as the rates of complete pathologic response (pCR) in surgical specimens post SBRT-this

 https://dx.doi.org/10.21037/tcr-22-232

means that the removed tumor will be evaluated under the microscope to determine how effective SBRT was in eradicating the cancer. Other outcomes that will be assessed include: overall survival (OS) at 3 years, disease free survival (DFS) at 3 years, local recurrence rates, radiation related toxicity, postoperative complications.

What is the purpose of the study?

The goal of this study is to determine the effectiveness of SBRT on reducing tumor viability at a pathologic level. We hope to extrapolate this information to both primary and secondary lung cancer.

What will happen during the study?

If you choose to participate in this study, treatment will be delivered within 2 weeks, with planning and delivery parameters following the standard guidelines. Following completion of SBRT, you will be assessed at the 4–6-week mark by the treating radiation oncologist and thoracic surgeon with a post-treatment computed tomography (CT) of the chest.

If no disease progression is identified, you will undergo scheduled surgical resection of all metastatic tumors at 8–12 weeks post SBRT. The choice of lobar *vs.* sublobar resection (type of surgery) will be determined by the participating surgeon, based on tumor size and location. The choice of surgical approach (MIS *vs.* thoracotomy) will be left to the discretion of the operating surgeon.

You will be seen Post SBRT and Post Surgery between Radiation and Surgery 8 to 12 weeks and post-operative at 30 days for 36 months after surgery. Routine post lung cancer resection required interval surveillance CT scan to be performed at internals of 6 months for at least 3 years. You will be typically followed by both Thoracic Surgery and medical oncology.

What are the possible risks of participating in the study?

Both SBRT and surgical wedge resection are well established as safe and effective modalities in the treatment of pulmonary malignancies. This trial utilized well established treatment protocols that are currently routinely applied to day-to-day clinical practice. So we do not anticipate that there will be any harm or discomfort from taking part in this study. Radiation prior to surgery can increase scarring during surgery and made surgery more challenging. This is less likely to affect your type of operation given the decreased amount of lung tissue being removed, and the fact that SBRT if focal radiation with less spread and less effects to the local area. In addition, we routinely operate on patients after they had radiation treatment.

You should know that the addition of SBRT to surgery will necessitate a delay to surgery, but we do not anticipate this delay to be of any significance, and some research has shown that radiation may have benefits in cancer treatment throughout the body (abscopal effect). Our own research has already shown, that delays ins patients with lung cancer who are completing necessary work-up is not associated with worsened outcomes.

Will I be paid to Participate in this study?

You will not be paid or compensated in any way for participation.

Will there be any costs to me in this study?

There will be no costs associated with taking part in this study.

What will happen to my personal information?

Your data that is collected will not be shared with anyone except with your consent or as required by law. All personal information such as your name or phone number will be removed from the data by research staff and be replaced with a study identification (ID) number (de-identified) before the data is analyzed by research staff. A password protected document is kept by the research team linking your study ID with your name on a password protected computer. This linking of your name to your study ID number is needed to link information from the study.

Once the study is complete and the data analyzed, all identifying information will be permanently removed and destroyed, and the remaining study records will be kept confidential and secure for 10 years. Following this, all study records will be destroyed in a confidential manner.

For the purposes of ensuring the proper monitoring of the research study, it is possible that a member of the Hamilton

 https://dx.doi.org/10.21037/tcr-22-232

Integrated Research Ethics Board and this institution and affiliated sites may consult your research data for quality assurance purposes. However, no records that identify you by name or initials will be allowed to leave the research office. By signing this consent form, you authorize such access.

What happens if I choose not to participate?

Your participation in this study is entirely voluntary. You may refuse to take part in the study, or you may stop participation at any time, without affecting future treatment. In no way does signing this consent form waive your legal rights nor does it relieve the investigators, sponsors or involved institutions from their legal and professional responsibilities. If during the course of the study, information becomes available that might affect whether you choose to continue your participation in the study, the research staff will give this information to you.

Can participation in the study end early?

You can stop taking part at any time and your doctor will continue to treat you with the best means available. If you decide to stop participating in the study, we encourage you to talk to your doctor first. If you do choose to stop your participation in the study, we ask that we have your permission to retain the data collected to date and to continue to follow you via your medical records for survival and hospital readmissions.

What if I have questions about the study?

If you have any questions or concerns about this study, please feel free to contact the Principal Investigator, Dr. John Agzarian at 905-522-1155 x32701 or the study coordinator Housne Begum at 905-522-1155 x35338.

https://dx.doi.org/10.21037/tcr-22-232

Post SBRT Pulmonary Metastasectomy (PSPM) Trial

Lead investigator: Dr. John Agzarian
Division of Thoracic Surgery
St. Joseph's Healthcare Hamilton
T2105-50 Charlton Ave E. Hamilton ON Tel: 905-522-1155 x 32701

CONSENT STATEMENT

Participant:

I have read the preceding information thoroughly. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I agree to participate in this study as stated in the above information. I understand that I will receive a signed copy of this form.

Name (printed)	*Signature*	*Date*

Person obtaining consent:

I have discussed this study in detail with the participant. I believe the participant understands what is involved in this study.

Name (printed)	*Signature*	*Date*

Investigator:

In my judgment, this participant has the capacity to give consent, and has done so voluntarily.

Name (printed)	*Signature*	*Date*

Witness: *(required if participants are unable to read, or if translation is necessary)*

I was present when the information in this form was explained and discussed with the participant. I believe the participant understands what is involved in this study.

Name (printed)	*Signature*	*Date*

This study has been reviewed by the Hamilton Integrated Research Ethics Board (HIREB). The HIREB is responsible for ensuring that participants are informed of the risks associated with the research, and that participants are free to decide if participation is right for them. If you have any questions about your rights as a research participant, please call the Office of the Chair, Hamilton Integrated Research Ethics Board at 905.521.2100 x 42013.

https://dx.doi.org/10.21037/tcr-22-232