Title: SYNCHROTRON MICROBEAMS FOR THE TREATMENT OF LUNG CANCER: A LESSON FROM THE FIRST PRECLINICAL TRIAL

Author Names: Verdiana Trappetti MSc[1], Cristian Fernandez-Palomo PhD[1], Lloyd Smyth PhD[2], Mitzi Klein VMD[3], David Haberthür PhD[1], Duncan Butler PhD[3], Micah Barnes MSc[3,4], Nahoko Shintani PhD[1], Michael de Veer PhD[5], Jean A. Laissue MD[1], Marie C. Vozenin PhD[6], Valentin Djonov MD[1].

Author Institutions: 1- Institute of Anatomy, University of Bern, Switzerland; 2- Department of Obstetrics and Gynaecology, University of Melbourne, Royal Women's Hospital, Melbourne 3- Imaging and Medical Beamline, Australian Nuclear Science and Technology Organisation - Australian Synchrotron, Clayton, VIC, Australia; 4- Department of Physical Sciences, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; 5- Monash Biomedical Imaging, Monash University, Clayton, Australia; 6- Department of Radiation Oncology/CHUV, Lausanne University Hospital and University of Lausanne, Switzerland

Synchrotron Microbeam Radiation Therapy (S-MRT) consists of Synchrotron X-rays fractionated into an array of quasi-parallel beamlets delivered in FLASH mode. S-MRT achieves excellent tumour control and normal tissue sparing. This study aimed to evaluate S-MRT efficacy in a preclinical mouse lung carcinoma model.

Lewis-lung carcinoma implanted C57BL/6J mice were treated with two cross-fired arrays of S-MRT or Synchrotron-Broad Beam (S-BB) at 11 days after implantation. An array composed of seventeen microbeams 50 µm wide, spaced 400 µm apart was employed. S-MRT peak-dose was 400 Gy with a valley-dose of 4.76 Gy (delivery 361 ms, dose-rate 991.7 Gy/s). S-BB delivered a homogeneous dose of 5.16 Gy (delivery 129 ms, dose-rate 37.0 Gy/s). In addition, mouse lungs without tumours were irradiated with S-MRT, and radiation-related effects were assessed up to 6 months post-treatment.

Mice in the S-MRT group had notably smaller tumour volumes compared to the S-BB group however, there was no difference in animal survival. This was attributed to pulmonary oedema found around the S-MRT-treated tumours. A mild transient form of fluid effusion was also observed in the S-MRT-treated normal lungs. Six months after S-MRT, the lungs of healthy mice were completely absent of radiation-induced pulmonary fibrosis.

Our study indicates that FLASH S-MRT is a promising tool for treating mouse lung carcinoma, i.e. reducing tumour size compared to mice treated with FLASH S-BB and sparing healthy lung from pulmonary fibrosis. Future experiments should focus on optimizing S-MRT parameters to minimize pulmonary oedema and maximize its therapeutic ratio.