Author's response to reviews

Title: Functional lung avoidance for individualized radiotherapy (FLAIR): Study protocol for a randomized, double-blind clinical trial

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Version: 2
Date: 16 September 2014

Author's response to reviews: see over
September 4, 2014

Dear Editors of BMC Cancer,

Please find enclosed our manuscript “Functional Lung Avoidance for Individualized Radiotherapy (FLAIR): Study Protocol for A Randomized, Double-Blind Clinical Trial”

Although radiotherapy is a key component of curative-intent treatment for locally advanced, unresectable non-small cell lung cancer (NSCLC), it can be associated with substantial pulmonary toxicity in some patients. Current radiotherapy planning techniques aim to minimize the radiation dose to the lungs, without accounting for regional variations in lung function. Many patients, particularly smokers, can have substantial regional differences in pulmonary ventilation patterns. It has been hypothesized that preferentially avoiding functional lung when prescribing radiotherapy may reduce toxicity, but this hypothesis has never been previously tested in a randomized clinical trial.

In our study, we will use sophisticated functional-lung imaging techniques in conjunction with advanced radiation dose-delivery platforms in a randomized, double-blind trial. Our study will comprehensively assess the impact of functional lung avoidance on pulmonary toxicity and quality of life in patients receiving chemoradiotherapy for locally advanced NSCLC.

We confirm that this study has received ethics approval and has received funding from a major external granting agency (documentation attached) and as such may qualify for publication without additional peer review. It is also registered at clinicaltrials.gov (NCT02002052).

Thank-you for your consideration of our manuscript.

Sincerely,

Dr. Brian Yaremko

Dr. Brian Yaremko, MD, MSc, FRCPC, PEng
Use of Human Participants - Initial Ethics Approval Notice

Principal Investigator: Dr. Brian Yaremko
File Number: 104834
Review Level: Full Board
Protocol Title: Functional Lung Avoidance for Individualized Radiotherapy (FLAIR): A Randomized, Double-Blind Clinical Trial
Department & Institution: Schulich School of Medicine and Dentistry/Oncology, London Health Sciences Centre
Sponsor: Ontario Institute for Cancer Research

Ethics Approval Date: February 11, 2014
Ethics Expiry Date: December 31, 2020

Documents Reviewed & Approved & Documents Received for Information:

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This is to notify you that the University of Western Ontario Health Sciences Research Ethics Board (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines, and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced study on the approval date noted above. The membership of this HSREB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB’s periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the University of Western Ontario Upated Approval Request form.

Member of the HSREB that are named as investigators in research studies, or declare a conflict of interest, do not participate in discussions related to, nor vote on, such studies when they are presented to the HSREB.

The Chair of the HSREB is Dr. Joseph Gilbert. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Signature

Ethics Officer to Contact for Further Information

This is an official document. Please retain the original in your files.
July 2 2014

Doug Hoover
Lawson Heath Research Institute

Dear Dr. Hoover

At its recent meeting, the Ontario Thoracic Society Research Advisory Committee considered your grant application entitled, "Individualized, Function-Guided Radiotherapy to Improve Quality of Life in Patients with Chronic Obstructive Pulmonary Disease and Advanced Lung Cancer". Your aforementioned grant was sent forward to the Ontario Lung Association Board of Directors at its meeting on June 21, 2014.

We are pleased to inform you that the Board was unanimous in its approval of the Grant-In-Aid as recommended. Your study has been approved for 1 – year of funding in amount $49,920.

The award will be issued in two installments: 50% of the funds will be sent to your university finance office in August 2014 and the remaining half will be sent in January 2015. However, prior to releasing these funds, we ask that you review and sign a copy of the attached Acknowledgement of Funding and return it to the OTS in the enclosed envelope. The second copy is for your records.

Please notify the OTS as soon as possible if there is any overlap between this grant and funding from another source.

Thank you for considering the Ontario Lung Association as a funding source for this interesting project. Enclosed are copies of the reviewers' comments from the National Review process for your perusal.

We look forward to receiving the following reports by the noted due dates. Please mark your calendar accordingly.

- **Final Progress Report:** due no later than October 31, 2015
- **Financial Statement:** due no later than October 31, 2015

Please forward a copy of any acknowledgement of OTS funding in publications arising from the grant. We wish you continued success in your research.

Sincerely,
George Habib
President & CEO
Ontario Lung Association

Encl.

Shawn Aaron, MD., MSc., FRCPC
Chair, Research Advisory Committee
Ontario Thoracic Society
LAWSON FINAL APPROVAL NOTICE

LAWSON APPROVAL NUMBER:  R-14-192

PROJECT TITLE:  Functional Lung Avoidance for Individualized Radiotherapy (FLAIR):  A Randomized, Double-Blind Clinical Trial

PRINCIPAL INVESTIGATOR:  Dr. Brian Yaremko

LAWSON APPROVAL DATE:  May 16, 2014

Health Sciences REB#:  104834

Please be advised that the above project was reviewed by the Clinical Research Impact Committee and Lawson Administration and the project:

Was Approved

Please provide your Lawson Approval Number (R#) to the appropriate contact(s) in supporting departments (eg. Lab Services, Diagnostic Imaging, etc.) to inform them that your study is starting. The Lawson Approval Number must be provided each time services are requested.

Dr. David Hill
V.P. Research
Lawson Health Research Institute

All future correspondence concerning this study should include the Lawson Approval Number and should be directed to Sherry Paiva, Research Administration Officer, Lawson Approval, Lawson Health Research Institute, 750 Baseline Road, East, Suite 300.

cc: Administration