MMND & ITRO 2018

Mini-Micro-Nano-Dosimetry and
Innovative Technologies in Radiation Oncology Workshops

Mantra Mooloolaba-Beach, Queensland Australia, February 6th-11th 2018

mmnditro2018.com

CENTRE FOR MEDICAL RADIATION PHYSICS

UNIVERSITY OF WOLLONGONG

cmrp@uow.edu.au

GOLD SPONSORS

HITACHI
Inspire the Next

THE ST. GEORGE HOSPITAL
TU SOUFFRES CELA SUFFIT

Australian Government | ansto

THE CROWN PRINCESS MARY CANCER CENTRE, WESTMEAD

proudly supports
RADIATION ONCOLOGY
TARGETING CANCER
targetingcancer.com.au
targetingcancer.co.nz

LIVERPOOL HOSPITAL

CENTRE FOR MEDICAL RADIATION PHYSICS

UNIVERSITY OF WOLLONGONG

THE PRINCE OF WALES HOSPITAL

PHILIPS

SILVER SPONSORS

MMND 2018

Mantra Mooloolaba-Beach, Queensland Australia, February 6th-8th 2018

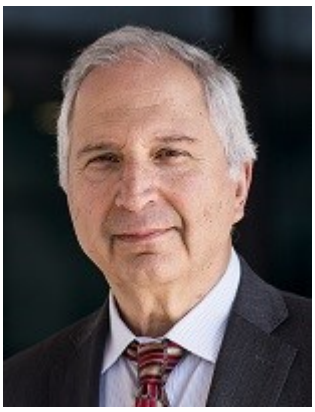
mmnditro2018.com

CENTRE FOR MEDICAL RADIATION PHYSICS

UNIVERSITY OF WOLLONGONG

cmrp@uow.edu.au

Welcome from the Chair



Distinguished Professor Anatoly Rozenfeld, PhD

Continuing our series of biennial meetings, the Micro-Mini & Nano Dosimetry (MMND) workshop (6th - 8th February) brings together both international and Australian radiation oncologists, medical physicists, radiation scientists and nanomedicine experts to discuss advancement in radiation oncology modalities and radiation dosimetry technologies for quality assurance in radiation therapy, radiobiological optimisation of treatments, and other relevant technologies, to further improve clinical outcomes of radiation therapy.

For the first time in the history of the MMND workshop series, we will be holding a special "Brachytherapy Day". This will be led by Dr Michael Zelefsky, Memorial Sloan Kettering Cancer Center (MSKCC), New York.

MMND—International Faculty

Professor Reinhard Schulte, MD

Reinhard Schulte, MD, is Professor of Radiation Medicine in the School of Medicine of Loma Linda University, and works as Translational Researcher on proton and ion therapy related technology and clinical developments in the James M. Slater Proton Treatment and Research Center, Department of Radiation Medicine, Loma Linda University Medical Center. He received his graduate degree in Physics (Diploma) from Dortmund University, Germany and his Doctorate in Medicine (Dr. med., summa cum laude) from the University of Cologne, Germany. He is Principal Investigator on an NIH-funded project to develop proton CT and participates in two large European Research Consortia related to proton therapy research. Dr. Schulte also has over 25 years of experience in clinical proton therapy and is licensed physician and board certified in radiation oncology and radiology in the United States and Germany.

Professor Vladimir Feygelman, PhD

Vladimir M. Feygelman graduated from the Department of Physics at Rostov State University in the former U.S.S.R in 1982 with a degree in Laser Physics. In 1985 he was awarded a PhD in Physical Chemistry at the same university. Since 1990 Dr. Feygelman is involved in Medical Physics, first as a Post Doc at the University of Florida (Gainesville), and then as a clinical radiotherapy physicist in Canada and USA. In 2006 he joined the faculty of Moffitt Cancer Center. Currently he is a Senior Faculty Member at Moffitt and Professor at USF Department of Oncologic Sciences. Dr. Feygelman divides his time between clinical duties, research, and teaching physics PhD students and medical residents. As a senior physicist, he is responsible for implementation of all major technological developments at the Department of Radiation Oncology. His research interests are primarily focused on quality assurance of complex advanced treatments. Dr. Feygelman was a member of the AAPM Task Group 244 on commissioning of dose calculations. He was the principal writer of the IMRT/VMAT section. Currently he serves as a Co-Chair of the AAPM working group on reference dose specification in treatment planning systems. Dr. Feygelman is an author of over 50 peer-reviewed papers on Medical Physics and was an invited speaker at various national and international meetings such as AAPM, ESTRO, and IEEE.

MMND—International Faculty

Professor Wolfgang Tomé, PhD

Professor Tomé works at Montefiore Medical Center and the Albert Einstein College of Medicine in New York City. He is the Director of the Division of Therapeutic Medical Physics of Montefiore Medical Center and the Director of Medical Physics of the Institute for Onco-Physics at the Albert Einstein College of Medicine. In addition, he also holds appointments as Visiting Professor of Medical Physics at the Centre of Medical Radiation Physics at the University of Wollongong, Australia and the University of Wisconsin at Madison. He has over 200 peer-reviewed publications, 16 book chapters, 2 books, over 200 abstracts, 5 patents to his credit, and is a Fellow of the American Association of Medical Physics. His current research interests include: techniques to mitigate normal tissue injury; bio-effects of focused-ultrasound; biologically guided therapy, MR guided therapy, SBRT, as well as immunoadjuvant cancer therapies.

Professor Mauro Carrara, PhD

Mauro Carrara works as Medical Physicist at the Department of Diagnostic Imaging and Radiotherapy at National Cancer Institute of Milano (Italy) where he is responsible for brachytherapy physics. He conducts research in several fields concerning quality control and dosimetry in high dose rate brachytherapy and the application of US or MR imaging for treatment planning. He has been invited to several national and international conferences to lecture on these subjects. Being part of the multidisciplinary Prostate Program of his Institution, he is as well involved in the development of non-linear models for acute and late toxicity prediction and the study of highly hypofractionated treatment schemes in prostate high dose radiotherapy.

In 2006, he was officially awarded by the Major of Milan with the International Young Researcher Award “Amici di Milano”. He is a member of the European Society for Therapeutic Radiology and Oncology (ESTRO) and Italian Association of Medical Physics (AIFM). For ESTRO and AIFM he was invited to conduct several courses in the fields of dosimetry, radiotherapy physics and mathematical non-linear models for pattern classification. Since 2007 he is Professor at the Department of Medicine and Surgery of the University of Milano. He is member of the Editorial Board of Physica Medica: European Journal of Medical Physics (Elsevier) and Section Editor for Tumori Journal (Wichtig).

MMND—International Faculty

Professor Katia Parodi, PhD

Katia Parodi received her Ph.D. in Physics from the University of Dresden, Germany, in 2004. She then worked as postdoctoral fellow at Massachusetts General Hospital and Harvard Medical School in Boston, USA. In 2006 she returned to Germany as tenured scientist and group leader at the Heidelberg Ion Therapy Center, obtaining in 2009 her Habilitation from the Heidelberg University. Since 2012 she is full professor and Chair of Medical Physics at the Physics Faculty of the Ludwig-Maximilians-University (LMU) in Munich, where she initiated a dedicated curriculum for Medical Physics within the Physics MSc. She also retained a secondary affiliation with the Heidelberg Ion Therapy Center.

Her main research interests are in high precision image-guided radiotherapy with a special focus on ion beams, from advanced computational modeling to experimental developments and clinical evaluation of novel methods for in-vivo ion range monitoring. Katia Parodi has been invited speaker and committee member at many conferences, and contributed to over 90 publications in peer reviewed journals, more than 150 conference contributions, 5 book chapters and a couple of patents. For her work she received several national and international recognitions, including the Behnken Berger Award in 2006, the IEEE Bruce Hasegawa Young Investigator Medical Imaging Science Award in 2009 and the AAPM John S. Laughlin Young Scientist in 2015. Since 2015 she is also vice president of the German Society for Medical Physics (DGMP).

Doctor Suzie Sheehy, PhD

Dr. Suzie Sheehy is an accelerator physicist and Royal Society University Research Fellow at the University of Oxford, UK. She leads research in high intensity hadron beams within the John Adams Institute for Accelerator Science, where she also teaches graduate level accelerator physics. Her research uses a combination of theoretical, experimental and simulation-based approaches to address questions in beam dynamics and the design of future accelerators. Her career has led her to study accelerators for a range of applications from proton/ion therapy to accelerator driven nuclear waste transmutation. In addition to her research and teaching of graduate level accelerator physics, Dr. Sheehy is also an award winning science communicator and presenter, bringing physics to wider audiences through TV, radio, podcasts, major live shows and demonstration lectures.

MMND—International Faculty

Professor Taiga Yamaya, PhD

Taiga Yamaya, Ph. D, is a Team Leader of Imaging Physics Team at National Institute of Radiological Sciences (NIRS), National Institutes for Quantum and Radiological Science and Technology (QST) in Japan. His research interest is the development of next generation positron emission tomography (PET) systems as well as development of radiation detectors and image reconstruction algorithms. He obtained his Ph. D degree in 2000. He has been awarded more than 10 prizes, one of which was the 1st prize of German Innovation Award (2012). He has accomplished more than 100 peer reviewed publications and more than 50 registered patents. He has also visiting professor positions in Chiba University and Yokohama City University. In Yamaya's laboratory at NIRS-QST, using their core technologies of depth-of-interaction (DOI) measurement, they are developing a new equipment concept of "OpenPET" for joint PET - therapy imaging and a brain-dedicated PET scanner for earlier diagnosis of dementia.

Professor Richard Maughan, PhD

Richard Maughan graduated from the University of Birmingham, England with an honors degree in physics in 1970. He completed his Ph.D. in Nuclear Physics at the same institution in 1974. From 1974 to 1983 he worked as a member of the scientific staff of the Cancer Research Campaign Gray Laboratory at Mount Vernon Hospital in England, where he was involved in basic radiation physics, chemistry and biology research. He moved to the USA in the fall of 1983, where he took a position as a medical physicist and a member of the faculty in the Radiation Oncology Department of Wayne State University (WSU), in Detroit. He played a major role in the development and application of a superconducting cyclotron as a neutron source for neutron radiation therapy.

In July 2000 Dr. Maughan moved to the University of Pennsylvania where he was appointed Professor, Director of Medical Physics and Vice Chair in the Department of Radiation Oncology. In this role he was a key member of the proton therapy development team, participating in the specification of the system, vendor selection and overseeing acceptance and commissioning. Under his direction the Medical Physics division expanded from about 30 people to a staff of over 80. He stepped down as Division Director in June 2013 and is currently a Professor and Vice Chair in the department.

MMND—International Faculty

Professor Zuofeng Li, PhD

Zuofeng Li is a Professor of Radiation Oncology at the University of Florida College of Medicine, and serves as the Director of Physics at the University of Florida Health Proton Therapy Institute. He graduated from Washington University in St. Louis with a degree of D.Sc. in Systems Science and Mathematics, and entered medical physics field as a post-doctoral research associate at Washington University School of Medicine. Following completion of medical physics residency training from Washington University, he held successive faculty appointments at University of Florida and Washington University, during which time he led the brachytherapy physics services at these institutions and performed Monte Carlo brachtherapy dosimetry research. Dr. Li returned to University of Florida in 2005 to lead its proton therapy system installation, acceptance testing and commissioning, and subsequent clinical physics operations. Dr. Li had served on various AAPM task groups on brachytherapy and proton therapy topics, and as the chairman of the AAPM Brachytherapy Subcommmittee, among other AAPM appointments. Dr. Li participated in the training and supervision of 8 PhD graduate students, and more than 20 medical physics residents; and is an author or co-author of over 120 peer-reviewed journal publications. He is a co-recipient of the 1993-1994 Farrington Daniel Award of Medical Physics Journal, and was named a Fellow of AAPM in 2012.

MMND ITRO 2018
PROGRAM

Tuesday 6th February 2018

MMND multidisciplinary (micro- nano-dosimetry, radiobiology, synchrotron MRT and EBRT, Monte Carlo Modelling)

07:50-08:00	**Introduction/Welcome** **Anatoly Rozenfeld/Tomas Kron /Michael Lerch**
Physics in Heavy Ion Therapy (Microdosimetry) ***Session chairs: Anatoly Rozenfeld, CMRP*** ***Rui Qiu, Tsinghua University***	
08:00–08:30	**(Invited) Larry Pinsky** ***Update on the status of MEDIPIX in space and an introduction to the Timepix 2*** **University of Houston, USA**
08:30–08:45	**Kenta Takada** ***Evaluation of RBE-weighted doses for various radiotherapy beams based on a microdosimetric function implemented in PHITS*** **University of Tsukuba, Japan**
08:45–08:55	**Davide Bortot** ***Microdosimetry on nanometric scale with a new low-pressure avalanche-confinement TEPC*** **Politecnico di Milano, Italy**
08:55-09:05	**Davide Mazzucconi** ***A FPGA-based software for microdosimetric data processing*** **Politecnico di Milano, Italy**
09:05-09:15	**Anatoly Rozenfeld** ***Progress in Silicon microdosimetry and its applications*** **CMRP UOW**
09:15-09:25	**Jeremy Davis** ***Progress in diamond microdosimetry*** **CMRP UOW**
09:25-09:30	**Ben James** ***3D Sensitive Volume Microdosimeter with Improved Tissue Equivalency: Charge Collection Study and its Application in ^{12}C Ion Therapy*** **CMRP UOW**
09:30-09:35	**Emily Debrot** ***Mini Beam C 12 therapy: simulations and first experimental results with SOI micro dosimeters*** **CMRP UOW**
Radiobiology & Monte Carlo Simulations ***Session chairs: Michael Lerch, CMRP;*** ***Larry Pinsky, University of Houston***	
09:35-10:00	**(Invited) Roger Martin** ***Topical radioprotection of radiation induced oral mucositis***

	Peter MacCallum CC
10:00–10:30	**Morning Tea**
10:30-10:45	**Moeava Tehei** ***Progress in Radiobiology*** **CMRP UOW**
10:45-11:00	**Susanna Guatelli** ***Recent developments in Geant4 for medical physics applications*** **CMRP UOW**
11:00-11:15	**Dousatsu Sakata** ***Development of track structure models in GEANT 4 on nanometre scale gold*** **CMRP UOW**
11:15-11:25	**Hilary Byrne** ***Nanotheranostic Radio-Enhancement*** **University of Sydney**
11:25-11:30	**David Bolst** ***Modelling HIMAC biomedical beamline*** **CMRP UOW**
11:30-11:50	**(Invited) Rui Qiu** ***Latest development and applications of the Chinese reference phantoms*** **Tsinghua University, Beijing, China**
Synchrotron Radiation ***Session chairs: Enbang Li, CMRP; Yoshinori Sakurai, Kyoto University***	
11:50-12:05	**Michael Lerch** ***Progress in MRT research towards clinical implementation*** **CMRP UOW**
12:05-12:20	**Olga Martin** ***Localised synchrotron radiation in mice induced persistent systemic genotoxic events mediated by the functional immune system*** **Peter MacCallum CC**
12:20-12:25	**Elette Engels** ***Towards image guided MRT*** **CMRP UOW**
12:25-12:30	**James Archer** ***Fibre optic dosimetry in synchrotron microbeam radiation therapy*** **CMRP UOW**
12:30 – 13:30	**Lunch**

Space Dosimetry ***Session chairs: Dale Prokopovich, ANSTO; Kenta Takada, University of Tsukuba***	
13:30–14:00	**(Invited) Taku Inaniwa** ***Progress of the microdosimetric kinetic model in heavy-ion therapy*** **National Institute for Quantum and Radiological Science and Technology, Japan**
14:00–14:15	**Stuart George** ***High Precision Track Geometry Calculation in Hybrid-Pixel Detectors*** **University of Houston, USA**
14:15–14:25	**Stefania Peracchi** ***Simulation of cosmic radiation spectra for personal microdosimetry at the International Space Station altitude*** **CMRP UOW**
Radiation Therapy ***Session chairs: Tomas Kron, Peter McCullum CC; Wolfgang Tome, AECM***	
14:25–14:45	**(Invited) Vladimir Feygelman** ***Preview of AAPM Working Group recommendations for TPS reference dose specification*** **Moffitt CC, USA**
14:45-15:00	**Nicholas Hardcastle** ***The liver INSPECTR trials: towards improved understanding of liver function following radiotherapy.*** **Peter MacCallum CC**
15:00-15:30	**Afternoon Tea**
15:30-15:45	**Yang Wang** ***Characterisation Evaluation for Different QA techniques Clinically Used for IMRT, VMAT and SBRT/SRS Treatment Plan dosimetry verification*** **ICON-Cancer Care**
15:45-16:00	**Prabhakar Ramachandran** ***A comprehensive phantom with multi-detector inserts for Pre-treatment quality assurance in stereotactic ablative radiotherapy*** **Peter MacCallum CC**

MRI-LINAC ***Session chairs: Peter Metcalfe, CMRP; Grazia Gambarini , INFN***	
16:00 – 16:15	**Taghreed Al-Sudani** ***Build up dose characteristics with eXaSkin bolus during 6MV radiotherapy: MOSkin dosimetry results*** **CMRP UOW**
16:15 - 16:25	**Trent Causer** ***Characterization of monolithic silicon strip detectors for MRI-Linac dosimetry*** **CMRP UOW**
16:25- 16:35	**Natalia Roberts** ***Modelling the X-ray source for the Australian MRI-linac*** **CMRP UOW**
Boron Neutron Capture Therapy ***Session chairs: Susanna Guatelli, CMRP; Richard Maughan, University of Pennsylvania***	
16:35–16:55	**(Invited) Yoshinori Sakurai** **Fundamental knowledge for microdosimetry in boron neutron capture therapy** **Kyoto University, Japan**
16:55–17:15	**(Invited) Grazia Gambarini** ***BNCT Dosimetry: Peculiarities and Methods*** **University of Milan, Italy**
17:15–17:25	**James Vohradsky** ***Evaluation of silicon and diamond based microdosimetry for boron neutron capture therapy applications*** **CMRP UOW**
17:25–17:35	**Andrew Chacon** ***Neutron Capture Enhanced Particle Therapy: Opportunistic Dose Amplification via Capture of Thermal Neutrons Produced During Heavy Ion and Proton Therapy*** **CMRP UOW and ANSTO**

MMND ITRO 2018
PROGRAM

Wednesday 7th February 2018
Brachytherapy Day

07:50-08:00	**Introduction and Welcome** **Anatoly Rozenfeld, Michael Zelefsky and Josh Yamada**
What is New In Brachytherapy? ***Session chairs: Josh Yamada, MSKCC; Michael Jackson , POWH***	
08:00–08:30	**(Invited) Mira Keys** ***20 minutes + 10 min QA/Discussion*** ***Why Brachytherapy? Implication on long term outcomes*** **University of British Columbia, Vancouver, BC, Canada**
08:30–09:00	**(Invited) Michael Zelefsky** ***Improving Dosimetric Outcomes of Prostate Cancer with Real Time Imaged-Based Feedback*** **Memorial Sloan Kettering Cancer Center, New York**
09:00 – 09:40	**(Invited) Antonio Damato** ***Advances in brachytherapy physics* (30 min+10 min Q/A Discussions)** **a. US/EM guidance** **b. Active MRI guidance** **Memorial Sloan Kettering Cancer Center, New York**
09:40 – 10:00	**(Invited) Mauro Carrara** ***New Trends in dose calculations, delivery and in vivo verification in brachytherapy* (20 min+5 min Q/A Discussions)** **Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy**
10:00 – 10:30	**Morning Tea**
Physics Innovations ***Session chairs: Anna Ralston, SG CCC; Mauro Carrara , National CC Milan***	
10:30 – 11:00	**(Invited) Antonio Damato** ***Directional brachytherapy*- (20 min + 10 min discussion/QA)** **Memorial Sloan Kettering Cancer Center, New York**
11:00 – 11:15	**Anatoly Rozenfeld** ***BrachyView: new technology for online source tracking in brachytherapy*** **CMRP UOW**
11:15 – 11:30	**Yu Sun** ***Use of Contemporary imaging methods in brachytherapy applications*** **University of Sydney**
11:30 – 11:40	**Taylah Brennen** ***Eye brachytherapy: new technology for fast QA of eye plaques*** **CMRP UOW**

11:40 – 11:50	**Anna Romanyukha** ***Gynaecological HDR BT applicator for treatment delivery and online QA verification of source dwell positions and times*** **CMRP UOW**
11:50 – 12:00	**Dean Cutajar** ***End to End (E2E) QA phantom for TRUS guide HDR brachytherapy*** **CMRP UOW and SG CCC**
12:00 – 12:20	**(Invited) Prabhakar Ramachandra** ***Brachytherapy utilising miniaturised X-ray tubes – An evolving technology*** **Peter MacCallum Cancer Centre**
12:20 – 12:30	**Adam Yeo** ***On line IGBT for prostate cancer ultrasound based real time solution*** **Peter MacCallum Cancer Centre**
12:30 – 13:30	**Lunch**
Debate: SBRT vs Brachytherapy for localised prostate cancer ***Session chairs:Michael Folkert , UT Southwestern Medical Center; Michael Jackson , POWH***	
13:30 – 14:00	**(Invited) Michael Zelefsky** ***20 minutes + 10 min QA/Discussion*** **Memorial Sloan Kettering Cancer Center, New York**
14:00 – 14:30	**(Invited) Mira Keyes** ***20 minutes + 10 min QA/Discussion*** **University of British Columbia, Vancouver, BC, Canada**
Tumour Board: Challenging Cases ***Session chairs: Josh Yamada, MSKCC***	
14:30 – 15:00	**Michael Zelefsky, Mira Keyes, Joe Bucci, Michael Folkert/other incl. local Doctors**
15:00 – 15:30	**Afternoon Tea**
Skin Brachytherapy: ***Session Chairs: Bryan Burmeister, Radiation Oncology Centres(ROS) Fraser Coast and Redland Australia***	
15:30 – 16:00	**(Invited) Chris Barker,** ***New Approaches to Skin Cancer Brachytherapy*** **MSKCC, New York**
Partial Breast Brachytherapy ***Session chairs: Mira Keys, University of British Columbia , Joseph Bucci , SG CCC***	
16:00 – 16.25	**(Invited) Sean Park** ***Same Day OperatioN and Intraoperative Catheter placement for Partial Breast Irradiation (SONIC-PBI)*** **Mayo Clinic, USA**

16:25 – 16:50	**(Invited) Michael Folkert** ***Ablative interstitial high-dose rate brachytherapy for localised visceral primary and metastatic lesions*** **UT Southwestern Medical Center, USA**

Thursday 8th February 2018
Particle Therapy Day

Advanced Heavy Ion and Proton Therapy Technology ***Session chairs: Anatoly Rozenfeld, CMRP; Michael Jackson , POWH***	
08:00 – 8:25	**(Invited) Koji Noda** ***Recent progress and future plan of heavy-ion-cancer radiotherapy with HIMAC*** **National Institute for Quantum and Radiological Science and Technology, Japan**
08:25 – 8:50	**(Invited) Richard Maughan** ***Recent Developments at the University of Pennsylvania's Roberts Proton Therapy Center*** **Penn University, USA**
08:50 – 9:15	**(Invited) Zuofeng Li, *IBA*** ***Image-Guided Adaptive Proton Therapy*** **IBA: Proton Therapy Center, Florida University, USA**
09:15 – 9:40	**(Invited) Masumi Umezawa *Hitachi*** ***Recent developments in Hitachi's Hybrid Therapy Solution*** **Hitachi**
09:40 – 10:00	**(Invited) Mauro Carrara** ***Italian medical physicists' and radiation oncologists' view on hadron therapy*** **Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy**
10:00 – 10:30	**Morning Tea**
QA in Proton Therapy and Treatment Optimization ***Session chairs: Carl Rossi , Scripps Proton Therapy Center; Tomas Kron , Peter MacCallum CC***	
10:30 – 10:45	**Irene Gudowska** ***Out-of-field doses associated with proton therapy*** **Stockholm University, Stockholm, Sweden**
10:45 – 11.00	**Tina Pfeiler** ***4D Robust optimization in pencil beam scanning proton therapy for hepatocellular carcinoma*** **The West German Proton Therapy Centre Essen, Germany**
11:00 – 11:15	**Jed Johnson** ***Efficient patient-specific QA for spot-scanned proton therapy using nozzle-integrated detectors and fast Monte Carlo dose calculations*** **Mayo Clinic, USA**

11:15 – 11:30	**(Invited) Roberto Sacchi** ***Test of innovative silicon detectors for the monitoring of a therapeutic proton beam*** **University of Torino and INFN, Italy**
11:30 – 11:45	**Daniel Mundy** ***Development of the Dose Magnifying Glass for clinical proton range measurements*** **Mayo Clinic, USA**
11:45-12:10	**(Invited) Marco Silari** ***GEM detectors for use in particle therapy*** **CERN**
12:10-12:30	**(Invited) Benjamin Clasie** ***Installation of a compact comprehensive proton therapy unit via an elevator shaft into existing standard radiotherapy centre*** **MGH, USA**
12:30 – 13:30	**Lunch**
Imaging with Protons and Ions ***Session chairs: Marie-Claude Gregoire, ANSTO; Scott Penfold , RAH***	
13:30 – 13:55	**(Invited) Katia Parodi** ***Ionoacoustics for range monitoring of proton therapy*** **LMU Munich, Germany**
13:55 – 14:20	**(Invited) Taiga Yamaya** ***In-beam OpenPET imaging for RI beams*** **National Institute for Quantum and Radiological Science and Technology, Japan**
14:20 – 14:45	**(Invited) Katia Parodi** ***Prompt gamma range monitoring of proton therapy status and perspectives*** **LMU Munich, Germany**
14:45 – 15:00	**Melek Zarifi** ***In-vivo range verification in hadron therapy using prompt gamma rays: A Geant4 simulation study*** **CMRP UOW**
15:00 – 15:30	**Afternoon Tea**
15:30 – 15:45	**Brad Oborn** ***MRI guided proton therapy: current status of development*** **CMRP UOW**
15:45 – 16:00	**Mitsutaka Yamaguchi** ***Simulation study on imaging of a monochromatic carbon beam by measuring secondary electron bremsstrahlung*** **National Institute for Quantum and Radiological Science and Technology, Japan**

16:00 – 16.20	**(Invited) Dieter Roehrich** ***The Bergen proton CT project – proton tracking in a high-granularity digital tracking calorimeter*** **University of Bergen, Norway**
Australian Proton Therapy Project ***Session chairs: Koji Noda, National Institute for Quantum and Radiological Science and Technology; Verity Ahern . The Crown Princess Mary CC Westmead***	
16.20 – 16:40	**(Invited) Michael Penniment** ***Australian Proton Therapy Project*** **Royal Adelaide Hospital, South Australia**
16:40 – 16:55	**Scott Penfold** ***Dual Energy yCBCT for adaptive proton therapy: A feasibility study*** **Royal Adelaide Hospital, South Australia**
Fundamental Physics of Ions Interaction and New Accelerator Technology in Particle Therapy ***Session chairs Igor Bray, Curtin University; Dale Prokopovich, ANSTO***	
16:55-17:10	**(Invited) A.S. Kadyrov** ***Comprehensive approach to hadron interactions with matter*** **Curtin University, Perth Western Australia**
17:10-17:25	**Edward Simpson** ***Nuclear reaction cross sections for Hadron therapy*** **ANU, Canberra ACT**
17:25-17:50	**(Invited - Special Closing) Suzie Sheehy** ***Can novel accelerator technology improve proton/ion therapy?*** **Oxford University, UK**
17:50-18:00	**Anatoly Rozenfeld** ***Close and future meeting*** **CMRP UOW**

Physics in Heavy Ion Therapy (Microdosimetry)

UPDATE ON THE STATUS OF MEDIPIX IN SPACE AND AN INTRODUCTION TO THE TIMEPIX2

Lawrence Pinsky[1]

[1] Physics Department, University of Houston, Houston, TX 77204-5005 USA, pinsky@uh.edu

Introduction: This paper updates the status of the use of technology developed by the CERN-based Medipix Collaborations in space radiation monitoring coupled with future plans including a look at the promise of the long anticipated Timepix2 device.

Background: NASA has flown Timepix-based Radiation Environment Monitors (REMs) onboard the International Space Station (ISS) since 2012[1]. Furhter, Timepix-based devices were the sole active radiation monirors onboard the first test on the new Multi-Purpose Crew Vehicle (MPCV, or "Orion") in December, 2014. Another Timepix-based device, the Hybrid Electroic Radiation Assessor, (HERA), is being deployed on the upcoming full trans-lunar test of the Orion spacecraft on Exploration Mission-1 (EM-1), and plans are in place to use the same or similar hardware on EM-2, the first manned mission above Low Earth Orbit (LEO) since Apollo. In addition to NASA's use of this technology in space, a number of satellite experiments have flown Timepix-based devices, including Proba V, Satram, and LUCID on the UK's TechDemo1 mission. Similar future applications of this and follow-on versions of this technology are actively being pursued within a number of upcoming projects

Timepix: The Timepix from the CERN-based Medipix2 Collaboration[1] is a hybrid pixel device consisting of detector chip having 256 x 256 pixels, each of which are 55 μm square using 250 nm IBM CMOS. The top surface of the chip has a solder pad enabling the connection of the chip to an overlying sensor chip with cooresponding solder pads using the Flip-Chip® solder-bump bonding technology. The sensor chip typically is a bulk semi-conductor with opposing polarity implants over each solder-bump pad. A reversed bias voltage is applied between the top surface of the sensor and the solder bumps via the front-end amplifiers in the Timepix chip. This allows the digitization of the total net charge collected from the electron-hole pairs produced by the deposition of energy in the bulk semiconductor of the sensor by an ionizing charged particle. The Timepix pixels each contain the analog and digital circuitry to digitize the amount of charge deposited using a Wilkison-type Time-Over-Threshold (TOT) technique. This allows the visualization of the tracks of penetrating charged particles and the determination of the energy deposited during each charged particle's transit within the sensor volume.

Timepix2: The Medipix2 Collaboration has been in the process of designing a second generation of the Timepix chip, motivated by the widespread success of the Timepix in its application to a wide variety of situations. The Timepix2 is a complete re-design of the Timepix using 135 nm TSMC CMOS. In addition to including simultaneous recording of both TOT charge measurement and Time Of Arrival (TOA) within 10 ns encoding, several and improvements have also been added. These include provisions for excluding residual charge collection from events that occurred prior to the "Shutter Open" and including the continuation of readouts for pixels that are still digitizing after the "Shutter Closes."

Another important change regards the analog input treatment. A new design with active feedback extends the input range to well over 3 MeV of energy deposited in the sensor being collected per pixel within the dynamic range for digitization. Charge depositions greater than that limit will be clamped to a constant plateau value, avoiding so-called "volcano effect" seen in the current Timepix.

Acknowledgments: The contrbutions and support of Stuart George, Thomas Campbell-Ricketts, and Anton Empl, from the University of Houston, asa well as Daniel Turecek (Also with ADVACAM s.r.o.), and Lukas Tlustos (also with CERN). Contributions and support also comes from the members of the Space Radiation Analysis Group at NASA's Johnson Space Center (JSC) including Edward Semones, Martin Kroupa, Nicholas Stoffle, Ryan Rios, Dan Fry, Ramona Gaza, and all of the support personnel at JSC who have contributed to the success of the Timepix-based devices in space radiation monitoring.

References:

1. A semiconductor radiation imaging pixel detector for space radiation dosimetry, M. Kroupa, et al., *Life Sci Space Res*. 6, 69-78 (2015).
2. Timepix, a 65k programmable pixel readout chip for arrival time, energy and/or photon counting measurements, (Llopart, X., et al.), *Nucl. Inst. And Meth. Phys. Res.* A 581, 485-494 (2007); and erratum *Nucl. Instr. and Meth*. A 585, 106 (2008).

EVALUATION OF RBE-WEIGHTED DOSES FOR VARIOUS RADIOTHERAPY BEAMS BASED ON A MICRODOSIMETRIC FUNCTION IMPLEMENTED IN PHITS

Kenta Takada[1], Tatsuhiko Sato[2], Hiroaki Kumada[1], Hideyuki Sakurai[1], Takeji Sakae[1]

[1] Faculty of Medicine, University of Tsukuba, 1-1-1, Tennodai, Tsukuba, Ibaraki, 305-8575, Japan
[2] Japan Atomic Energy Agency, 2-4, Shirakata, Tokai, Ibaraki 319-1195, Japan
Corresponding author: k-takada@md.tsukuba.ac.jp

Introduction: The University of Tsukuba developed a treatment planning system (TPS) for boron neutron capture therapy (BNCT) that uses a Monte Carlo algorithm as a dose calculation engine. In the near future, the use of this TPS will be expanded into radiation therapies other than BNCT (i.e., X-ray therapy, and particle therapies). Based on this TPS, we will conduct a biological dose estimation and a physical dose evaluation considering the relative biological effectiveness (RBE). To achieve this purpose, we constructed a Monte Carlo calculation geometry for various radiotherapy beams and calculated the dose probability density of lineal energy (y): $d(y)$ and the biological dose using the appropriate geometry and PHITS code.

Materials and Methods: The $yd(y)$ spectra for the various types of radiation beams, namely X-ray beams (10 MV, 200 keV), a proton beam (200 MeV), a carbon-ion beam (290 MeV/u), and an accelerator-based BNCT beam, were calculated. The $yd(y)$ spectra were calculated using the microdosimetric function implemented in PHITS code [1]. The RBE-weighted dose distributions for a charged particle beam were also calculated in combination with the microdosimetric kinetic model [2]. The double scatterer method and the wobbler irradiation methods were assumed to be the irradiation methods of the proton and carbon-ion beams, respectively. The width of the spread-out Bragg peak was 60 mm. With regard to the BNCT beam, an accelerator-based neutron source developed by the University of Tsukuba, which was a neutron beam generated by irradiating a proton beam of 8 MeV onto a beryllium target [3], was evaluated.

Results: Figure 1 shows the relative comparison of the $yd(y)$ spectra for various beams. Sharp peaks were observed at approximately a y-value of 1 (keV/μm) in the calculated $yd(y)$ spectrum of the 10 MV X-rays. This peak was attributed to the production of Auger electrons from an oxygen atom. In the yd(y) spectrum of the carbon-ion beam, two peaks were observed in the yd(y) spectrum calculated by PHITS. These two peaks were caused by the contribution of the primary component of the carbon-ion and δ rays. The peak around 5 keV/μm can not be observed with a thick-walled detector. Figure 2 presents the calculated physical and RBE-weighted dose distributions for the carbon-ion beam in the water phantom.

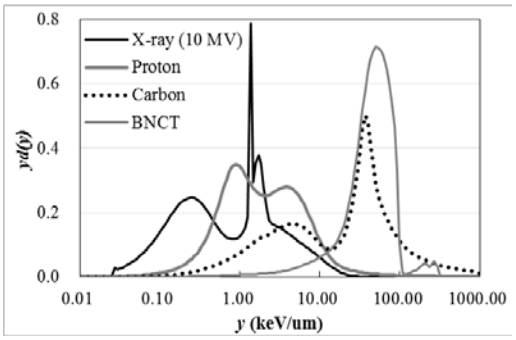


Figure 1. Calculated *yd(y)* spectra for various radiotherapy beams.

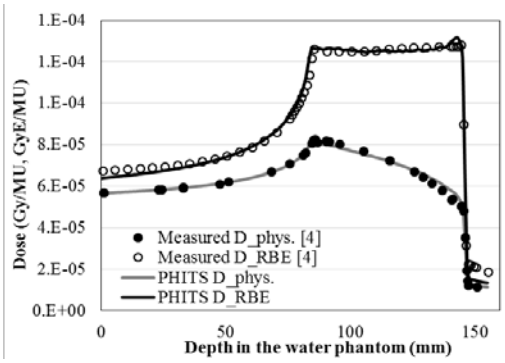


Figure 2. Comparison of physical and RBE-weighted dose for carbon-ion beam.

The calculated depth doses were nearly agreed with the measured data obtained by using a tissue equivalent proportional counter [4].

Conclusions: The microdosimetric $yd(y)$ spectra and the RBE-weighted dose for various radiation beams were calculated. By implementing this method, the newly developed TPS at the University of Tsukuba can be expected to calculate the RBE-weighted dose along with the physical dose for various radiotherapy beams.

References:

1. Sato T, Watanabe R and Niita K 2006 *Radiat. Prot. Dosim.* **122** 41-5
2. Hawkins R B 1998 *Med. Phys.* **25** 1157-70
3. Kumada H, Matsumura A, Sakurai H, et al. 2014 *Appl. Radiat. Isot.* **88** 211-5
4. Kase Y, Kanai T, Sakama M, et al. 2011 *J. Radiat. Res.* **52** 59-6

MICRODOSIMETRY ON NANOMETRIC SCALE WITH A NEW LOW-PRESSURE AVALANCHE-CONFINEMENT TEPC

D. Bortot[1,2], D. Mazzucconi[1,2], S. Agosteo[1,2], A. Pola[1,2], S. Pasquato[1,2], A. Fazzi[1,2], P. Colautti[3],V. Conte[3]

[1] Politecnico di Milano, Energy Department, via La Masa 34, 20156 Milano, Italy, davide.bortot@polimi.it
[2] INFN, Sezione di Milano, via Celoria 16, 20133 Milano, Italy.
[3] INFN, Laboratori di Legnaro, viale dell'Università 2, Legnaro, Padova, Italy.

Introduction: The tissue equivalent proportional counter (TEPC) is the most accurate device for measuring the microdosimetric properties of a particle beam, nevertheless no detailed information on the track structure of the impinging particles can be obtained, since the lower operation limit of common TEPCs is about 0.3 μm[1]. On the other hand, the pattern of particle interactions is measured by track-nanodosimetry, which derives the single-event distribution of ionization cluster size at the nanometric scale. However, only three nanodosimeters are available worldwide, showing stringent limitations: complexity, dimension and associated lack of transportability. In order to fill the gap between standard TEPCs and nanodosimeters, an innovative avalanche-confinement TEPC capable of simulating biological sites down to the nanometric region was designed and constructed.

Materials and Methods: Since the lower operation limit of single-wire TEPCs is equal to about 300 nm in order to maintain an acceptable energy resolution, it is necessary to modify the geometry of the sensitive volume by embedding a third electrode for confining the electronic avalanche within a defined region. An extensive study, based on a prototype described elsewhere[2], allowed designing and developing an avalanche-confinement TEPC (sensitive volume 13 mm in diameter and length) which houses three electrodes biased independently: a central anode wire (graphite), a cylindrical cathode shell (conductive plastic A-150 type) and a helix (gold-plated tungsten), which surrounds the anode and subdivides the sensitive volume into an external drift zone and an internal multiplication region (Figure 1). Two aligned cavities embed a removable ^{244}Cm alpha source and a very compact solid-state detector: this configuration allows calibrating the TEPC by also varying the simulated site size and the polarization of the three electrodes. It guarantees that only signals due to alpha particles with a straight path inside the sensitive volume, i.e. the drift region, are collected[3].

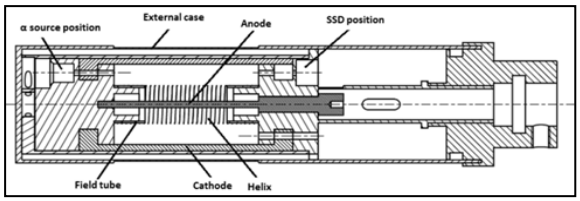


Figure 1. Cross-sectional view of the new TEPC.

A customized and transportable vacuum and gas flow system guarantees vacuum conditions and ensures a continuous replacement of tissue equivalent gas inside the chamber. Dimethyl ether (DME: $(CH_3)_2O$), which can be considered as a tissue-equivalent gas apart from the lack of nitrogen, is the selected filling gas for this TEPC.

Results: The TEPC response in the range 0.3 μm-25 nm against a fast neutron field produced by a calibrated ^{241}Am-Be source and quasi-monoenergetic neutron beams produced through the ^{7}Li(p,n)^{7}Be reaction on a LiF target was assessed experimentally. Two further characterizations with 62 MeV/u carbon ion and helium ion beams were performed at the INFN-Laboratori Nazionali del Sud (LNS-INFN). The experimental response of the microdosimeter for different simulated site sizes in the range 300-25 nm at several points across the depth dose distribution was measured and compared with Monte Carlo simulations performed with the FLUKA code. The obtained results show a rather good agreement.

Conclusions: The irradiation campaigns with different neutron beams and low-energy hadrons (helium and carbon ions) give confidence about the capability of this novel avalanche-confinement TEPC of measuring microdosimetric distribution at simulated site ranging from 0.3 μm down to 25 nm. Further irradiations with other particles are necessary to study deeply the charge collection efficiency of the TEPC at low simulated site sizes, i.e. down to 25 nm. Moreover, further comparisons between FLUKA simulation and experimental data measured with other particles are foreseen.

Acknowledgements: This work was supported by the Italian National Institute for Nuclear Physics - INFN – Scientific Commission V in the framework of the MITRA (Microdosimetry and TRAck structure) and NADIR (biologically relevant NAno-Dosimetry of Ionizing Radiation) projects.

References:

1. B. Hogeweg, *Proc. 4th Symp. on Microdosimetry* **5122**, 843-854 (1973).
2. V. Cesari et al., *Radiat. Prot. Dosim.* **99**, 337-342 (2002).
3. D. Bortot et al., *Radiat. Meas.* (2017). https://doi.org/10.1016/j.radmeas.2017.01.01

A FPGA-BASED SOFTWARE FOR MICRODOSIMETRIC DATA PROCESSING

D. Mazzucconi[1,2], M. Bonfanti[1,2], D. Bortot[1,2], S. Agosteo[1,2], A. Pola[1,2], S. Pasquato[1,2], A. Fazzi[1,2]

[1] Politecnico di Milano, Energy Department, via La Masa 34, 20156 Milano, Italy, davide.mazzucconi@polimi.it
[2] INFN, Sezione di Milano, via Celoria 16, 20133 Milano, Italy.

Introduction: Microdosimetry describes the statistical fluctuations of the imparted energy in a micrometric site[1]. The tissue equivalent proportional counter (TEPC) is the most accurate device for measuring the microdosimetric properties of a particle beam. Since microdosimetric quantities (i.e. the specific energy and the lineal energy) may span over several decades, the electronic and acquisition chain should meet further requirements with respect to the conventional one. Usually, in order to cover the wide dynamic range of the signals generated by the TEPC and to ensure a good resolution throughout this range, the output signal from the preamplifier is fed in parallel to three linear amplifiers which shape and amplify the signal with different gains. In such a way, very low energy deposition events are filtered in the high-gain stage, and high-energy deposition events, which necessarily saturate in the high-gain stage, are processed in the low-gain stage. The acquisition chain should be capable of processing and merging the signals coming from the three amplifiers. A new system with high acquisition performance, in terms of real time calculations, and compact hardware was developed for this purpose.

Materials and Methods: The analog-to-digital conversion is performed by a commercial acquisition system produced by National Instruments, the 4 channels, 14 Bit-Oscilloscope NI PXIe-5170R, which is a configurable digitizer including a user-programmable FPGA (Field Programmable Gate Array) module for the on-board signal processing. The FPGA module is an integrated circuit that contains a matrix of reconfigurable gate array logic circuitry that is programmed via software. When an FPGA is configured, the internal circuitry is connected in a way that creates a hardware implementation of the software application. In this way, the FPGA is capable of performing high speed parallel computations on the acquired data. The FPGA circuitry is programmed thanks to LabVIEW FPGA module[2], which belongs to the high-level LabVIEW graphical programming environment. LabVIEW FPGA development tools also contain a built-in FIFO (First In First Out) transfer and memory read/write functions for storing data in the FPGA application. The FIFO transfer is the connecting bridge between the FPGA and the elaboration software which gives the microdosimetric spectrum. Thanks to the FPGA module a parallel high speed acquisition on the three channels can be performed. Moreover, the implemented software can merge together the three electronic chains and compute a real time microdosimetric spectrum.

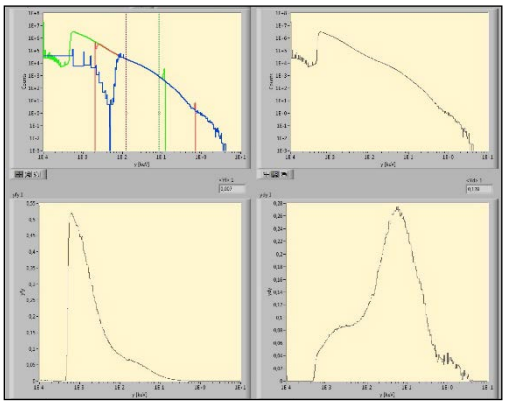


Figure 1. Graphical interface of the software showing a spectrum from an Am-Be fast neutron source.

Results: The developed software has a graphical interface in which the user can set the acquisition parameters (e.g. sampling rate and acquisition thresholds) and visualize the microdosimetric spectrum. The FPGA software can perform analog-to-digital conversion and digital signal processing at a sampling rate up to 15 MS/s (i. e. Mega Samples per second) per each of the three channels (The ADC speed is 45 MS/s). The software can plot a real time microdosimetric spectrum in order to have a prompt information about the irradiation field (Figure 1).

Conclusions: The new FPGA-based hardware and software, allow to reach a significant high acquisition speed that is needed in the presence of a high counting rate. This is because, for intense fields, a shorter shaping time is mandatory in order not to cause a pulse pile-up. The new acquisition software was tested irradiating a TEPC with an intense quasi-monoenergetic neutron beam and a 62 MeV/u helium ion beam. Further optimization on the FPGA architecture is foreseen in order to achieve an improvement on the computation performances.

Acknowledgements: This work was supported by the Italian National Institute for Nuclear Physics - INFN – Scientific Commission V in the framework of the MITRA (Microdosimetry and TRAck structure) and NADIR (biologically relevant NAno-Dosimetry of Ionizing Radiation) projects.

References:

4. Microdosimetry. ICRU Report 36 (1983).
2. National Instruments. http://www.ni.co

PROGRESS IN SILICON MICRODOSIMETRY AND ITS APPLICATIONS

Linh T. Tran[1], David Bolst[1], Emily Debrot[1], Susanna Guatelli[1], Marco Petasecca[1], Michael Lerch[1], Lachlan Chartier[1], Dale Prokopovich[1], Marco Povoli[2], Angela Kok[2], Charlot Vandevoorde[3], J. Slabbert[3], Naruhiro Matsufuji[4], Tatsuaki Kanai[5], Anatoly B. Rosenfeld[1]

[1]Centre for Medical Radiation Physics, University of Wollongong, Australia. anatoly@uow.edu.au
[2]SINTEF, Norway
[3]Radiation Biophysics Department, NRF iThemba LABS, South Africa
[4]National Institutes for Quantum and Radiological Science and Technology, Chiba, Japan
[5]Gunma Heavy Ion Medical Centre, Gunma, Japan

The solid state microdosimeters with 3D micron sized sensitive volumes (SVs) mimicking dimensions of cells, known as the "Bridge" and "Mushroom" microdosimeters, were fabricated using MEMS technology [1,2]. The silicon microdosimeters provide extremely high spatial resolution and were used for evaluating the relative biological effectiveness (RBE) of 290 MeV/u ^{12}C, 180 MeV/u ^{14}N and 400 MeV/u ^{16}O passive ion beams as well as 290 MeV/u ^{12}C mini ion beams at Heavy Ion Medical Accelerator in Chiba (HIMAC), Japan. Additionally, the variation of RBE in-field was investigated for a passive proton beam delivery system at iThemba labs, South Africa including radiobiological and microdosimetry measurements.

For a 180 MeV/u ^{14}N pristine BP, the $\overline{y_D}$ changed from about 29 keV/µm at the entrance to 92 keV/µm at the BP, with a maximum value 438 keV/µm at the distal edge. For a 400 MeV/u ^{16}O ions, the dose-mean lineal energy $\overline{y_D}$ changed from about 24 keV/µm at the entrance to 106 keV/µm at the BP, with a maximum value of approximately 381 keV/µm at the distal edge. The maximum derived RBE_{10} values for ^{14}N and ^{16}O ions are 3.10 ± 0.47 and 2.93 ± 0.45, respectively.

The $\overline{y_D}$ and RBE_{10} values are compared for 290 MeV/u ^{12}C broad beam and minibeams produced by brass multi-slit collimator where microdosimetric spectra were measured in peaks and valley and out of field with a recently developed single 3D SV microdosimeter.

The RBED (D=2Gy) derived from survival of the Chinese Hamster Ovary (CHO) cells and the predicted RBE from the microdosimetric measurements using MKM in proton beam at iThemba labs indicate that there is a strong increase in the biological effectiveness with depth along the SOBP particular in the distal fall off of the SOBP (Fig 1, 2). Both RBED are matching reasonably well.

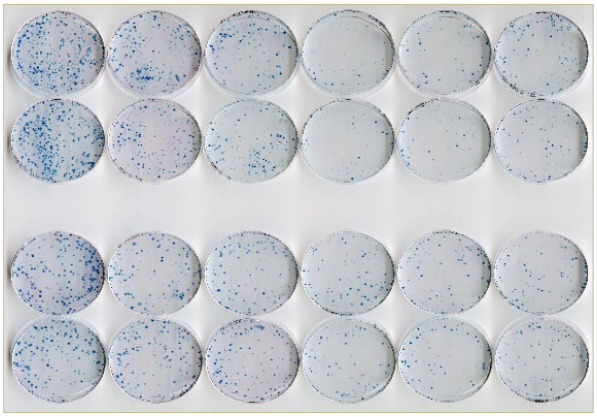


Fig. 1 Petri-dishes representing colony survival in CHO-K1 cells at 6 positions (from left to right: 74.88%, 101.10%, 83.44%, 57.18%, 39.76% and 18.98% of along the Bragg curve, exposed to doses of 4 Gy (2 top rows) and 8 Gy (2 bottom rows).

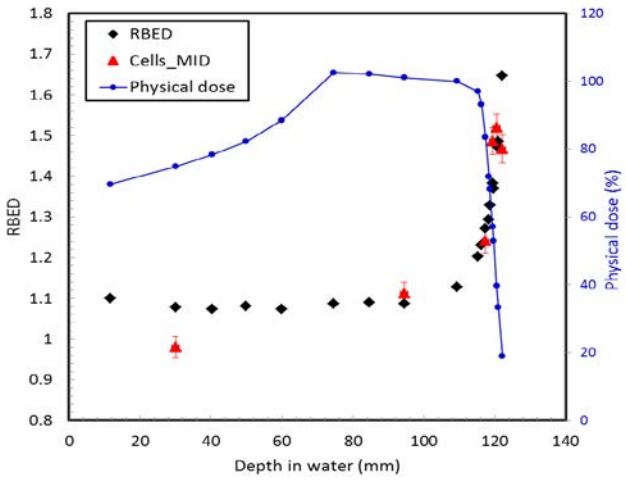


Fig. 2 Comparison of RBED obtained with microdosimetric probe and radiobiological experiment with CHO cells

References:

1. Novel detectors for silicon based microdosimetry, their concepts and applications (A. Rosenfeld), *Nucl. Instrum. Methods., Phys. Res.* A **809**, 156–170, (2016).
2. 3D Silicon Microdosimetry and RBE study using ^{12}C ion of different energies (L. Tran et al.), *IEEE Trans. on Nucl. Sci. vol.* **62**, no. 6, pp 3027-3033, (2015).

3D SENSITIVE VOLUME MICRODOSIMETER WITH IMPROVED TISSUE EQUIVALENCY: CHARGE COLLECTION STUDY AND ITS APPLICATION IN ^{12}C ION THERAPY

Benjamin James[1], Linh T. Tran[1], David Bolst[1], Dale Prokopovich[2], Michael Lerch, Marco Petasecca, Susanna Guatelli, Mark Reinhard[2], Marco Povoli[3], Angela Kok[3], Naruhiro Matsufuji[4] and Anatoly Rozenfeld[1]

[1]Centre of Medical and Radiation Physics, University of Wollongong, bj197@uowmail.edu.au
[2]NSTLI Nuclear Stewardship, Australian Nuclear Science and Technology Organization, Australia
[3]SINTEF, Norway
[4]National Institutes for Quantum and Radiological Science and Technology, Chiba, Japan

Introduction: Particle therapy has many advantages over conventional photon therapy, particularly for treating deep-seated solid tumours due to its greater conformal energy deposition achieved in the form of the Bragg Peak (BP). Successful treatment with heavy ions depends largely on knowledge of the relative biological effectiveness (RBE) of the radiation produced by primary and secondary charged particles. Different methods and approaches are used for calculation of the RBE-weighted absorbed dose in treatment planning system (TPS) for heavy ion therapy. The RBE derived based on microdosimetric approach using the tissue equivalent proportional counter (TEPC) measurements in ^{12}C therapy has been reported, however the large size of commercial TEPCs averages RBE values which dramatically changes close to and in the distal part of the BP, which may have significant clinical impact. The Centre for Medical Radiation Physics (CMRP), University of Wollongong, has initiated the concept of silicon microdosimetry to address the shortcomings of the TEPC[1]. In the course of this research, a new 3D SV microdosimeter covered with a tissue equivalent material has been investigated and its application in C-12 therapy has been studied.

Methods: A new generation 3D microdosimeter design was proposed by CMRP, it has 3D cylindrical sensitive volumes, known as "Mushrooms". The Mushroom microdosimeter is fabricated on silicon on insulator material with a buried oxide layer that isolates the sensitive volumes from the support wafer. An array of n+ electrodes and surrounding ring p+ electrodes are produced using deep reactive ion etching, followed by polysilicon deposition and doping[1]. In order to improve the tissue equivalence of the new microdosimeters, they have been covered with a 12µm layer of polymide. While the polymide layer will serve to improve the tissue equivalence of the microdosimeter, charge collection and uniformity studies were required to understand how the microdosimeter output would be affected by this new layer.

The charge collection efficiency was investigated using ion beam induced charge collection (IBICC) technique with the 6MV SIRIUS Tandem Accelerator at Australian Nuclear Science and Technology Organisation (ANSTO). Median energy maps showing the charge collection characteristics of the device were then created[1]. Finally to study its possible applications in ^{12}C therapy, the new polymide mushroom microdosimeters were placed in various positions along the central axis of the SOBP of a 290 MeV/u ^{12}C ion beam at the Heavy Ion Medical Accelerator in Chiba (HIMAC), Japan.

Results: Results presented will include IBIC MCA spectra and median energy maps obtained using the scanning 5.5 MeV He^{2+} microbeam. These results will demonstrate a uniform charge collection and some issues with the polymide coating deposition, which have been investigated. Based on the irradiations conducted at HIMAC, microdosimetric spectra, dose mean lineal energy (y_D) and RBE results will also be presented. RBE values obtained in the SOBP at HIMAC showed a dramatic increase, with values of 1.3 observed at the entrance and increasing to 2.7 at the end of the SOBP.

Conclusions: These results will serve to prove that the new generation, tissue equivalent, polymide mushroom microdosimeters are an excellent tool for quality assurance in heavy ion therapy applications

References:

1. Tran, L. T., Chartier, L., Prokopovich, D. A., Reinhard, M. I., Petasecca, M., Guatelli, S., Lerch, M. L. F., Perevertaylo, V. L., Zaider, M.,Matsufuji, N., Jackson, M., Nancarrow, M. & Rosenfeld, A. B. (2015). 3D-mesa 'bridge' silicon microdosimeter: charge collection study and application to RBE studies in 12C radiation therapy. IEEE Transactions on Nuclear Science, 62 (2), 504-511.

Radiobiology & Monte Carlo Simulations

TOPICAL RADIOPROTECTION OF RADIATION-INDUCED ORAL MUCOSITIS

Pavel N. Lobachevsky[1], Andrea Smith[1], Laura Munforte[1], Nevena Vasilijevic[1], Sarah Foenander[1], Jonathan M. White[2], Colin Skene[2], Seb Marcuccio[3], Roger F. Martin[1,3]

[1]Peter MacCallum Cancer Centre, Melbourne, VIC, Australia, rfm@unimelb.edu.au
[2]School of Chemistry and Bio21 Institute, The University of Melbourne, Melbourne, VIC, Australia,
[3]Advanced Molecular Technologies, Scoresby, VIC, Australia,

Introduction: Even with the most modern radiotherapy techniques, some dose to nearby normal tissues cannot be excluded. Many of the normal tissues "at risk" in RT are accessible topically, and the topical application route provides the opportunity to selectively protect normal tissues to the exclusion of the tumour. Examples include oral mucosa, rectal mucosa, oesophagus, lung (aerosol), urethra and bladder, hair follicles and skin. We have developed new radioprotecting drugs that can be applied topically to ameliorate normal tissue toxicities in cancer radiotherapy (RT) patients. The initial focus is the clinical scenario of topical application of radioprotector to oral mucosa of H&N RT patients, as a spray, or mouth wash/swish/gargle, prior to each radiation dose. Apart from clinical need, this choice was driven by the availability of a suitable preclinical model, in which the radiobiological model is radiation-induced ulceration of mouse tongue (1).
The compound family can be described as DNA-binding antioxidants, the first lead compound being methylproamine (2). The mechanism of radioprotection involves charge transfer along DNA, between a transient radiation-induced oxidising species (such as a Guanine radical cation) and the reducing radioprotector molecule bound in the minor groove (3). By analogy, the radioprotector acts like a "sacrificial anode" diverting the transient radiation-induced damage from DNA to the ligand, which presumably then dissociates from the DNA.
The oral mucosa includes a barrier to drug penetration, not unlike the stratum corneum, and thus has necessitated the design of molecules that can penetrate the barrier to enable topical delivery to stem cells in the basal layer of the mucosa. Fortunately, since all the drugs are fluorescent, delivery to basal cell nuclei can be monitored by fluorescence microscopy.

Materials and Methods: A library of >200 new compounds with a characteristic bisbenzimidazole scaffold exemplified by a minor-groove binders Hoechst 33342 and methylproamine, have been synthesised and characterised by standard methods (2). Each compound was evaluated using an in vitro clonogenic survival assay that assesses both radioprotection and cytotoxicity.
To assess topical delivery, drug formulation was applied to the ventral surface of mouse tongue, and at various times after application, cryostat sections were taken for fluorescence microscopy.
The radiobiological model involved irradiation with 25 keV X-rays of a 3mm x 3mm field on the ventral surface of mouse tongue, and monitoring of ulcers which appeared about 10 days after irradiation. For the fractionated version of the model, mice were exposed to daily snout irradiations with 160 keV X-rays prior to a single top-up/boost to the tongue, as for the single-fraction model.

Results: A clinical candidate emerged from screening for radioprotective activity and cytotoxicity using the in vitro clonogenic survival assays, and evaluation of topical delivery.
Proof-of-principal of topical radioprotection has been established in a mouse tongue model, for both single-fraction and fractionated irradiation. The extent of radioprotection (a Dose Reduction Factor of > 1.2) is such that based on a low-power retrospective clinical study, Grade-2 oral mucositis would be reduced to Grade 0/1.

Discussion and Conclusions: A clinical trial is planned, but compound manufacture and toxicology remain as pre-requisite milestones. All 3 members of the compound family evaluated in the Ames test have proved negative, but a broad toxicology profile is a priority. However there are grounds for optimism. Under a Licensing Agreement (LA) to OrthoBiotech (a J&J subsidiary) during 1999-2001, the licensee commissioned toxicology studies on the then lead compound (methylproamine), and the results satisfied their requirements to proceed with the LA. Nevertheless, a new sponsor needs to be identified to progress to clinical studies.

References:

1. A. Gehrisch A & W. Dörr W. *Strahlenther Onkol.* **183**:36-42 (2007).
2. R. F. Martin et al, *Cancer Res.* **64**:1067-70 (2004)
3. R.F Martin & R. F. Anderson *Int. J. Radiat. Oncol. Biol. Phys.*, **42***:* 827-831 (1998).

DEVELOPMENT OF TRACK STRUCTURE MODELS IN GEANT4 FOR NANO-METER SCALE GOLD

D. Sakata[1,2,3], I. Kyriakou[4], S. Okada[5], H. N. Tran[6], N. Lampe[2], S. Guatelli[1], M.C. Bordage[7,8], V. N. Ivanchenko[9,10], K. Murakami[11], T. Sasaki[11], D. Emfietzoglou[4] and S. Incerti[2,3]

[1] University of Wollongong, Centre For Medical Radiation Physics, Wollongong, Australia
[2] Univ. Bordeaux, CENBG, UMR 5797, Gradignan, France, dousatsu-univtky@umin.ac.jp
[3] CNRS, IN2P3, CENBG, UMR 5797, Gradignan, France
[4] University of Ioannina Medical School, Medical Physics Laboratory, 45110, Ioannina, Greece
[5] Kobe University, Organization for Advanced and Integrated research, Kobe, Japan
[6] Irfu, CEA, Universite Paris-Saclay, Gif-sur-Yvette, France
[7] INSERM, UMR1037 CRCT, Toulouse France
[8] Universite Toulouse III-Paul Sabatier, UMR1037 CRCT, Toulouse, France
[9] Geant4 Associates International Ltd, Hebden Bridge, United Kingdom
[10] Tomsk State University, Tomsk, Russia
[11] KEK, Tsukuba, Japan

Introduction: Gold NanoParticles (GNPs) are known to boost the effectiveness of photon based radiation treatments by increasing the absorbed dose in their vicinity. To investigate the effectiveness of GNPs, previous Monte Carlo simulation studies have explored GNP dose enhancement using mostly condensed history models. However, in general, such models are suitable for macroscopic volumes and for electron energies above a few hundreds electron volts. We have recently developed, for the Geant4-DNA extension of the Geant4 Monte Carlo simulation toolkit, discrete physics models for electron transport in gold [1]. In this talk, we show the impact of new discrete physics models in microscopic gold volume.

Materials and Methods: In this work, the new physics models are compared to the Geant4 Penelope and Livermore condensed history models, which are currently used for NP radioenhancement Geant4-based studies. Within this study, an ad-hoc Geant4 simulation application has been developed to calculate the absorbed dose in liquid water around a GNP and its radioenhancement, caused by secondary particles emitted from the GNP itself, when irradiated with a monoenergetic electron beam. The effect of the new physics models is also quantified in the calculation of secondary particle spectra, when originating in the GNP and when exiting from it.

Results: The new physics models show similar backscattering coefficients with Livermore and Penelope models in large volumes for 100 keV incident electrons. However, in submicron sized volumes, only the new physics models describe the high backscattering that should still be present around GNPs at these length scales. We found that the new physics models could be applicable to microscopic gold volumes down to 20 nm diameter at least.

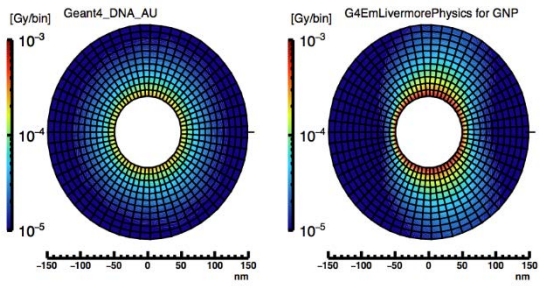


Figure 1. Two dimensional absorbed dose by secondary particles around GNPs irradiated by 100 keV monoenergetic electrons, in a 1 nm thick sampling plane. Left: Geant4_DNA_AU, Right: Livermore in Geant4.

Conclusions: Improved physics models for gold are necessary to better model the impact of GNPs in radiotherapy via Monte Carlo simulations. We concluded that the implemented discrete physics models are characterised by an improved performance for particle transport simulations in gold volumes with submicron dimensions.

Acknowledgements: This work is funded by the University of Bordeaux, via the 2015 international post-doctoral fellowship program, for the "Nano-Boost" project. The work is also supported by the "France- Japan Particle Physics Laboratory (FJPPL)" international associated laboratory (CNRS/KEK) and by the Greece-France "Projet International de Cooperation Scientifique (PICS)" #7340. This work is also supported by the Australian Research Council, ARC DP, DP170100967.

References:

5. Dousatsu Sakata et al, "An implementation of discrete electron transport models for gold in the Geant4 simulation toolkit", *J. Appl. Phys.* ***120****, 244901 (2016)*

NANOTHERANOSTIC RADIO-ENHANCEMENT

H L Byrne[1], A McNamara[2], F Lux[3], G le Duc[4], O Tillement[3], R Berbeco[5], Z Kuncic[1]

[1] School of Physics, University of Sydney, NSW 2006, Australia hilary.byrne@sydney.edu.au
[2] Department of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA
[3] ILM UMR 5306 CNRS, Claude Bernard-University, Lyon, FRA.
[4] NH TherAguix, SAS, France;
[5] Department of Radiation Oncology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02215, USA

Introduction: The ability to design and build functional nanoscale structures provides the tools for interaction with and manipulation of fundamental biological processes at the sub-cellular scale on which they operate.

The field of radiotherapy has developed a body of knowledge of the micro- and nano-scale mechanisms of radiation damage, relating characteristic ionisation patterns to biological effectiveness. This knowledge can now be exploited to explain and optimise the experimentally observed enhancement of radiation damage by high atomic number nanoparticles [1].

Herold et al. first demonstrated increased efficiency of kilovoltage radiotherapy in combination with small gold particles in 2000 [2]. Nanoparticle radio-enhancement has since been demonstrated for a wide range of incident particle types and energies [3,4]. While much attention has been paid to date to radio-enhancement with gold nanoparticles, recent studies have begun to focus on other high atomic number elements, for example bismuth [5].

The choice of element does not greatly affect the physical mechanisms of dose enhancement, but does offer the possibility of tailoring the addition of diagnostic or therapeutic function. For example, the incorporation of gadolinium, a contrast agent for magnetic resonance imaging (MRI), delivers diagnostic imaging and enhanced radiotherapy treatment in the same nanoparticle [6]. The recent emergence of MRI-guided radiotherapy affords the ideal platform for exploiting nanotheranostic radio-enhancement.

Materials and Methods: Nanoparticle radio-enhancement can be investigated and understood on several different physical scales.

At the macroscale, physical dosimetry of the nanoparticle radiation enhancement effect presents a challenge. Detectors must be able to record the enhanced numbers of short range photo-electrons from low energy photons which can be absorbed by only thin films of shielding.

At the nanoscale, biologically important locally inhomogeneous dose distributions are created by extremely short range of Auger electrons. Monte Carlo simulations (see figure 1) can be used to gain insights into the nanoscale physical phenomena at work in radio-enhancement that are otherwise difficult to obtain experimentally.

Results: Patterns of energy deposition on the nanoscale are linked to the biological effectiveness of radiation treatment. The presence of high atomic number nanoparticles gives rise to high dose gradients near their surface, which can be related to tumour control probabilities through models such as the Local Effect Model. However, the biological effectiveness is dependent on the nanoparticles' distribution relative both to each other, to important sub-cellular structures, and within the target tissue.

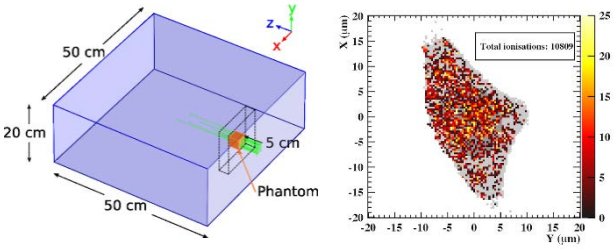


Figure 1. a) simulation geometry for macroscale dose enhancement b) sub-cellular ionisation distribution

Conclusions: High atomic number nanoparticles hold great promise for enhancing radiotherapy, through both compounding the radiation damage caused within the target tumour and enhancing image contrast for tracking nanoparticle uptake and improving radiotherapy targeting precision. The best clinical implementation of this emerging paradigm requires a deep understanding of the mechanisms at work to allow development of an optimal treatment.

References:

1. Kuncic, Z. and Lacombe, S. Nanoparticle radio-enhancement: principles, progress and application to cancer treatment. *Phys. Med. Biol.* In press (2017) doi:10.1088/1361-6560/aa99ced
2. Herold, D. M. *et al.* Gold microspheres: a selective technique for producing biologically effective dose enhancement. *Int J Radiat Biol* **76,** 1357 (2000).
3. Butterworth, K. T. *et al.* Physical basis and biological mechanisms of gold nanoparticle radiosensitization. *Nanoscale* **4,** 4830 (2012).
4. Lacombe, S. *et al.* Particle therapy and nanomedicine: state of art and research perspectives. *Cancer Nanotechnology* **8,** (2017).
5. Detappe, A. *et al.* Ultrasmall Silica-Based Bismuth Gadolinium Nanoparticles for Dual Magnetic Resonance–Computed Tomography Image Guided Radiation Therapy. *Nano Lett.* **17,** 1733 (2017).
6. Sancey, L. *et al.* The use of theranostic gadolinium-based nanoprobes to improve radiotherapy efficacy. *BJR* **87,** 20140134 (2014).

MODELLING THE HIMAC BIO BEAMLINE IN GEANT4 FOR MICRODOSIMETRY APPLICATIONS

D. Bolst[1], L. T. Tran[1], S. Guatelli[1], N. Matsufuji[2], A. B. Rosenfeld[1]

[1] Centre for Medical Radiation Physics, University of Wollongong, Australia, db001@uowmail.edu.au
[2] Research Centre for Charge Particle Therapy, National Institue of Radiological Scienc, Chiba, Japan

Introduction: ^{12}C therapy has had a growing interest thanks to its enhanced physical and biological dose properities, however, the ^{12}C beam produces a complex radiation field and it is important to characterise and understand the field which is produced. Monte Carlo simulations provide an insight to the radiation field but need to be accurate, in this work the modelling of the bio beamline at the Heavy Ion Medical Accelerator (HIMAC) in Japan is described and validated against experimental data.

Materials and Methods: The Bio Beamline is a passive beam and was modelled using the Monte Carlo toolkit Geant4 [1] version 10.2p2. The modelling of the beam starts after the beam nozzle as a pencil beam with an energy of 290 MeV/u, the beam is then formed to a circular shape by a pair of wobbler magnets, operated using the single wobbling method. After the wobbler the lateral dose uniformity is improved by passing through a scatterer, the contribution of neutrons present in the beam are then reduced by passing through a neutron shutter (vacuum tube). For a spread out Bragg Peak (SOBP), after the neutron shutter the beam passes through an aluminium ridge filter to form the SOBP. The beam is then shaped by an aluminium four leaf collimator (FLC) and a brass collimator. After being collimated the beam is either incident upon a phantom or a scoring plane to generate a phase space file.

The physics models used in the simulation included the *G4StandardOption3* for electromagnetic interactions, the Bincary Intranuclear Cascade (BIC) for hadronic fragmentation and the neutron High Precision (HP) model for neutron interaction up to 20 MeV.

To validate the Geant4 application the lateral and depth dose profiles were compared to experimental measurements using an ionisation chamber. To investigate whether simplifying the beamline by excluding the wobbler magnets had a noticeable impact on the beam profile alternative methods were simulated including: passing the initial point beam without the wobbler being active, having a uniform 100 mm diameter circular beam generated and finally generating a cone beam.

Results: The lateral dose comparison between the experiment and simulation can be seen in figure 1 for both a mono-energetic and a SOBP taken at iso-centre before the phantom with both the FLC and brass collimator fully opened. Excellent agreement is observed between experiment and simulation for both beams. The simplified beam simulation methods were compared to the full wobbler setup for a collimated 100 × 100 mm^2 field size. It was found that the cone beam provided good agreement with the full wobbler setup while both of the alternatives gave poor agreement.

For the depth dose comparisons the mono-energetic beam was found to have a excellent agreement with experiment for all simulation methods. The SOBP depth dose is shown in figure 2 and had slightly less agreement with experiment than the mono-energetic beam with a slight over-response in the dose towards the end of the SOBP. Unlike with the mono-energetic beam the different simulation methods had a drastic impact on the depth dose distribution, with the point and circle beams producing a flatter response while the cone beam matched the full wobbler setup very well.

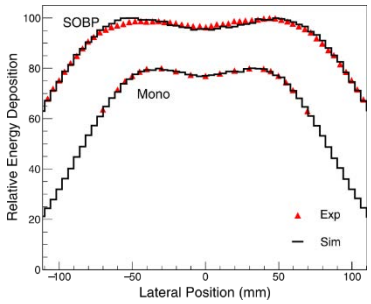


Figure 1. Comparison of the lateral profile of the experiment and the simulation for a mono and SOBP.

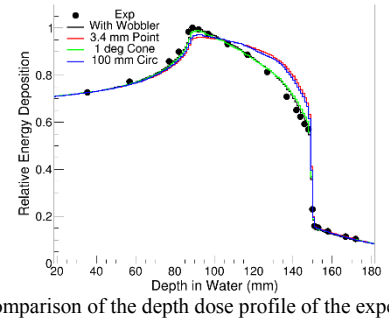


Figure 2. Comparison of the depth dose profile of the experiment and the simulation for a SOBP

Conclusion: A Geant4 application modelling the Bio Beamline has been described and validated against experimental lateral and depth dose measurements for a mono-energetic and SOBP ^{12}C beam. Excellent agreement was observed between simulation and experiment for both lateral beam profiles and for the depth dose distribution. Simplifed simulation methods without the wobblers were compared and it was found that a cone beam gave good agreement for both lateral and depth dose profiles.

References: 6. Geant4 Collaboration (S. Agostinelli et al.), *Nucl. Instrum. Meth. Phys. Res.* A **506**, 250-303 (2003).

LATEST DEVELOPMENT AND APPLICATIONS OF THE CHINESE REFERENCE PHANTOMS

Rui Qiu[1,2,*], Zhen Wu[3], Chunyan Li[3], Li Ren[1,2], Wenjing Wang[1,2], Hongyu Zhu[1,2], Mingliang Dai[1,2], Yuxi Pan[1,2], Ruiyao Ma[1,2],An kang Hu[1,2],Junli Li[1,2]

[1] Department of Engineering Physics, Tsinghua University, Beijing, China
[2] Key Laboratory of Particle & Radiation Imaging (Tsinghua University), Ministry of Education, Beijing, China
[3] Nuctech Company Limited, Beijing, China
[*] Corresponding author: qiurui@mail.tsinghua.edu.cn

Abstract: The Chinese adult reference male (CRAM) and female (CRAF) phantoms have been developed in previous work. Latest development and applications of the Chinese reference phantoms are introduced in this paper.

A Chinese male phantom library was constructed with 7 different heights ranging from 155 cm to 185 cm and 12 phantoms with different total body masses in each height. Chinese pediatric reference phantoms were constructed for 3 months, 1 year, 5 years, 10 years, and 15 years male and female respectively based on the CT medical images of different ages. The heights of the six established phantoms were 62 cm, 77 cm, 110 cm, 139 cm, 168 cm and 158 cm, respectively, and the weights were 7 kg, 10 kg, 19 kg, 32 kg, 55 kg and 50 kg, complied with the reference value. Each mesh-type phantoms consists of 108 different tissues and organs, which includes all the radiation-sensitive organs.

A set of three-dimensional detailed breast models based on the realistic structures in the breast and the Chinese female breast parameters were built. A mathematical model was established and then converted to a voxel model. First the breast shape was built, and then it was divided into skin, adipose tissue region, and fibroglandular tissue region. Detailed structures such as Cooper's ligaments, intraglandular fats, and ductal lobes were built in different regions.

A mathematical model for human respiratory tract was first established based on the anatomic bronchial parameters of adult Chinese male. Then it was voxelized to build a numerical voxel model, and integrated into the CRAM. This model featured by consecutive 16-generation bronchial structures, could represent the structure of entire lung trachea and bronchus structure.

A detailed eye model was built based on the characteristic anatomic parameters of the Chinese adult male. This eye model includes seven main structures, which are scleral, choroid, lens, iris, cornea, vitreous body and aqueous humor. The lens was divided into sensitive volume and insensitive volume based on different cell populations. The detailed eye model was incorporated into the converted polygon-mesh version of the CRAM_S.

The phantoms were applied in radiation protection, including dose estimation from external exposure and internal exposure, in normal situations and in accidental situations. Detailed dose distributions in radiation-sensitive organs can also be obtained. The phantoms were also applied in medical imaging field such as dose estimation in mammography and CT. A series of organ dose conversion coefficients for dose estimation in CT scanning and X-Ray radiology were calculated with the Chinese adult and pediatric reference phantoms. A series of glandular tissue dose conversion coefficients for dose estimation in mammography were calculated with the 3D detailed breast models. These data will provide references for the revision of the national standard for the estimation of the examinee's organ doses generated by X-ray diagnosis in China.

Key words: Chinese reference phantom; detailed organ model; Monte Carlo; radiation protection; medical imaging

Synchrotron Radiation

LOCALISED SYNCHROTRON RADIATION IN MICE INDUCES PERSISTENT SYSTEMIC GENOTOXIC EVENTS MEDIATED BY THE FUNCTIONAL IMMUNE SYSTEM.

Jessica Ventura[1,2], Pavel Lobachevsky[1,3], Jason Palazzolo[1], Helen Forrester[4], Nicole Haynes[1,3], Alesia Ivashkevich[5], Andrew W. Stevenson[6,7], Christopher J. Hall[7], Vassilis Gorgoulis[8,9], John Hamilton[3], Alexandros G. Georgakilas[10], Carl N. Sprung[4], Olga A. Martin[1,3] (olga.martin@petermac.org).

[1]Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; [2]Royal Women's Hospital, Melbourne, VIC, Australia; [3]The University of Melbourne, Melbourne, VIC, Australia; [4]Hudson Institute of Medical Research, Clayton, VIC, ia; [5]Canberra Hospital, Garran, ACT, Australia; [6]CSIRO, Clayton, VIC, Australia; [7]Australian Synchrotron, Clayton, VIC, Australia; [8]University of Athens, Athens, Greece; [9]University of Manchester, Manchester Academic Health Science Centre, Manchester, UK; [10]National Technical University of Athens, Athens, Greece.

Introduction: The discovery of the radiation-induced bystander effect (RIBE) (1) has expanded knowledge of radiobiological mechanisms beyond the scope of the central dogma of radiation biology, i.e. that only cells that absorbed a dose of ionising radiation (IR) are affected and the response is dose-dependent. The RIBE is now a well-established phenomenon comprising cyto- and genotoxic effects in out-of-field cells associated with irradiated cells. A counterpart *in vivo* phenomenon, a change in an organ or tissue distant from the irradiated region, was termed the radiation-induced abscopal effect (RIAE) (2). The mechanisms of the RIAE are only beginning to be understood, however the immune system has been proposed as the main mediator.

It is not known how radiation settings affect non-targeted normal tissues and therefore the risk of radiation-related adverse abscopal effects. At the Imaging and Medical Beamline (IMBL), the Australian Synchrotron, we examined systemic effects of microbeam radiotherapy (MRT) and broad beam (BB) configurations, in mice that were locally exposed to a very short pulse of a high dose-rate synchrotron beam (49 Gy/sec). We determined how radiation volume and dose impact the RIAE. We associated the propagation of these systemic effects with the induction of innate and adaptive immune effector responses and with modulations of plasma cytokine concentrations. Finally, we compared the RIAE in mice with the functional immune system and in immune-deficient mice.

Materils and Methods: C57BL/6 mice were irradiated with 10 or 40 Gy incident dose of MRT or BB in an 8x8, 8x1, or 2x2-mm area of the right hind leg For irradiation with MRT, a collimator produced beam widths of 25 μm and microbeam centre-to-centre spacings of 200 μm. The absorbed doses of incident and scattered radiation were measured with the radiochromic EBT3 and XRQA2 films. Blood samples, irradiated skin and a variety of normal unirradiated tissues were collected for DNA damage analysis of double-strand breaks (DSBs) quantified as γ-H2AX foci in tissue sections and oxidatitive clustered DNA leasions (OCDL) measured by constant field gel electrophoresis of genomic DNA treated with pyrimidine- and abasic site-specific enzymes. We also measured the systemic immune response (plasma cytokine concentrations) and the local immune response (*in-situ* quantification of immune cells). The 10 Gy 8x8 mm MRT irradiation experimet was repeated in immune-deficient mice; (i) NOD SCID gamma (NSG), (ii) CCL2/MCP1 knock-outs, and (iii) in C57BL/6 mice treated with anti-CSF1R ASF98 antibody which effectively depletes macrophages.

Results: OCDLs elevated in a wide variety of unirradiated normal tissues. In out-of-field duodenum, a trend for elevated apoptotic cell death was observed under most irradiation conditions, however DSBs elevated only after exposure to lower doses (10 Gy peak dose, but not 40 Gy). These genotoxic events were accompanied by changes in concentrations of MDC, CCL2/MCP1, Eotaxin, IL-10, TIMP-1, VEGF, TGFβ-1 and TGFβ-2 plasma cytokines and by changes in frequencies of macrophages, neutrophils and T-lymphocytes in duodenum. Overall, systemic radiation responses were dose-independent (3). Strikingly, these effects and the abscopal innate and adaptive immune effector responses were completely or partially abrogated in the mice with various immune deficiencies, highlighting the role of the functional immune system in propagation of systemic genotoxic effects of localised irradiation.

Conclusion: These findings have implications for the planning of therapeutic and diagnostic radiation treatment to reduce the risk of radiation-related adverse systemic effects.

References:

1. KM Prise & JM O'Sullivan, *Nature Reviews. Cancer.* **9**:351-360 (2009).
2. S. Siva et al, *Cancer Letters* **356**:82-90 (2015).
3. J. Ventura et al, *Cancer Research*, in press (2017

TOWARDS IMAGE-GUIDED MICROBEAM RADIATION THERAPY

E Engels[1,2], S Corde[1,2,3], M Westlake[1,2], N Li[1,2], M Lerch[1,2], , M Tehei[1,2]

[1] Centre for Medical Radiation Physics (CMRP), Wollongong, NSW, Australia 2522, ee215@uowmail.edu.au
[2] Illawarra Health and Medical Centre (IHMRI), Wollongong, NSW, Australia 2522
[3] Prince of Wales Hospital, Randwick, Australia 2031

Introduction: Gliomas and glioblastomas are challenging tumours to treat due to their radio-resistance and residence in healthy brain tissue. In paediatric patients, conventional radiotherapy is often implemented, but tends to provide only short-term benefits.

Synchrotron generated, high dose and high flux microbeams are however better tolerated by normal tissue. Microbeam radiation therapy (MRT) implements spatially fractionated, sub-millimetre x-rays to treat tumours, with great potential for successful glioma and CNS tumour therapy [1].

Nanoparticles are promising candidates for diagnosis and radio-therapy. High-Z and paramagnetic nanoparticles not only improve the visibility of tumours for CT and MRI, but increase the dose conformity to tumour tissue with clinical X-ray beams [2]. The ongoing use of paramagnetic gadolinium nanoparticles for MRI contrast has led to the removal of linear Gd products from the EU market due to toxicity concerns [3]. New metal oxide nanoparticles have properties that include lower toxicity, potential drug attachment, radiation enhancement and preferential uptake into tumour cells [4,5].

This work examines the coupling of metal oxide nanoparticles with MRT, for better tumour control, less toxicity, and the capability of image-guided MRT with CT and MRI.

Methods: To characterize the potential of metal oxide nanoparticles for MRT, Geant4 simulations were performed (version 10.1) to determine optimum conditions for nanoparticle-enhanced MRT. Absorbed dose was measured in cell volumes and nanoparticle enhancement expressed by Dose Enhancement Ratio (DER).

Cell studies were performed with 9L gliosarcoma, grown in T12.5 flasks. Nanoparticles were sonicated and added 24 hours before MRT irradiation in hutch 2B at the IMBL, Australian Synchrotron. A pink beam spectrum with mean energy of 66 keV to optimise thulium oxide photon absorption (Figure 1) was produced by a 2T wiggler field. Surviving cell colonies were fixed and stained with crystal violet (30%) and ethanol (70%) and counted after 14 doubling times.

Results: Nanoparticle-enhanced MRT was characterised with Geant4 simulations. Higher energy microbeams (above 90 keV) allowed a greater number of secondary electrons to extend the damage of a microbeam to the valley regions. Targeting the maximum photon absorption of the nanoparticle led to localised and more selective damage.

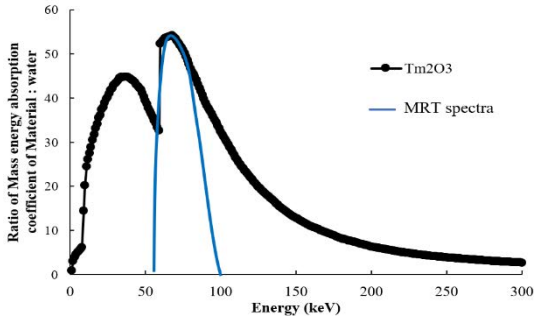


Figure 1. Comparing the Ratio of the mass energy absorption coefficient of Tm_2O_3

In vitro experiments confirmed that refining the beam energy selection, led to significant increases in MRT damage towards 9L tumour cells (Figure 2).

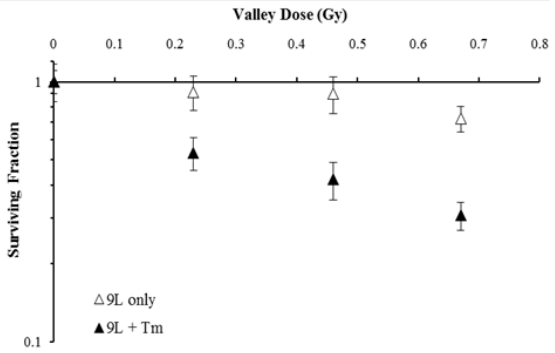


Figure 2. MRT treatment of 9L gliosarcoma expressed as surviving fraction with and without Tm nanoparticles.

References:

1. Microbeam Radiation Therapy: Clinical Perspectives (Grotzer et al.) *Phys Med* **31**, 564-567 (2015).
2. Nanoparticles in Cancer Imaging and Therapy, *J Nanomater* (Smith, et al.) Article ID 891318, 7 pages (2012).
3. European group recommends to stop using 4 linear GBCAs (Williams) *Gadolinium Toxicity* (2017).
4. Optimizing dose enhancement with Ta2O5 nanoparticles for synchrotron microbeam activated radiation therapy. (Engels et al.) *Phys Med* **32** (12), 1852-1861 (2016).
5. Nanostructures, concentrations and energies: an ideal equation to extend therapeutic efficiency on radioresistant 9L tumor cells using Ta2O5 ceramic nanostructured particles. (Brown et al.) *Biomed. Phys. Eng. Expres*, **3**(1), 015018 (2017)

FIBRE OPTIC DOSIMETRY IN SYNCHROTRON MICROBEAM RADIATION THERAPY

James Archer[1], Enbang Li[1], Anatoly Rosenfeld[1,2], Michael Lerch[1,2]

[1] Centre for Medical Radiation Physics, University of Wollongong, NSW, Australia 2522, jarcher@uow.edu.au
[2] Illawarra Health and Medical Research Institution. University of Wollongong, NSW, Australia, 2522

Introduction: Synchrotron microbeam radiation therapy is a novel pre-clinical therapy method that uses high brilliance, spatially fractionated, low energy synchrotron x-rays to deliver a very high dose rate within the microbeams. A conventional spatial fractionation for these beams is 50 μm microbeam width at 400 μm peak-to-peak separation. To perform dosimetry on these beams, a dosimeter with a high spatial resolution is required. We present a plastic scintillator fibre optic dosimeter that has been demonstrated to be able to resolve the microbeam structure. The advantages of such a dosimeter is the water equivalence, passive components exposed to the radiation field, relatively inexpensive components and simple fabrication.

Materials and Methods: We use cylindrical BC-400 plastic scintillator optically coupled to a 1 mm diameter core plastic optical fibre. BC-620 reflective paint was coated on the end of the probe to maximise the capture of light. A silicon photomultiplier (SensL MiniSM) was used to measure the light output of the probe. The use of plastic components ensures that the probe is water equivalent for radiation interaction. BC-400 is energy independent over a large range of energies, linear, and temperature independent over 0-60 ˚C [1]. The maximum one dimensional spatial resolution of the probe is determined by the thickness of scintillator used. We present the results from two probes, with 50 μm and 20 μm spatial resolutions, with measurements of the intrinsic microbeam profile, and depth dose curves.

The experiments were performed at the Australian Synchrotron, on the Imaging and Medical Beam-Line. The 50 μm probe was tested using Gammex Solid Water to provide attenuation and back-scatter, while the 20 μm probe was tested in a water tank. To test the effect of the BC-620 paint on the light capture, the depth dose measurements with the 20 μm probe were repeated with and without the paint.

Results: We were able to resolve microbeams with both resolution probes (shown for the 50 μm probe in Figure 1) [2]. The average microbeam widths measured with the 50 μm probe was (63 ± 2) μm, which compares favourably with a silicon strip detector of the same resolution (62.4 ± 0.9) μm. The 20 μm probe measured the widths to be (52.1 ± 6.5) μm. The depth dose measurements with the 50 μm probe matched that of a Pinpoint ionisation chamber except for an over-response at lower depth. This result was similar to the 20 μm probe in water. The effect of removing the BC-620 paint has no significant effect on the depth dose shape, but reduced the total light output by 24%.

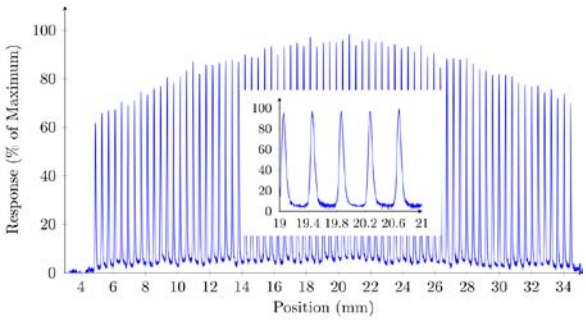


Figure 1. The intrinsic microbeam profile measured with the 50 μm resolution probe. Inset shows the centre section of the microbeam scan.

Conclusions: The results presented here demonstrates the ability for the fibre optic dosimeter probe to be able to effectively resolve microbeams. The depth dose results show a consistent discrepancy to the ionisation chamber results at low depths. The comparison with and without the BC-620 paint demonstrates that any radiation hardening effects cannot explain this discrepancy. The higher sensitive volume of the ionisation chamber makes a direct comparison of the results challenging.

The reduction in light output by removing the BC-620 paint has two reasons; a lower amount of light being reflected back into the fibre, and the higher Z material of the paint (TiO_2) having a higher dose enhancement. As one of the main advantages of using a probe of this design is the water equivalence, not using the BC-620 paint is justified to remove any possible unwanted dose enhancements.

Acknowledgements: This project was supported by UOW's Global Challenges Program. This research was undertaken on the Imaging and Medical beamline at the Australian Synchrotron, Victoria, Australia (AS162/IMBL/10829). Authors JA, EL, AD, MC and ML acknowledge the support of the Australian NH&MRC (APP1093256). This research has been conducted with the support of the Australian Government Research Training Program Scholarship.

References:

1. Water-equivalent plastic scintillation detectors for high-energy beam dosimetry (A.S. Beddar et al.), *Phys. Med. Biol.* **37(10)**, 1883-1913 (1992).
2. X-ray microbeam measurements with a high resolution scintillator fibre-optic dosimeter (J. Archer et al.), *Sci. Rep.*, **7**, 12450 (2017).

Space Dosimetry

PROGRESS OF THE MICRODOSIMETRIC KINETIC MODEL IN HEAVY-ION RADIOTHERAPY

Taku Inaniwa[1]

[1] Department of Accelerator and Medical Physics, National Institute of Radiological Sciences, QST, 4-9-1 Anagawa, Inage-ku, Chiba 263-8555, Japan, inaniwa.taku@qst.go.jp

Introduction: To date, more than 10,000 patients of vaious tumour sites have been treated with therapeutic carbon-ion beams at the National Institute of Radiological Sciences (NIRS). In carbon-ion radiotherapy treatment planning, the biological effectiveness of the therapeutic beams have to be predicted based on one of biological models. The microdosimetric kinetic (MK) model[1,2] has been used for this purpose at the NIRS. For further development of heavy-ion radiotherapy, we started a research project of a hypo-fractionated multi-ion radiotherapy, namely a "quantum knife". In the quantum knife, heavy ions up to neon are assumed as therapeutic ion species. Recent study revealed that the MK model may overestimate the biological effectiveness of heavy ions with linear energy transfer (LET) > 150 keV/μm, especially at high dose region.[3] Thus, the MK model should be updated so that it is applicable in treatment planning of the quantum knife. In this study, a biological model, namely a stochastic microdosimetric kinetic (SMK) model, will be reviewed and tested for in-vitro cell-survival fraction data.

Materials and Methods: The ion-species dependences obserbed in the relation between LET and relative biological effectiveness (RBE) deduced from cell-survival data indicate that the LET is not an ideal index for expressing the biological effectiveness of heavy ions. Instead, microdosimetric quantities such as specific energy z may be better indices for this purpose, since they directly relate to ionizing density within microscopic sites. The microdosimetric kinetic (MK) model is one biological model used to predict the cell-survival fraction from the specific energy z_d absorbed by a microscopic subnuclear structure "domain".[1] In the MK model, the survival fraction of cells S can be calculated by

$$\ln S(D) = -\left(\alpha_0 + \beta z_d^{*}\right)D - \beta D^2 \qquad (1)$$

where α_0 and β are cell-type specific parameters, and the variable z_d^{*} is the dose-averaged saturation-corrected specific energy absorbed by a domain. In the derivation of equation (1), the stochastic nature of the specific energy within the domain z_d was considered, while that within the cell nucleus z_n was neglected by assuming a constant value $z_n = D$. Sato and Furusawa indicated that this approximation was valid only for radiations with LET < 150 keV/μm.[3] They developed a computation method to numerically determine the cell-survival fractions by considering the stochastic natures of specific energies both in a domain z_d and a cell nucleus z_n, namely a stochastic mocrodosimetric kinetic (SMK) model. With the SMK model, the cell-survival fractions can be predicted accurately even for heavy ions with LET > 150 keV/μm. However, the computation based on the SMK model is too time-consuming to do in daily treatment planning especially with an iterative inverse planning. We updated the SMK model to be applicable in daily treatment planning. The updated SMK model was tested to the in-vitro cell-survival data of HSG cells irradiated by helium, carbon, and neon ions.[4]

Results: Figure 1 shows the comparison between experimental and predicted cell-survival fractions of HSG cells irradiated by helium-, carbon-, and neon-ion beams at different LETs. The experimental data were reproduced by both the MK and the SMK models for low LET radiations. However, for neon ions at LET = 654 keV/μm, only the SMK model reproduced the experimental data, and the MK model underestimated the cell-survival fractions.

Conclusion: In this study, the SMK model was updated for a hypo-fractionated multi-ion radiotherapy, and was validated for helium-, carbon-, and neon-ion beams in wide LET and dose ranges.

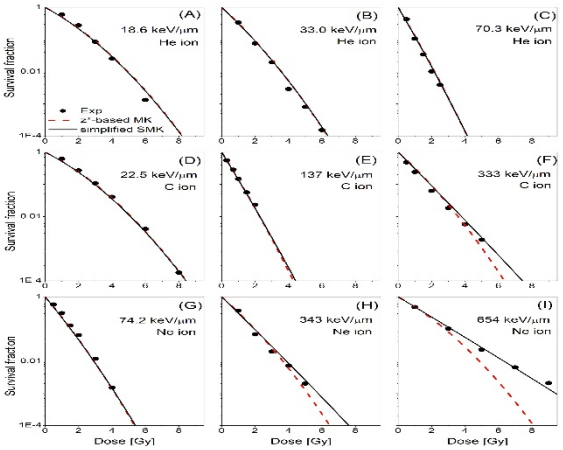


Figure 1. Experimental survival fractions of HSG cells irradiated by helium (A-C), carbon (D-F), and neon ions (G-I) compared with the predictions with the SMK (solid curves) and the MK models (dotted surves)

References:

7. R. B. Hawkins, *Radiat. Res.* **140**, 366-374 (1994).
2. T. Inaniwa et al., *Phys. Med. Biol.* **55**, 6721-6737 (2010).
3. T. Sato and Y. Furusawa, *Radiat. Res.* **178**, 341-356 (2012).
4. Y. Furusawa et al., *Radiat. Res.* **154**, 485-496 (2000).

HIGH PRECISION TRACK GEOMETRY CALCULATION IN HYBRID-PIXEL DETECTORS

Stuart P. George[1*], Lawrence Pinsky[1]

[1] University of Houston, Department of Physics, 3507 Cullen Blvd, Houston, TX 77204, USA
[*] spgeorg4@central.uh.edu

Introduction: Timepix Hybrid-pixel detectors are now being used for several applications in space and aerospace dosimetry by NASA and other organisations [1]. These include radiation monitoring on the International Space Station and the Orion spacecraft, measurement of LET spectra as part of the Biosentinel satellite as well as flights on high altitude balloons and commercial aircraft.

Hybrid pixel detectors consist of an array of semiconductor pixels coupled to an dedicated asic for readout. This means that hybrid pixel detector technology acts like solid state nuclear emulsion and can provide detailed tracking information [2] for particles crossing the sensor such as the 600 MeV/A Silicon Ion shown in Figure 1.

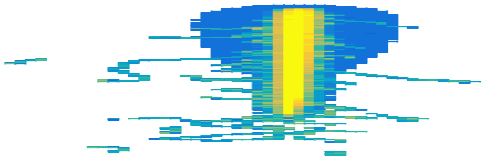


Figure 1, Example 600 MeV/A Silicon ion at high polar angle measured with a Timepix detector, color scale denotes deposited charge.

This information can be used for particle charge and energy identification, especially when a particle has a long track extending over many pixels. Calculating charge and energy is important both for validating radiation transport models and calculation of the NASA 2012 radiation quality factors which are functions of charge and energy. Highly important to these calculations are precise measurements of the particle LET or stopping power which is used to directly infer the possible energies and charge of any given track. The LET is calculated by measuring both the length and the deposited energy in the track. While quite some work has been done on improving the measurement of deposited energy [3,4] in the Timepix, the same effort has not been duplicated for high precision measurements of track geometry, especially for longer tracks.

This talk provides an overview of the current 'state of the art' for track LET measurement with hybrid pixel detectors, discusses some of the pitfalls in calculating track lengths and presents a novel methodology for accurately calculating the track geometry. This is done by calculating the 'length' and 'width' of the track by building histograms along and perpendicular to the central line of the track. An empirical formula for calculating the track length from these quantities is derived based on a large dataset of different ion tracks gathered at the HIMAC facility in Chiba, Japan. This new procedure results in more accurate track length calculation as shown in figure 2. This in turn leads to more accurate LET distributions which are verified by comparison to both theoretical Landau-Vavilov distributions as well as Geant4 Monte Carlo calculations. This method is shown to work well for a wide variety of different ions. Finally we show how this improved LET calculation also improves the calculation of other quantities such as the reconstructed track energy.

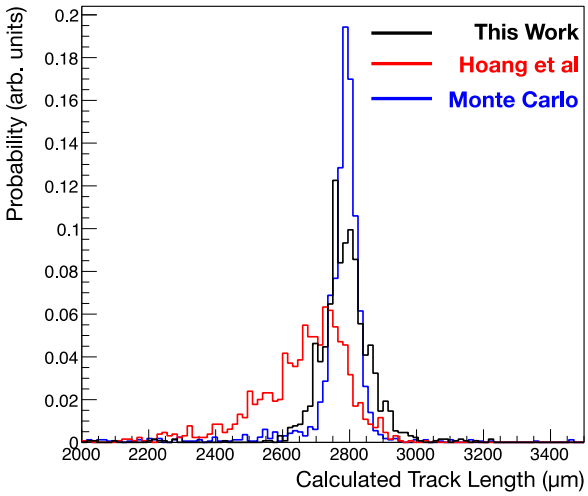


Figure 2. Plot showing measured track length distributions using the new (black), and old (red) calculation methods, compared to Geant4 Monte Carlo simulations (blue).

References:

8. N. Stoffle et al, Timepix based radiation environment monitor measurements aboard the international space station *Nucl. Instrum. Meth. Phys. Res.* A 762, 143-148 (2015)
9. S. Hoang et al, Data analysis of tracks of heavy ion particles in Timepix Detector *J. Phys Conf Series* 523, 1 (2014)
10. M. Kroupa et al, Energy resolution and power consumption of Timepix detector for different detector settings and saturation of front end electronics *J. Phys Conf Series* 523, 1 (2014)
11. M. Kroupa et al, Techniques for precise energy calibration of particle detectors *Rev. Sci. Inst* 88 033301 (2017)

Tuesday 6th of February 14:15

SIMULATION OF COSMIC RADIATION SPECTRA FOR PERSONAL MICRODOSIMETRY AT THE INTERNATIONAL SPACE STATION ALTITUDE

S. Peracchi[1], J. Vohradsky[1], S. Guatelli[1], L. T. Tran[1], A. Rosenfeld[1]

[1] Centre for Medical Radiation Physics, University of Wollongong, NSW, Australia 2522, sp009@uowmail.edu.au

Introduction: Latest researches predict the cosmic rays exposure during long space missions outside the Earth's geomagnetic sphere, as to the Moon and Mars, can double the cancer risk. The need to characterize cosmic radiation and its effects on astronauts' health motivated the development of new sensible instruments capable to evaluate the dose at cellular level, strongly damaged by radiation. The Center for Medical Radiation Physics (CMRP) developed a Silicon On Insulator (SOI) microdosimeter whose response needs to be studied in such mixed radiation field and whether its response can be used for biological risk prediction based on existing models.

Firstly, a detailed characterization of different radiation environment has been performed through Geant4 simulations.

Material and Methods: The Low Earth Orbit (LEO) radiation environment, where the International Space Station (ISS) is currently orbiting, has been characterized through Geant4 simulations to obtain particles spectra inside and outside the ISS. We considered different sources present in space as trapped protons and electron, Galactic Cosmic Ray (GCR) and Solar Particle Events (SPEs). They are mainly composed of protons, alpha particle and heavy ions with energy up to 100GeV/n.

Our geometry is based on Columbus Module, as a component of ISS, represented by a multi-layer cylinder (1), surrounded by a sphere where particles are injected inward it with an isotropic distribution.

Input spectra have been simulated in open Space at the altitude of ISS orbits with SPENVIS, an online tool to model space environment and its effects. The NASA AP8/AE8 models have been used for trapped radiation, the CREME96 model for GCR and the JPL-91 model for SPEs (2). Otherwise, for spectra inside Columbus, we use Geant4 toolkit, storing all primary and secondary particles produced through the interaction with shielding material, behind the innermost layer of Columbus shielding wall. We did not consider propagation in the air volume because we wanted to store the maximum kinetic energy available for a particle to propagate inside the astronauts' habitat. Those spectra will be used as input in following simulations where the microdosimeter will be positioned at different distance from the wall.

Results: Because of their low energy up to 7MeV, all trapped electrons have been stopped during the propagation through the Columbus wall. Trapped protons survived mostly at energy>10MeV, accompanied by a significant production of secondary low energy neutrons. Incident GCR protons with energy up to 100GeV are not totally shielded and they can reach the inside habitat. For example, Figure 1 shows the high flux of neutrons from spallation reaction and a not negligible flux of alpha particles due to disintegrations of the light and heavy nuclei of walls materials that are produced.

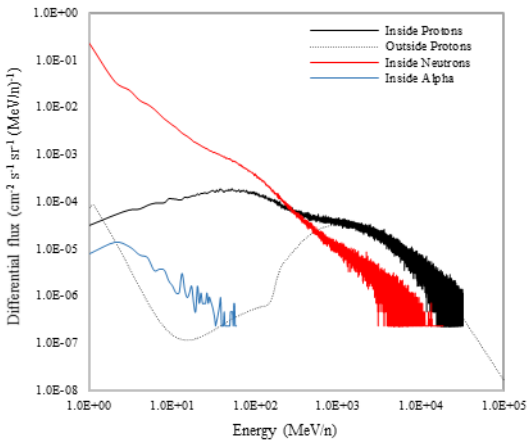


Figure 3. GCR protons inside and outside Columbus module.

Similarly, incident GCR alpha particles in the same energy range have not been totally shielded, indeed they produced a significant flux of secondary neutrons and protons of hundreds MeV.

Conclusion: The first characterization of cosmic radiation field inside the Columbus Module orbiting at LEO altitude has been performed by simulation with Geant4 toolkit. Results from spectra inside the spacecraft show relevant fluxes of primary and secondary particles traversing the shielding wall. Future simulations will be done modelling the microdosimeter SOI inside ISS to obtain the microdosimetric spectrum in term of lineal energy and to calculate the dose equivalent H(10) and H(0.07) for astronauts to predict radiation hazard risk of Space missions.

References:

1. Space environment characterisation of Kevlar®: good for bullets, debris and radiation too (R. Destefanis et al.), *Universal Journal of Aeronautical & Aerospace Sciences*, 80-113 (2014).
2. Space Environment Information System SPENVIS (ESA), https://www.spenvis.oma.be.

Radiation Therapy

PREVIEW OF AAPM WORKING GROUP RECOMMENDATIONS FOR TPS REFERENCE DOSE SPECIFICATION

S. Kry[1], V. Feygelman*[2], P. Balter[1], T. Knöös[3], C.-M. C. Ma[4], M. Snyder[5], B. Tonner[6], O.N. Vassiliev[1]

[1] MD Anderson Cancer Center
[2] Moffitt Cancer Center, vladimir.feygelman@moffitt.org
[3] Skåne, University Hospital and Lund University
[4] Fox Chase Cancer Center
[5] Wayne State University
[6] Ackerman Cancer Center

Introduction: Linac calibration is done in water, but patients are comprised primarily of soft-tissue. Conceptually, (and specified in NRG/RTOG trials[1]) dose should be reported as dose-to-muscle to describe the dose to the patient. Historically, the dose-to-water of the linac calibration was often converted to dose-to-muscle for patient calculations through manual application of a 0.99 dose-to-water to dose-to-muscle correction factor, applied during the linac clinical reference calibration. However, many current treatment planning system (TPS) dose calculation algorithms approximate dose-to-muscle (tissue), making application of a manual scaling unnecessary. At present, based on IROC Houston monitoring, 75% of institutions define their output as dose-to-water, while 25% indicate that they report dose-to-muscle (through application of a multiplicative 0.99 correction to reference dose-to-water), and these percentages are consistent across different TPS platforms. This highlights the variability in the community.There is little guidance on when application of a scaling factor is appropriate, resulting in highly inconsistent application of this scaling by the community. In this report we provide guidance on the steps necessary to go from the linac absorbed dose-to-water calibration to dose-to-muscle in patient, for various commercial treatment planning system algorithms. If the treatment planning system does not account for the difference between dose-to-water (D_w) and dose-to-muscle (D_m), then TPS reference dose scaling is warranted.

Methods: We have tabulated the major vendors' TPS in terms of whether they approximate dose-to-muscle or calculate dose-to-water and recommend the correction factor required to report dose-to-muscle directly from the treatment planning system algorithm. Different algorithms were analyzed one-by-one, based on the available peer-reviewed literature, manufacturer user guides and white papers, interviews with vendors, and comparisons with the Monte Carlo (MC) simulations done for this work. The output is a table specifying whether a multiplicative manual correction (0.99) to the TPS reference dose-to-water is necessary to obtain dose-to-tissue for each algorithm.

Results: For the photons, MC- and Boltzmann equation solver-based algorithms, as a rule, organically report dose to tissue and no manual correction is necessary, except for one system where the patient is inherently treated as water of varying density in MC simulations. Pencil beam (PB) algorithms, including AAA, report dose to water and require a manual correction. Superposition/Convolution (S/C) algorithms are most complicated in terms of dose reporting. Many, but not all, use tissue-specific mass attenuation coefficients for TERMA calculations and in theory report dose-to-tissue, although numerically this is not exact. For consistency we do not recommend a manual correction for S/C, except when final dose is unequivocally reported in water. A sample of recommendations for the photon algorithm correction application is listed in the Table.

Vendor	System	Algorithm	Dose by TPS D_w	Dose by TPS D_m	CF
Elekta	Monaco	XVMC		X	1.00
	Monaco	Collapsed Cone		X	1.00
	Oncentra	Collapsed Cone		X	1.00
	Xio	Multi-Grid Superposition	X		0.99
Philips	Pinnacle	CCC		X	1.00
Raysearch	RayStation	Collapsed Cone	X		0.99
Varian	Eclipse	Acuros XB		X	1.00
	Eclipse	AAA	X		0.99
	Eclipse	PBC,CDC	X		0.99
ViewRay	ViewRay	Monte Carlo	X		0.99

Conclusions: Linac reference calibration should be reported in water and never converted to muscle *per se*.

If necessary, a 0.99 times the dose-to-water correction should be applied in the TPS reference dose specification. This should be done on an algorithm-by-algorithm basis, bearing in mind that in a general family of algorithms specific implementation may change the approach.

A qualified medical physicist should ascertain if the specific TPS algorithm reports dose-to-water or dose-to-tissue and accordingly set the TPS reference dose for that algorithm

TPS vendors are encouraged to evolve their algorithms to calculate and report dose-to-tissue.

References:

1. Gladstone, D.J., et al., *Dose specification for NRG radiation therapy trials.* Int J Radiat Oncol Biol Phys, 2016. **95**(5): p. 1344-1345.

THE LIVER INSPECTR TRIAL: TOWARDS IMPROVED UNDERSTANDING OF LIVER FUNCTION FOLLOWING RADIOTHERAPY

Nicholas Hardcastle[1], Carol Haddad[2], Geoff Schembri[3], Dale Bailey[3], Brett Jones[4], Adam Briggs[2], George Hruby[2], Andrew Kneebone[2]

[1] Peter MacCallum Cancer Centre, Melbourne, VIC, Australia, nick.hardcastle@petermac.org
[2] Northern Sydney Cancer Centre, Royal North Shore Hospital, St. Leonards, NSW, Australia
[3] Department of Nuclear Medicine, Royal North Shore Hospital, St. Leonards, NSW, Australia
[4] Department of Hepatology, Royal North Shore Hospital, St. Leonards, NSW, Australia

Introduction: Stereotactic ablative body radiotherapy (SABR) is an emerging treatment option for primary liver cancer and liver metastases. Safety and efficacy has been demonstrated in a number of Phase II trials [1], [2]. Strict dose constraints on the liver are adhered to via use of isotoxic prescription regimes. Current constraints are based on dose to anatomical liver, without knowledge of underlying liver function apart from that provided from serum liver function tests and clinical examination. We describe a pilot study to evaluate the use of a hepatocyte single photon emission tomography (SPECT) tracer [3] for evaluation of liver function before and after liver SABR.

Materials and Methods: Liver function Investigation with Single Photon Emission Computed Tomography after Radiotherapy (Liver INSPECTR) is a Phase I pilot study investigating 99m-Tc Mebrofenin SPECT in the context of liver SABR. Previous experience with this imaging technique has been limited to estimation of future remnant liver prior to surgical resection. Patients who are to receive SABR for treatment of primary liver cancer or liver metastases are eligible for the study. Participants receive a mebrofenin SPECT-CT image at time of CT simulation, and at 1 and 6 months post SABR treatment. Indocyanine green (ICG) and ultrasound elastography of the liver is performed at the same time points. The change in 99m-Tc Mebrofenin uptake 1 month post SABR was measured for the first patient enrolled.

Results: Three of a planned 20 patients have consented to participate and have undergone pre-SABR SPECT imaging, ICG and elastography examinations. At time of writing one patient has completed 1 month post-treatment imaging and functional tests. Visual inspection of the pre and 1 month post-treatment SPECT images show decreased uptake in irradiated volumes (Figure 1). Mebrofenin uptake decreased as a function of dose received (Figure 2).

Conclusions: The Liver INSPECTR trial has the potential to improve understanding of radiation damage to functional liver and the ability to avoid functionally important regions of the liver through advanced treatment plan optimisation [4].

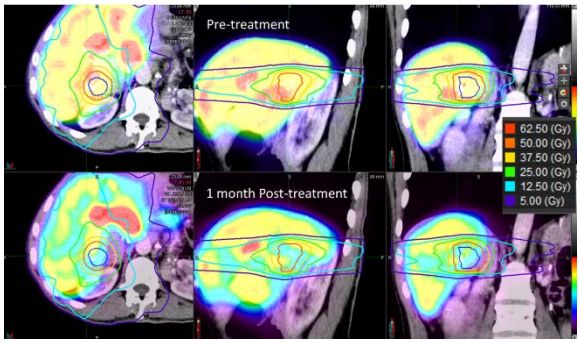


Figure 4: Pre (top) and post-treatment 99m-Tc Mebrofenin SPECT images overlaid on the treatment planning CT scan. Isodose lines from a 50 Gy in 5 fx treatment are shown. SPECT colourmaps are normalized to the counts in liver receiving < 5 Gy.

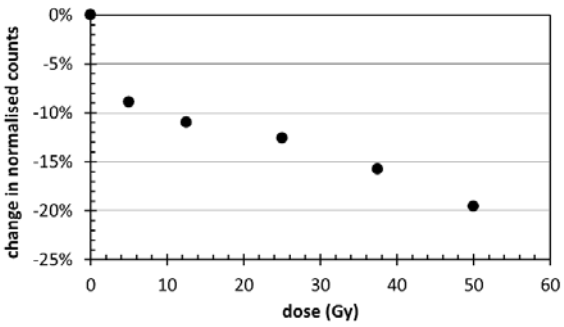


Figure 5: Change in normalized SPECT counts in regions of liver receiving 5 - 50 Gy in 5 fractions. The counts in each image have been normalized to the counts in the region of liver receiving less than 5 Gy.

References:

1. J. Klein and L. A. Dawson, "Hepatocellular carcinoma radiation therapy: Review of evidence and future opportunities," *Int. J. Radiat. Oncol. Biol. Phys.*, vol. 87, no. 1, pp. 22–32, 2013.
2. D. T. Chang *et al.*, "Stereotactic body radiotherapy for colorectal liver metastases: A pooled analysis," *Cancer*, vol. 117, no. 17, pp. 4060–4069, 2011.
3. W. de Graaf, K. P. van Lienden, T. M. van Gulik, and R. J. Bennink, "99mTc-Mebrofenin Hepatobiliary Scintigraphy with SPECT for the Assessment of Hepatic Function and Liver Functional Volume Before Partial Hepatectomy," *J. Nucl. Med.*, vol. 51, no. 2, pp. 229–236, 2010.
4. S. R. Bowen *et al.*, "Differential hepatic avoidance radiation therapy: Proof of concept in hepatocellular carcinoma patients," *Radiother. Oncol.*, vol. 115, no. 2, pp. 203–210, 2015.

CHARACTERIZATION EVALUATION FOR DIFFERENT QA TECHNIQUES CLINICALLY USED FOR IMRT, VMAT AND SBRT/SRS TREATMENT PLAN DOSIMETRY VERIFICATION

Emma Cai [1,2], Guilin Liu [1], Yang Wang [1,2]

[1] ICON Cancer Care – Radiation Oncology Centres NSW
[2] CMRP, School of Physics, University of Wollongong, NSW, Australia 2522

Introduction: Different QA techniques commonly used in clinic for planning dose verification for radiotherapy treatment include IMRT, VMAT, SBRT/SRS etc. different dosimetry measurement method and analysis techniques may bring QA results with different characterizations. This study is compared the measurement and analysis results via different dosimetry QA planning dose verification performed using ArcCheck, Varian PDIP on TrueBeam, IBA Dolphin system, and film dosimetry.

Materials and Methods: selected clinical treatment plans planned by Eclipse planning system, cases include head & neck, lung, breast cases and treatment techniques included IMRT, VMAT, SBRT, and gating treatment. Each cases delivered on Varian TrueBeam will QA performed to each case with all techniques listed in introduction.

Results and discussion: ArcCheck in past many years commonly being clinical used for IMRT and VMAT QA check with QA result gives sufficient consistency to routine clinical work, however in comparison it is showing the robust dosimetry results in dose distribution check and the limitation of measurement resolution showing the weakness in using for SBRT/SRS QA cases.

Varian PDIP portal dosimetry in recent years successfully working on TrueBeam machine with provided QA results for IMRT, VMAT, and SBRT/SRS in very friendly simply using but reliable consistency in dosimetry response and dose distribution analysis results. An important challenge it needs to maintaining good QA accuracies for both flat-panel alignment and detector calibrations.

IBA Dolphin with high resolution ion-chamber in 2D matrix mounted to collimator with entry dose delivered by treatment delivery, via the 3D dosimetry analysis result indicated good reliable target dose reconstruction quality with sufficient resolution for dose analysis.

Film dosimetry gives highest dosimetry analysis resolution however in common concerns with lower result reliability. However with involved scanning signal control and relative darkness calibration technique, the analysis result is showing good reliability and consistency for dose distribution check, made film dosimetry giving advantage in SBRT/SRS and dynamical gating treatment especially for small volume target plans.

Conclusion: Common used ArcCheck with good reliability however may not be suitable for smaller volume target dose check, both PDIP and Dolphin with good result reliability and reasonable resolution for most cases of small volume SBRT cases. Film dosimetry is suggesting to be used for small volume and dynamic delivery plan dosimetry check especially for SRS and gating treatment delivery check.

A COMPREHENSIVE PHANTOM WITH MULTI-DETECTOR INSERTS FOR PRE-TREATMENT QUALITY ASSURANCE IN STEREOTACTIC ABLATIVE RADIOTHERAPY

Prabhakar Ramachanran[1]

[1] Peter MacCallum Cancer Centre, Melbourne, VIC, Australia, Ramachandran.Prabhakar@petermac.org

Stereotactic ablative radiotherapy (SABR) is an advanced high precision radiotherapy procedure where a high dose of radiation is delivered in few fractions. Pre-treatment quality assurance (QA) is conducted prior to treatment to ensure the planned dose is delivered precisely. Several types of detectors have been explored for the use of pre-treatment QA in SABR. This study discusses the design of an in-house phantom with inserts designed to accommodate multiple detectors such as ion chambers, films, alanine, optically stimulated luminescence (OSLs), thermoluminescence dosimeter (TLDs), diodes, diamond detectors, and presage dosimeter. It also presents some of the measurement results performed for selective treatment sites. The results were compared to dose measured with an ArcCheck device. An in-house phantom originally designed for pre-treatment QA of SABR was modified to accommodate multiple dosimeters such as OSLs, diodes, diamond detectors, and presage dosimeters. The inserts were designed using Perspex, and 3D printed materials. The Presage dosimeter provided a three-dimensional view of the delivered dose for SABR plans and matched closer to the planned dose distribution. Most of the detectors/dosimeters explored in this study demonstrated measured results within 3% of the planned dose

MRI-LINAC

BUILD UP DOSE CHARACTERISTICS WITH EXASKIN BOLUS DURING 6MV RADIOTHERAPY: MOSKIN DOSIMETRY RESULTS

Taghreed Al-sudani[1], Peter Metcalfe[1,2], Dean Cutjar[1], Kananan Utitsarn[1], Abdurrahman Ceylan[2], Jeremy Davis[1] and Anatoly Rosenfeld[2]

[1] Centre for Medical Radiation Physics, University of Wollongong, NSW, Australia 2522, tahas274@uowmail.edu.au
[2] Illawarra Cancer Care Centre, Wollongong, NSW, Australia

Introduction: Skin dose evaluation is important to ensure adequate dose to the superficial target volume and to avoid severe skin toxicity[1]. The purpose of this study is to investigate the build-up dose characteristics of eXaSkin bolus for 6MV photon beams and evaluate this material for use in skin tumour treatment.

Methods: Using a 6MV Varian LINAC with field size of 10x10cm^2, the surface and build up dose characteristics of eXaSkin (thickness=3, 5, 8, 10, 15 and 26 mm) was investigated in comparison with solid water (thickness=2, 5, 15, 20 and 26 mm), see Fig. 1. Dose measurements were performed using a MOSkin dosimeter. Additionally, the percentage surface dose measurements for various oblique incident beams with 3mm thick of both bolus was investigated. Measurements were performed using MOSkin dosimeter and compared with advanced Markus chamber.

Results: D_{max} of eXaSkin for 6MV was approximately 0.9 cm that is consistent with the higher density of this material (ρSW=1.04 g/cm^3 ρeXa=1.7±0.03 g/cm^3). This bolus also exhibits higher dose in the build-up region between 2-10 mm depths (Fig. 2) and higher dose at oblique incident beams (Fig. 3).

Fig. 1: eXaSkin material

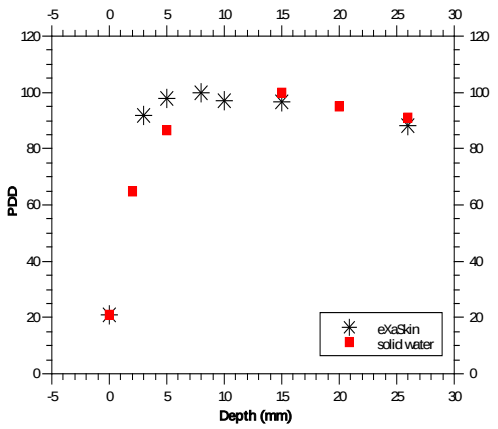


Fig. 2 Build up region for solid water vs eXaSkin using MOSkin dosimeter for 6MV LINAC with field size of 10x10 cm^2.

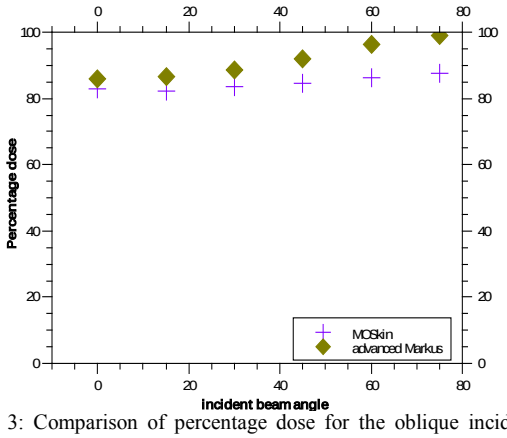


Fig. 3: Comparison of percentage dose for the oblique incident beam using advanced Markus chamber and MOSkin dosimeter at 3 mm eXaSkin bolus.

Conclusion: Preliminary results suggest that eXaSkin is a promising candidate for use in the treatment of superficial tumors without producing excessive skin reaction.

References:

1. Q. Shang, et al, Appl. Radiat. Oncol, 2015

CHARACTERIZATION OF MONOLITHIC SILICON STRIP DETECTOR FOR MRI-LINAC DOSIMETRY

T. Causer[1,2], T. Chapman[1], B. Oborn[1,2], J.A. Davis[1], M. Petasecca[1], A.B. Rosenfeld[1], P. Metcalfe[1]

[1] Centre for Medical Radiation Physics, University of Wollongong, NSW, Australia 2522
[2] Illawarra Cancer Care Centre, Wollongong, NSW, Australia

Introduction: Multiple vendors are now offering real-time MRI-guided radiotherapy systems. Quality assurance of small fields delivered with an MRI-linac system requires detectors with high spatial/temporal resolution, and magnetic insensitivity. High spatial resolution is required to characterise the asymmetric penumbra that transverse designs demonstrate [1].

In this work the authors describe the characterisation of the dosimetric performance of a monolithic silicon strip detector mounted to a flexible polymide (Kapton) printed circuit board intended for use in MRI-linac dosimetry.

Materials and methods: The monolithic silicon strip detector, (DMG-256A) consists of 256 phosporous implanted (n+) strips of 20x2000μm^2 with 200 μm pitch (Fig 1). Dosimetric characterization of sDMG-256A included dose linearity, dose per pulse dependence, angular dependence, uniformity of detector channel response, comparision of PDD and output factors with CC13 ionisation chamber. The effect of air gap width in detector packaging for small field output factor (OF) measurements in the presence of 1.2T transverse magnetic field was investigated. Measurements were performed on a Clinac iX, Varian Medical Systems using 6MV and 10MV beams. Measurement of dose linearity, dose per pulse dependence, uniformity of detector channel response, PDD and output factors were made using Soild Water®, with the detector housed in a bespoke PMMA phantom. Measurement of angular response was made using the Dosepoint RT-smartIMRT® phantom. The magnetic field for the air gap investigation was generated using a portable permanent magnet system (Fig. 2).

Results: The dose response (20-1000)cGy shows a linear responce (R^2 = 1). The dose per pulse dependence displays a 10.3% variation over the range (0.29-4.65)x10^{-4} Gy/pulse. The variation of the detectors channel response relative to the central channel for 99% of channels were within ±5% prior to the correction factor being applied. After correction the variation of all channels was within 0.2%. The angular response of the sDMG-256A has a maximum 20% decrease in response for beam angles parallel to the long axis of the detectors monolithic silicon chip. An increase in airgap width results in a decreased in measured OF with the effect being larger for smaller field sizes (Fig 3.).

Conclusions: The preliminary dosimetric characterisation of a monolithic silicon strip detector mounted to flexible polymide carrier has been carried out. The sDMG-256A has been designed to meet the needs of MRI-linac beam dosimetry and its dosimetric characteristics shows its applicability.

References:

1. Gargett et. al, Med Phys, 2015 vol: 42 (2) pp: 856-865

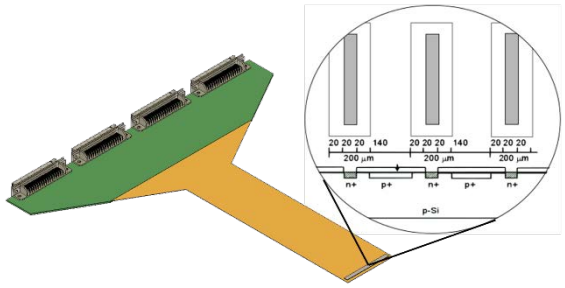


Figure 1. sDMG-256A, green is FR4 section of PCB, orange is the flexible polymide.

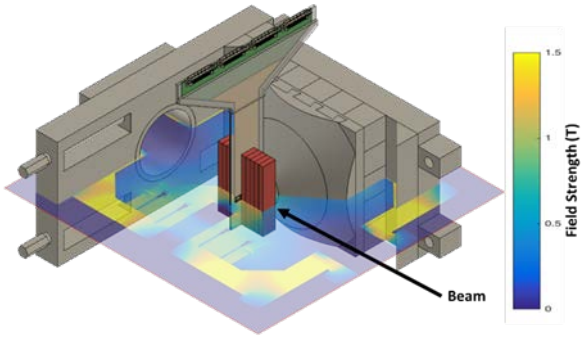


Figure 2. Output factor measurement setup with portable permanent magnet system

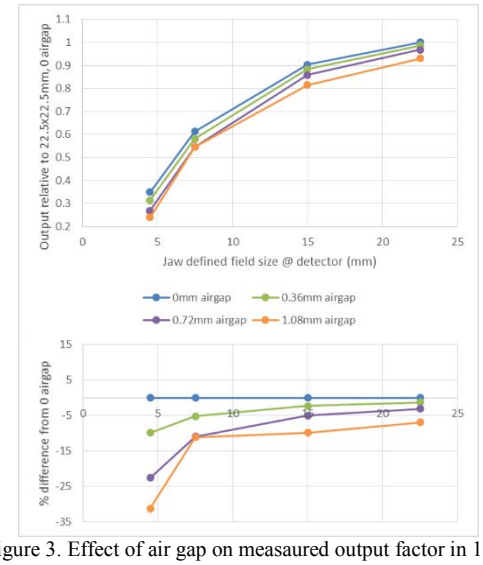


Figure 3. Effect of air gap on measaured output factor in 1.2T transverse magnetic field.

MODELLING THE X-RAY SOURCE FOR THE AUSTRALIAN MRI-LINAC

Natalia Roberts[1,5], Brad Oborn[1,2], Jarrad Begg[3,5], Urszula Jelen[5], Bin Dong[5], Armia George[3], Sarah Alnaghy[1,5], Trent Causer[1,2,5], Thahabah Alharthi[4,5], Lois Holloway[1,3,4,5], Peter Metcalfe[1,5]

[1] Centre of Medical and Radiation Physics, University of Wollongong, NSW, Australia 2522,
[2] Illawarra Cancer Care Centre, Wollongong Hospital, Wollongong, NSW, Australia
[3] Department of Medical Physics, Liverpool and Marcather Cancer Therapy Centre, Sydney, NSW, Australia
[4] Institute of Medical Physics, School of Physics, University of Sydney, Sydney, NSW, Australia
[5] Ingham Institute for Applied Medical Research, Sydney, NSW, Australia

Introduction: MR-guided radiotherapy offers superior soft tissue contrast and the potential to reduce current treatment margins while escalating dose to the tumour [1]. With the knowledge of tumour position and shape the radiotherapy beam can be adapted to deliver a more precise treatment. However, the magnetic field produced by the MRI impacts the dose distribution in the patient. These effects can be modelled using Monte Carlo methods. The focus of this work is to develop a model of the x-ray beam for patient radiotherapy treatment planning validation of the Australian MRI-linac system [2]. The novelty of our system is that dose can be calculated without the magnetic field using convolution and this dose can be compared against Monte Carlo dose both with and without the magnetic field [3].

Materials and Method: The initial commissioning of the linear accelerator was performed prior to the installation of the MRI, therefore the measurements presented were under 0 T conditions. The Monte Carlo toolkit Geant4 was used to model the beam to obtain a close match to the experiments. PDDs and profiles for the 6MV beam were taken in a water tank with a CC13 ion chamber and in solid water with Garchromic film. The model includes the linear accelerator treatment head, MLCs and the phantoms used during measurements. The electron beam parameters that were varied to match the simulation results were energy and spot size. Measurements were taken at an extended source to isocentre distance of between 1.8-3.2 m, so as to match the adjstable system when the MRI was to be installed. This will allow for studies of the impact of the linac position on MRI imaging performance and the dose peturbations in the phantom/patient.

Results: The current model of the beam has a match of PDDs within 2% (figure 1). The nominal energy of the beam was estimated to be 5.6MV with a high low energy component of photons present downstream of the linac, which was expected as the linac is flattening filter free. As seen in figure 2, the MLC model provides a close agreement with measured data in terms of the penumbral shape.

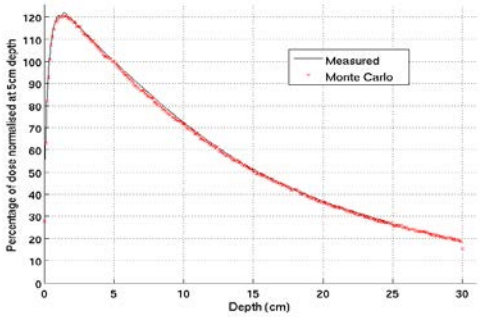


Figure 1: PDD for a 10x10cm^2 field (as set by the MLC controller), measurement taken with EBT3 film in solid water

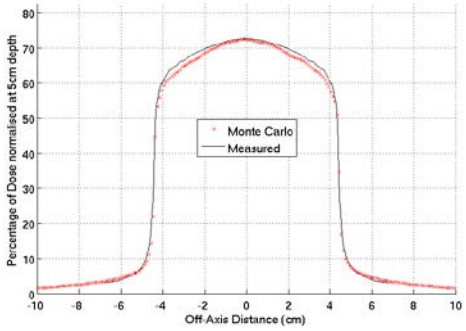


Figure 2: Profile at depth 10cm for a 10x10cm^2 field (as set by the MLC controller), measurements were taken with EBT3 film in solid water

Conclusion: A good Monte Carlo model of the x-ray beam for the Australian MRI-linac system has been developed. Simulations were performed to match the configuration of commissioning of this linear accelerator without a magnetic field. Profiles and PDDs matched well with measurements. Future work will include verification of the Monte Carlo model in the presence of the magnetic field from the MRI scanner.

Acknowledgements: This research has been conducted with the support of the Australian Government Research Training Program Scholarship and the Centre for Oncology Education and Research Translation (CONCERT).

References:

1. Menten M et al, *Phys. Med.* https://doi.org/10.1016/j.ejmp.2017.02.003 (2017)
2. Keall P J et al, *Semin. Radiat. Oncol.* **24** 203-6 (2014)
3. Oborn B et al, *J. Phys. Conf. Ser.* 489 012020 (2014)

Boron Neutron Capture Therapy

FUNDAMENTAL KNOWLEDGE FOR MICRODOSIMETRY IN BORON NEUTRON CAPTURE THERAPY

Yoshinori Sakura[1]

[1] Kyoto University Reseach Reactor Institute, yosakura@rri.kyoto-u.ac.jp

Introduction: At present, the development of the accelerator-based irradiation system for BNCT is energetically performed by various groups in the world [1]. Especially in Japan, BNCT using various accelerator-based irradiation systems may be carried out at plural facilities in the near future. Thus, it is the time when BNCT is shifting from a special particle therapy to a general therapy, now.

In order to promote this shift, not only the development and improvement for the irradiation system but also the preparation and improvement in the physical engineering and medical physics, such as dosimetry system, etc., is important. Especially, for the characterstic comparison among the several types of the irradiation fields, the microdosimtric estimation is necessary. Moreover, for the development of boron compounds, the microdosimtric viewpoint is important.

The fundamental knowledge for microdosimetry in BNCT is introduced divisionally for two parts: (1) for background dose and (2) for reaction of boron and neutron.

Fundamental Knowledge I : The results for the analytical estimation from the viewpoints of energy transfer to biological tissue are introduced for the interactions occurred in biological tissue due to the neutron irradiation with incidental gamma rays, and for the charged particles generated due to the interactions. For example, the energy distributions of generated protons for the epi-thermal neutron irradiation mode of the BNCT facility in Kyoto University Reactor (KUR) [2], is showin in Fig. 1.

The scattering reaction of hydrogen is the main source of protons for the wider energy region in the epi-thermal neutron irradiation. In the irradiation fields with the more incidental thermal neutrons, the number of protons originated from the (n,p) reactions of nitrogen exceeds the number of protons originated from the hydrogen reaction, nearly at 0.5 MeV. The number of high-energy protons originated from the hydrogen reaction is larger in the irradiation fields with the more incidental high-energy neutrons. For the protons originated from the (n,p) reactions of nitrogen and oxygen, the yields for the higher energy are larger.

Fundamental Knowledge II : At present, two kinds of boron cpompound, such as BPA (boronophenylalanine) and BSH (borocaptate sodium) are applied for BNCT clinical study. The distribution of boron compound for cell is different between BPA and BSH as shown in Fig.2 [3, 4]. BSH cannot enter the inside of the cell, and it just resides surround cell. For BPA, it is actively uptaken into tumorous cell by amino acid transporter. The degree of uptake for tumorous cell is expressed using T/B ratio based on whole blood, and T/B (tumor/blood) ratio is decided using the result by F-BPA-PET.

The cpompound biological effectiveness (CBE) for tumorous tissue is fixed to 3.8 for BPA and 2.5 for BSH. For BPA, it is thought that its CBE factor changes as T/B ratio changes. In some tumorous cells, BPA uptake is smaller than T/B ratio, or almost zero. In this case, BPA exists just surround the cell, so the CBE factor is thought to be nearly 2.5, the same for BSH.

Conclusion: The microdosimetric estimation in BNCT is important. It is hoped that studies for microdosimetry in BNCT will further proceed corresponding to the fundamental knowledge introduced here into consideration.

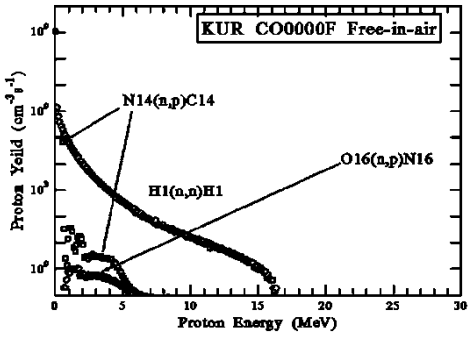


Figure 1. Energy distributions of generated protons for the epi-thermal neutron irradiation mode of KUR.

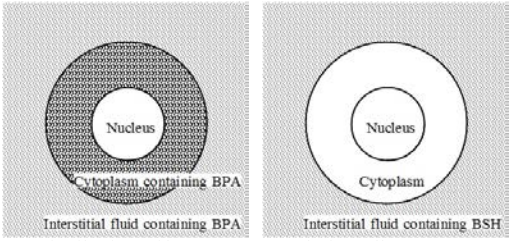


Figure 2. Distribution of boron compounds for cell.

References:

12. H. Tanaka, et al., *Nucl. Instr. Meth*. B **267**, 1970 (2009).
2. Y. Sakurai and T. Kobayashi, *Nucl. Instr. Meth*. A **453**, 569 (2000).
3. Y. Mishima, et al., *Pigment Cell Res.* **2**, 226-234 (1989).
4. A.H. Soloway, et al., *J. Med. Chem.* **10**, 714-717 (1967).

BNCT DOSIMETRY: PECULIARITIES AND METHODS

G. Gambarini[1,2], D. Bettega[1,2], A. Gebbia[1], E. Artuso[1], M. Felisi[1], D. Giove[1,2], V. Klupak[3], L. Viererbl[3] and M. Vins[4]

[1] Università degli Studi di Milano, Department of Physics, Milano, Italy. E-mail: grazia.gambarini@mi.infn.it
[2] INFN Istituto Nazionale di Fisica Nucleare, Section of Milan, Milano, Italy
[3] Department of Neutron Physics, Research Centre Řež, Czech Republic

Introduction: BNCT dosimetry is a challenging task, particularly in the case of irradiations with epithermal neutrons, as required for deep tumor treatments. In tissue, the epithermal neutrons are moderated mainly by the elastic scattering interactions with hydrogen nuclei $^{1}H(n,n)^{1}H$ and the energy spectrum of BNCT neutron beams is suitably designed in order to get high fluence of thermal neutrons in a volume centered at a depth of about 2 cm. The radiotherapy dose is due to the charged particles generated in the reactions of thermal neutrons with ^{10}B selectively accumulated in the tumor tissue ($^{10}B(n,\alpha)^{7}Li$).

In addition to the dose due to ^{10}B, for the patient dose calculations it is necessary to take into account all the secondary radiation generated by neutrons, both in tumor regions and in healthy tissues. The dose contributions that have to be considered can be divided into three general groups, each characterized by a different spatial distribution: the dose coming from the charged particles generated by thermal neutron reactions with particular isotopes, the gamma dose and the dose due to epithermal- and fast-neutron elastic or anelastic collisions (fast neutron dose).

The charged particles have short range and then a spatial distribution directly related to the distribution of thermal neutron fluence, and the absorbed dose can be evaluated, in each position, by means of the corresponding kerma factor. In addition to the dose due to ^{10}B, a not negligible contribution comes from the charged particles generated by the reactions of thermal neutrons with Nitrogen ($^{14}N(n,p)^{14}C$) whose concentration in tissue is of about 3% w/w.

A significant percentage of the absorbed dose comes from gamma radiation, partially due to background and partially to the photons of 2.2 MeV emitted in the reactions of thermal neutrons with hydrogen ($^{1}H(n,\gamma)^{2}H$). This emission, in each point of the irradiated volume, is linearly correlated to the thermal neutron fluence in that point and, owing to the long range in tissue of the 2.2 MeV photons, the resulting dose undergoes changes, due to the variation of shape or size of the irradiated volume, greater than those of the thermal neutron fluence.

A lower contribution is given by fast neutron dose. This dose is mainly due to knock-on recoil nuclei, mostly recoil protons, and is not greatly dependent on the geometry of the irradiated volume.

Both the charged-particle dose and the gamma dose have a spatial distribution that significantly depends on the irradiation geometry, i.e. size and shape of the irradiated volume, and also on the direction of the neutron beam. In order to estimate the influence of the unavoidable lack of precision of the input data for dose measurements or calculations, for the issues described above, apposite experimental and computational evaluations have been carried out.

Materials and Methods: Several measurements and calculations have been performed with the epithermal neutron beam of the LVR-15 research reactor, designed for BNCT at the Research Centre Řež.

Measurements of neutron fluences and absorbed doses were performed with Fricke-gel dosimeters, thermoluminescence detectors and activation foils and recent results are reported in previous papers (1-2). In order to better understand some peculiarities of the obtained results, proper evaluations have been computed by means of MCNP/MCNPX, 2006 (3).

Results: Dose measurements were performed in phantoms with different sizes and shapes. With the developed methods, the separation of boron, gamma and fast neutron doses have been done. From the boron dose, thermal neutron fluence has been inferred. The outcomes obtained with the various detectors were mutually consistent and complementary.

In order to attain a deeper understanding of the variability of the spatial distribution of the various dose components, a lot of calculations have been performed concerning neutron energy spectra, thermal and epithermal neutron fluence profiles and gamma dose in various water phantoms.

Also evaluations on neutron fluence and gamma dose in phantom containing ^{157}Gd have been done, owing to the high cross section (255000 b) of the reaction $^{157}Gd(n,\gamma)^{158}Gd$.

Conclusions: The results of the work have given useful information on the topic. In particular, they allow a first estimate of the extent of the changes that may occur by changing the shape or size of the irradiated volumes.

References:

13. A. Khajeali et al., *Appl. Radiat. Isot.* **103** 72 (2015).
2. G. Gambarini et al., *Radiat. Phys. Chem*. **116**, 21-27 (2015).
3. G. Gambarini et al. *Proc. of the Internat. Symp. of Reactor Dosimetry*, ASTM, STP1608 (in press)

EVALUATION OF SILICON AND DIAMOND BASED MICRODOSIMETRY FOR BORON NEUTRON CAPTURE THERAPY APPLICATIONS

James Vohradsky[1], Jeremy A. Davis[1,2], Linh T. Tran[1], Anatoly B. Rosenfeld[1], Susanna Guatelli[1,2]
[1] Centre for Medical Radiation Physics, University of Wollongong, Australia, jev720@uowmail.edu.au
[2] Illawarra Health and Medical Research Institute, University of Wollongong, Australia

Introduction: The shift from reactor to accelerator based neutron production has created a renewed interested in Boron Neutron Capture Therapy (BNCT). This method is typically used to treat inoperable brain tumours (glioblastoma [1]) that cannot be treated by traditional forms of radiotherapy or chemotherapy [2]. BNCT is reliant upon the favourable uptake of boron-10 by tumour cells along with the interaction with neutrons to produce high LET fragments (He^{2+} & Li^{3+}) that deposit energy locally within the tumour site. As with any radiation based treatment, Quality Assurance (QA) by means of dosimetric measurements is crucial in terms of patient safety. This study extends previous work regarding the application of solid state microdosimetry in the field of BNCT by means of a dedicated Monte Carlo simulation [3].

Materials and Methods: Geant4 was used to model and optimise the design of silicon on insulator and diamond based microdosimeters [4] [5] [6]. The CMRP Bridge microdosimeter was studied extensively. Detector optimisation in this context, pertains to the geometry and materials (i.e., sensitive volume size and probability of neutron activation) to be used in the construction of detectors. The applicability of previously determined correction factors to match the energy deposition response of charged particles within silicon/diamond to water was evaluated within the context of BNCT by analysis of microdosimetric spectra [7] [8].

Results: The study has shown conclusively that the materials currently used in the available silicon and diamond-based CMRP microdosimeters do not pose any radiation protection risk with the typical exposure times of BNCT. However, there are changes with respect to the sensitive volume thickness that must be addressed.

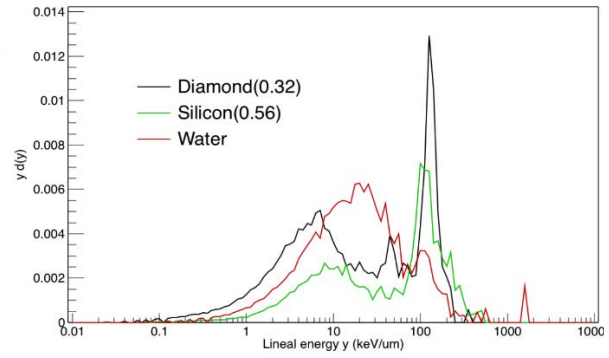


Figure 1. Comparison of microdosimetric spectra obtained with 0.1 µm thick SVs in the case of 25ppm ^{10}B concentration in the tumour volume.

Reduced SV thickness resulted in a higher rate of BNC products crossing the SV. The study of water equivalence conversion in BNCT using the current geometric scaling factors published for silicon, 0.56 [7], and diamond, 0.32 [8], produced a suitable result for high-LET radiation fields.

Conclusion: Three dedicated Geant4 applications were developed to characterise the BNCT radiation field, provide analysis of neutron activation and to obtain the microdosimetric response of optimised detector designs. Unfortunately, in the context of this project, it was not possible to validate the simulation against experimental measurements. With a 10 µm thick SV, the number of alpha particles classified as stoppers is about 96%. This is due to the short range of the alpha particles and ^{7}Li nuclei in comparison to the Bridge SV mean chord length. As the projected range of a 1.5 MeV alpha particle in silicon is 5.26 µm [9], thinner SVs are required to allow BNC products to cross the SV. The study of the water equivalence conversion concluded their suitability for high-LET radiation fields. However, it was found that their ability diminished in the lower lineal energy range where most events were due to stoppers. As the majority of particles in BNCT are stoppers, these correction factors do not provide a well-approximated water equivalent response for low-LET events. The solution is to develop thin SVs to have more crossers and eventually develop an ad hoc conversion factor for BNC. The results have shown that a Bridge microdosimeter fabricated with thinner SVs would provide a very suitable detector for dedicated BNCT QA for epithermal neutron sources, such as existing facilities at Tokai and KURRI in Japan.

References:

1. Current Status of Neutron Capture Therapy (D. Rorer et al.), *IAEA Tech. Rep.* **1223**, 3-63 (2001).
2. Current Status of Boron Neutron Capture Therapy (R.F. Barth et al.), *Rad. Onc.* **7.1**, 146-170 (2012).
3. Performance of Silicon Microdosimetry in BNCT (P.D. Bradley et al.), *Rad. Res.* **151**, 235-243 (1999).
4. GEANT4 Collaboration (S.Agostinelli et al.), *Nuc. Instrum. Meth. Phys. Res.* **506**, 250-303 (2003).
5. Novel silicon microdosimeter using 3D SVs (L.T. Tran et al.), *IEEE Trans. Nuc. Sci.* **61.4**, 1552-1557 (2014).
6. Characterization of a novel microdosimeter (J.A. Davis et al.), *IEEE Trans. Nuc. Sci.* **59.6**, 3110-3116 (2012).
7. TE Correction in Silicon Microdosimetry (S. Guatelli et al.), *IEEE Trans. Nuc. Sci.* **55.6**, 3407-3413 (2008).
8. TE Study of Diamond Microdosimeter (J.A. Davis et al.), *IEEE Trans. Nuc. Sci.* **61.4**, 1544-1551 (2014).
9. SRIM (J.F. Ziegler et al.), *Nuc. Instrum. Meth. Phys. Res.* **268**, 1818-1823 (2010).

NEUTRON CAPTURE ENHANCED PARTICLE THERAPY: OPPORTUNISTIC DOSE AMPLIFICATION VIA CAPTURE OF THERMAL NEUTRONS PRODUCED DURING HEAVY ION AND PROTON THERAPY

Andrew Chacon[1,2], Mitra Safavi-Naeini[2,1,3], Susanna Guatelli[1,4], Marie-Claude Gregoire[2] and Anatoly Rosenfeld[1,4]

[1] Centre for Medical Radiation Physics, University of Wollongong, NSW, Australia 2522,
[2] Australian Nuclear Science and Technology Organisation,
[3] Brain and Mind Centre, University of Sydney, NSW, Australia,
[4] Illawarra Health and Medical Research Institute, University of Wollongong, NSW, Australia 2522

Introduction: Proton and heavy ion therapy is a form of radiotherapy which works because a monoenergetic heavy ion beam will deposit most of its energy within a narrow depth range - known as the Bragg Peak - with the peak dose depth determined by the beam energy, ion species and target composition [1]. During proton and heavy ion radiotherapy, particles in the beam may undergo inelastic collisions with nuclei in the target, producing a range of nuclear fragments, including other nuclei, protons and neutrons [1]. The neutrons are typically regarded as a nuisance, as they indiscriminately irradiate non-target tissues.

In classical boron neutron capture therapy, the patient is administered a compound containing ^{10}B which is preferentially absorbed by the malignant target tissue [2]. The target volume is then irradiated with a beam of epithermal/thermal neutrons, which thermalise when reaching the target. The addition of ^{10}B has the effect of increasing the thermal neutron absorption cross section of the target, hence increasing the physical neutron dose absorbed by the tumour. The biological dose is enhanced even further due to the decay chain which results from boron neutron capture, which results in the high linear energy transfer (LET) particles lithium and alpha [2].

This work aims to demonstrate that a typical heavy ion or proton therapy treatment plan generates an approximately uniform thermal neutron field within the target volume and centred around the beam path, with sufficient fluence to be suitable for therapeutic boron neutron capture dose enhancement.

Materials and Methods: Utilising the Geant4 Monte Carlo toolkit, the spatial distribution of thermal neutron fluence generated through the process of fragmentation during proton and heavy ion therapy is evaluated. Total neutron fluence produced by irradiation according to a simple treatment plan is evaluated within the treatment volume. The biological effective dose contribution resulting from neutron capture inside and outside of the treatment volume is computed based on a range of published and theoretical boron concentrations (both in tumour and healthy tissue).

Results: The simulation results indicate that there is a strong correlation between the position of the Bragg peak and the maximum fluence of thermal neutrons which are internally generated within the phantom when using protons or heavy ions. Concentrations of ^{10}B the range of 200 to 400 ppm can then increase the biological effective dose in the treatment volume in excess of 10% for both protons and Carbon ions, with the exact enhancement depending on concentrations of Boron which is achievable with a full and comprehensive analysis to be presented at the conference.

Conclusion: Our results demonstrate that the neutron distribution resulting from proton and heavy ion fragmentation mostly originates within a point internal to the treatment volume. Importantly, our simulations have shown that the neutron flux per primary particle is such that a typical proton or heavy ion treatment plan will result in a total neutron fluence which can produce a dose enhancement of the 10% or more depending on boron tissue concentrations which are obtainable.

References:

1. Durante, M, Loeffler, J, 'Charged particles in radiation oncology', *Nature Reviews Clinical Oncology* 7.1 (2010), pp. 37–43.
2. Barth, R, Coderre, J, Vicente, M, & Blue, T 2005, 'Boron neutron capture therapy of cancer: current status and future prospects', *Clinical Cancer Research: An Official Journal Of The American Association For Cancer Research*, 11, 11, pp. 3987-4002

Acknowledgements: This research has been conducted with the support of the Australian Government Research Training Program Scholarship. The authors would like to acknowledge Monash University M3 High Performance Cluster (HPC), University of Wollongong HPC, National Computational Infrastructure (NCI) for computational support.

What is new in Brachytherapy?

NEW TRENDS IN DOSE CALCULATION, DELIVERY AND *IN VIVO* VERIFICATION IN BRACHYTHERAPY

Mauro Carrara[1], Annamaria Cerrotta[2], Emanuele Pignoli[1]

[1]Medical Physics Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan – Italy
[2]Radiation Oncology 2, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan – Italy

Introduction: In the recent years, the incorporation of 3D imaging into the clinical brachytherapy (BT) workflow with the replacement of the 2D approach has rapidly emerged, leading to image guided adaptive brachytherapy (IGABT). Interestingly, CT and/or MR image-assistance has opened not only clinical possibilities within the BT workflow, but also new physical opportunities. In particular, dose calculation, dose delivery and QA of radiation delivery (i.e., *in vivo* verification) have become main topics of research and development within the Scientific Community.

Dose calculation: The TG-43U1 [1] dose calculation formalism describes dose deposition around a single source centrally positioned in an homogeneous unbounded water phantom, using an algorithm-based approach. The dosimetric data are derived from source-model specific Monte Carlo simulations or TLD measurements according to specifications outlined in the AAPM TG-43U1 report. Doses in BT treatment planning are then estimated superposing precalculated dose distributions for single sources according to the specific pattern of source dwell positions and times. This method is fast and practical in the clinic; however, calculated dose distributions can be in numerous situations over- or underestimated by at least 5%.

In contrast, model-based dose-calculation algorithms (MBDCAs) offer the possibility of modelling radiation transport in non-water media (tissues, applicators, air-tissue interfaces), resulting in a much more accurate reconstruction of the dose distribution delivered to the patient (AAPM TG-186 [2]). MBDCA-based treatment planning systems have recently become commercially available, leading to a lot of new requisites and demanding physical tasks in terms of commissioning, QA and application, but at the same time opening a wide spectrum of innovative opportunities.

Dose Delivery: As it happened a few years ago in external beam radiotherapy with the advent of intensity modulated techniques, now that MBDCA-based treatment algorithms are available also BT will possibly move towards more sophisticated delivery techniques. In fact, new shielded applicators are currently under study allowing innovative modulated techniques such as directional modulated BT, interstitial rotating shield BT or dynamic modulated BT. The main idea, common to all these techniques, is to generate highly directional and selectable dose profiles through shielding designed with high-density alloys.

Such kind of applicators might enable to achieve consistent improvements in organ at risk sparing without any reduction of the dose delivered to the patients or they might enable to escalate the dose to the target while ensuring the recommended organs at risk sparing levels are not exceeded.

In vivo verification: With increased conformality of dose to the target and possible delivery innovations with more sophisticated technologies, reliability and precision of the achieved dose distribution has become even more important. Nevertheless, BT still involves some manual procedures during catheter/applicator insertion, treatment planning and treatment delivery that makes it prone to errors. Systems for delivery verification are consequently getting more and more importance. In particular, systems for real-time *in vivo* dosimetry or on line verification of source dwell positions and times are currently under study/development within the Scientific Community, aiming to the improvement of the overall treatment delivery accuracy. Translation of these new verification systems into improved clinical routine is still in progress.

Conclusions: IGABT has opened new possibilities within the BT workflow, with new dose calculation model-based modalities, modulated treatment delivery techniques and in vivo delivery verification systems, capturing the interest of the Scientific Community.

References:

1. Rivard MJ, Coursey BM, DeWerd LA et al. Update of AAPM Task Group No. 43 Report: A revised AAPM protocol for brachytherapy dose calculations. *Med Phys* 31 (2004), 633-74
2. Beaulieu L, Carlsson Tedgren A, Carrier JF et al. Report of the Task Group 186 on model-based dose calculation methods in brachytherapy beyond the TG-43 formalism: current status and recommendations for clinical implementation. *Med Phys* 39 (2012), 6208-36

Physics Innovations

BRACHYVIEW: VERIFICATION OF LDR BRACHYTHERAPY PATIENT PLANS

T. Brennen[1], M. Petasecca[1], D.L. Cutajar[1,2], S. Alnaghy[1], J. Bucci[2], A. Bece[2], M. Favoino[3], M. Carriero[3], J. Jakubek[4], S. Pospisil[4], M. Lerch[1], A.B. Rosenfeld[1]

[1] Centre for Medical Radiation Physics, University of Wollongong, Australia
[2] St George Cancer Care Centre, St George Hospital, Kogarah, Australia
[3] Advanced Computer System Pty Ltd, Rome, Italy
[4] Institute of Experimental and Applied Physics, Czech Technical University, Prague, Czech Republic

Introduction: BrachyView is a novel in-body imaging system developed with the objective to provide real-time intraoperative dosimetry for low dose rate prostate brachytherapy treatments. Seed positions can be reconstructed after implantation by the means of a high-resolution pinhole gamma camera. The obtained dataset is then combined with conventional trans-rectal ultrasound imaging (TRUS) to localise the effective implanted source position within the prostate volume[1].

Materials and Methods: The BrachyView probe consists of a 1mm thick tungsten cylindrical collimator, containing three single cone pinholes. This study utilised pinhole diameters of 500 µm and 800 µm to assess the effect of the pinhole diameter on seed reconstruction quality, as well as the feasibility to perform reconstruction prior to seed deployment from the treatment needles.

Two clinical LDR prostate brachytherapy plans were devised containing 98, and 96 seeds (I-125 with an average activity of 0.248mCi and 0.303mCi respectively), implanted into a prostate gel phantom. TRUS images, manual segmentation and rendering were performed to reconstruct the 3D shape and position of the prostate, utilising transversal 2.5mm ultrasound slices.

BrachyView data was acquired for an average of 2.5 minutes after each needles implantation to compensate for the low activity seeds. A post implant CT study with O-MAR (orthopaedic metal artefact reduction) was completed to provide a reference for comparison of the reconstructed seed positions.

Results: When compared to the seed positions obtained by the CT scan the BrachyView reconstruction showed average discrepancies of 2.4 mm, 1.35 mm and 1.2 mm in the x, y and z reference frames, respectively for the 500 µm collimator as shown in figure 1 (a).

For the 800 µm collimator average discrepancies of 4.3 mm, 4.8 mm and 2.5 mm in the x, y and z reference frames, respectively as shown in figure 2. 100% and 70% of seeds were reconstructed in the case of the 500 µm and 800 µm, respectively.

The 500 µm collimator provided a higher accuracy in seed position reconstruction, however due to the reduced pinhole size a longer acquisition time is required to obtain high quality projections for use in the reconstruction algorithm.

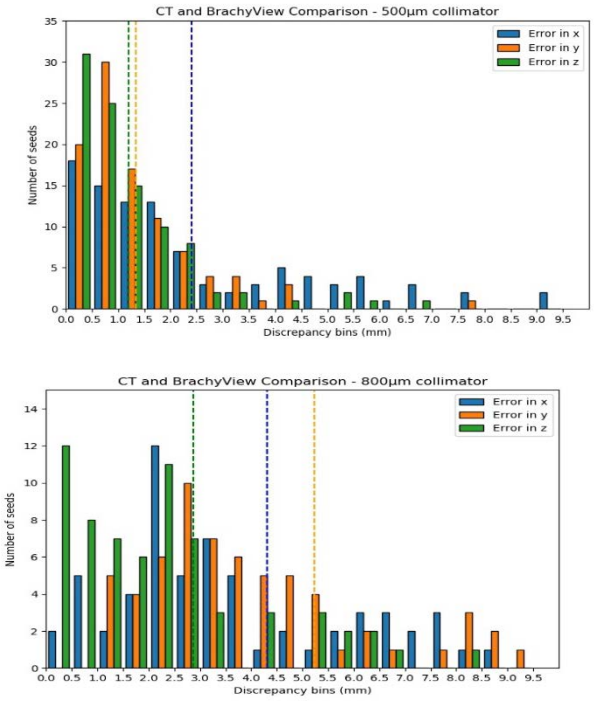


Figure 1: a) CT and BrachyView 500 µm collimator reconstructed seed discrepancies b) 800 µm collimator reconstructed seed discrepancies. With average discrepancies indicated.

Conclusions: A comparison of the BrachyView data utilising 500 µm and 800 µm pinhole diameters has allowed for optimisation of the collimator, with 100% of seeds being reconstructed by the means of the 500 µm collimator , with 74% within 2mm of their nominal positions. Results from the 800 µm-data showed increased scatter contribution and reconstructed positions with large inaccuracy, with only 70% of seeds reconstructed. This is an indicator that use of the 800 µm collimator for seed reconstruction before seed deployment from treatment needles is not feasible with the current methodology. The combination of the 500 µm collimator and TRUS imaging has shown that it is a unique tool for intraoperative verification for implantation quality.

Acknowledgements: This research has been conducted with the support of the Australian Government Research Traning Program Scholarhip.

References:

1. BrachyView: Combining Trans-rectal Ultrasound 3D imaging and Position Reconstruction of LDR seeds in a Prostate Gel Phantom (S.Alnaghy et al.), *Physica Medica* (2016)

USE OF CONTEMPORARY IMAGING METHODS IN BRACHYTHERAPY APPLICATIONS

A. Haworth[1], Y. Sun[1,2], M. Ebert[3,4], H. Reynolds[2,5], J. Betts[6], D Wraith[7], C Mitchell[5], D Murphy [2,5], B. Parameswaran[5], S. Williams[2,5]

[1] School of Physics, University of Sydney, NSW Annette.haworth@sydney.edu.au
[2] Sir Peter MacCallum Dept. of Oncology, University of Melbourne, Melbourne, Vic
[3] School of Physics, University of Western Australia, WA
[4] Department of Radiation Oncology, Sir Charles Gairdner Hospital, WA
[5] Peter MaCallum Cancer Centre, Melbourne, Viv
[6 3]Faculty of Information Technology, Monash University, Vic
[7] Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Qld

Introduction: Many reasons for the decline in prostate brachytherapy (BT) utilisation have been proposed. Competition with hypofractionated external beam radiotherapy is commonly cited. The BT community should embrace modern technology to ensure patients receive best quality care.

Methods: We present a framework for Biologically Optimised RadioTherapy (BiRT) that incorporates multiparametric MRI (mpMRI) and a focal approach to treatment[1] (Fig 1). The model requires knowledge of tumour location, tumour cell density, tumour aggressiveness and hypoxia. We describe a quantitative, voxel-by-voxel approach for extracting tumour characteristics from mpMRI. Predictive models were built from data derived from forty-five patients scheduled for radical prostatectomy who underwent pre-operative in vivo mpMRI

Results: Prediction of tumour location using support vector machines has demonstrated a prediction accuracy ranging from 70.4 to 87.1%[2] Logistic regression models demonstrated accuracies >83% in differentiating between high and low grade tumours. Regarding hypoxia, HIF1α and CAIX expression levels demonstrated significant correlations with pharmacokinetic maps generated from DCE. Low dose rate brachytherapy treatment planning using a biological optimization approach can produce plans robust to seed migration and predict superior clinical outcomes compared with conventional approaches.[3,4]

Conclusion: Parametric and pharmacokinetic maps generated from mpMRI and a sophisticated framework for co-registration of ground truth histology with mpMRI has provided a platform to develop predictive models for tumour location and biology.

We present a framework for a contemporary approach to prostate focal BT that incorporates mpMRI and a biological optimisation approach to treatment planning. Future clinical trials should consider such techniques for BT to remain an attractive option for treatment of localised prostate cancer.

References:

14. Haworth A, Williams S. Focal therapy for prostate cancer: the technical challenges. J Contemp Brachytherapy 2017;9(4):383-389
2. Sun Y, Reynolds H, Wraith D, et al. Predicting prostate tumour location from multiparametric MRI using Gaussian kernel support vector machines: a preliminary study. Australas Phys Eng Sci Med. 2017;40(1):39-49
3. Haworth A, Mears C, Betts JM, et al. A radiobiology-based inverse treatment planning method for optimisation of permanent l-125 prostate implants in focal brachytherapy. Phys Med Biol. 2016;61(1):430-44
4. Betts JM, Mears C, Reynolds HM, et al. Prostate cancer focal brachytherapy: Improving treatment plan robustness using a convolved dose rate model. Procedia Computer Science. 2017;108C:1522–31

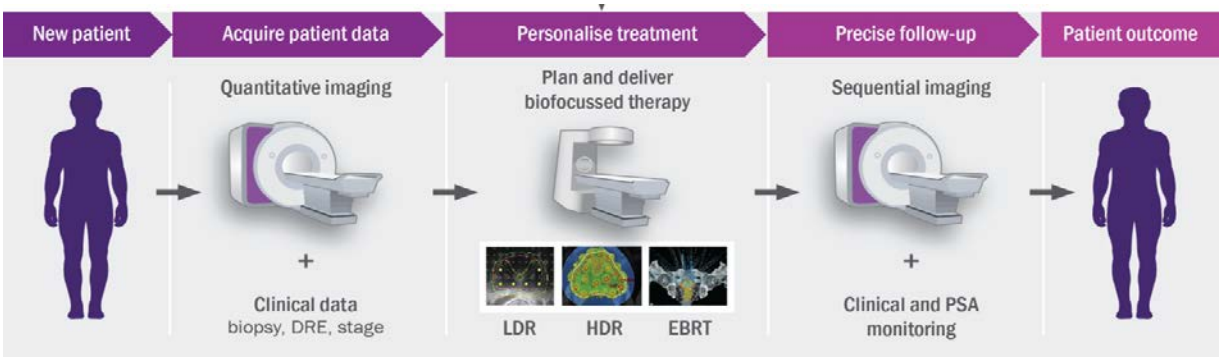


Figure 1. The BiRT framework

EYE BRACHYTHERAPY: NEW TECHNOLOGY FOR FAST QA OF EYE PLAQUES

T. Brennen[1], M. Petasecca[1], J. Poder[1], D.L. Cutajar[1], G. Cohen[2], A. Damato[2], A.B. Rosenfeld[1]

[1] Centre for Medical Radiation Physics, University of Wollongong, Australia 2522,
[2] Memorial Sloan Kettering Cancer Center, New York, USA

Introduction: Intraocular tumours can be difficult to treat due to their small size and extreme proximity to nearby healthy tissues, such as the optical nerve and lens. Though these cancers are rare, the prognosis due to their presence can be severe, resulting in the death of 45% of patients within 15 years[1]. Eye brachytherapy, is the most common treatment available, due to it's easy accessibility and high tumour control rates (84% after 5 years). Brachytherapy plaques, containing radioactive seeds, are sutured to the patients eye, directly above the tumour to deliver the therapeutic dose[1]. Fast and accurate quality assurance (QA) measures to verify source activity, placement and arrangement within the plaque currently do not exist, with visual inspection by a physicist being common practic. A novel approach utilising gamma camera imaging techniques with a high resolution Medipix device is presented.

Materials and Methods: The QA system developed consists of a single cone pinhole tungsten collimator, 800 µm in diameter. Situated directly below the pinhole at a variable distance is a Medipix detector, allowing for magnification and FoV adjustments for varying plaque sizes, as shown in Figure 1. The Medipix device is a silicon hybrid detector consisting of 256 x 256 pixels, with a pitch of 55 µm. This provides the means for high resolution imaging of the loaded plaque.

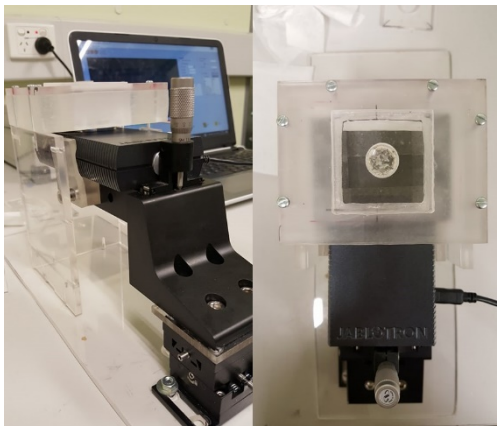


Figure 1: Eye Brachytherapy fast QA system design and construction.

As proof of principle, images were obtained for a range of varying conditions, such as uniform activity seeds (12, 14, 16, 18, 20, and 22 mm COMs plaques), non-uniform activity seeds loaded, and incorrectly loaded plaques (addition of an extra seed within the plaque). I-125 model AGX-10 seeds were utilised. Acquisition was performed in spectroscopic mode for 5 minutes for each plaque.

Results: The measurements confirmed the feasibility of utilising the current gamma camera arrangement with a Medipix device to provide high quality images to perform fast QA for eye brachytherapy.

Some of the results are pictured in Figure 2, where it is clear that the methodology can be applied to a range of plaque sizes, configurations and varying seed activities. It is clear that the system can easily identify incorrect loading and varying activies of seeds within plaques.

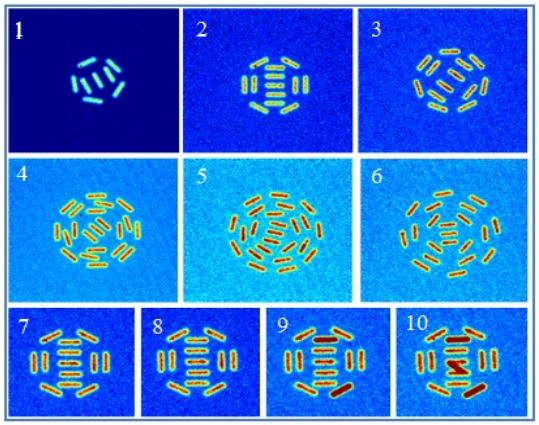


Figure 2: Prelimary results, uniform activity I-125 seeds (1- 6 uniformly loaded 12, 14, 16, 18, 20, and 22 mm COMS plaques), 14 mm COMS plaque silastic insert only (7), fully loaded plaque (8), mixed activity plaques incorrectly loaded (9) and an extra seed (10).

Conclusions: It has been demonstrated that it is possible to used a solid state silicon device, Medipix, to peform QA for eye plaque brachytherapy. It is invisaged that further development of the system will allow for verification of vendor plaques and absolute calibration of preloaded seeds.

Acknowledgements: This research has been conducted with the support of the Australian Government Research Traning Program Scholarhip.

References:

1. C. M. Vajdic, A. Kricker *et al*, "Incidence of ocular melanoma in Australia from 1990 to 1998.", *International Journal of Cancer*, vol. 105, no. 1, pp. 117-122, May 2003

GYNECOLOGICAL HDR BT APPLICATOR FOR TREATMENT DELIVERY AND ONLINE QA VERIFICATION OF SOURCE DWELL POSITIONS AND TIMES

Anna Romanyukha[1], Mauro Carrara[2], Marco Petasecca[1], Tebarak Al-Salmani[1], Dean Cutajar[1], Annamaria Cerrotta[2], Carlo Fallai[2], Emanuele Pignoli[2], Anatoly Rosenfeld[1]
[1] Centre for Medical Radiation Physics, University of Wollongong, Wollongong, Australia, ar947@uowmail.edu.au
[2] Medical Physics Unit, Department of Diagnostic Imaging and Radiotherapy, Istituto Nazionale dei Tumori, Milan, Italy

Introduction: While cancer treatment in the form of High Dose Rate (HDR) Brachytherapy (BT) is often prescribed to patients with gynaecological malignancies, there is no quality assurance (QA) procedure in practice to verify the administered treatment delivery. This means that potential errors can remain unknown to hospital staff, and may cause various post-treatment complications for the patient. BT source position and dwell time verification provide a robust QA measure of the treatment. An innovative prototype of a multichannel vaginal applicator has been designed for dose delivery and real-time source position and dwell time QA verification. The aim of this study was to develop the QA vaginal applicator prototype, calibrate, and test its ability to resolve dwell positions and times of the HDR BT ^{192}Ir source within the seven peripheral channels of the applicator.

Materials and Methods: The applicator prototype is modelled based on the Nucletron Multichannel Vaginal applicator that is 30 mm in diameter and contains seven peripheral and one central channel(s). Three p-type epi diodes with an active area of 1.5 x 1.5 mm^2 are attached to the applicator, selected due to their efficiency in the measurement of high-energy photons associated with the ^{192}Ir source. The diodes have been placed around the upper 55-mm region of the applicator, encompassing the most clinically relevant region of the applicator for HDR BT treatments. The readout system is a TERA and FPGA system capable of 100 µs online readout for up to four diodes at a time. The QA applicator system is fitted into a custom-made solid water phantom, mimicking scatter conditions taking place inside the patient throughout the treatment. Starting with the real-time readout signal of the three diodes, a prototype of the system was characterized to establish a method of source localization, and then tested to evaluate its performance for dwell positon verification in an arbitrary HDR BT plan (Fig.1). The treatment plan consisted of two dwell positions of 5 and 10 s in length per single catheter, with source localization evaluated for every one of the seven peripheral needles.

Results: The characterization of the system showed no significant dependence on radiation intensity throughout the entire "life" of the source once diode response was normalized for the source air kerma strength. Following characterization, the system has demonstrated its ability to resolve the HDR BT source position in the arbitrary plan for a range of 25-50 mm along the applicator, encompassing between 10 to 20 dwell positions of 2.5 mm step size, depending on the catheter number. Discrepancies between the nominal and measured positions and dwell times are provided in Table 1. The highest positional discrepancy was recorded as 0.6 mm in catheter 6, located at 57 mm along the applicator. The highest dwell time discprepancy was 0.6 s in catheter 5 at 39.5 mm along the applicator.

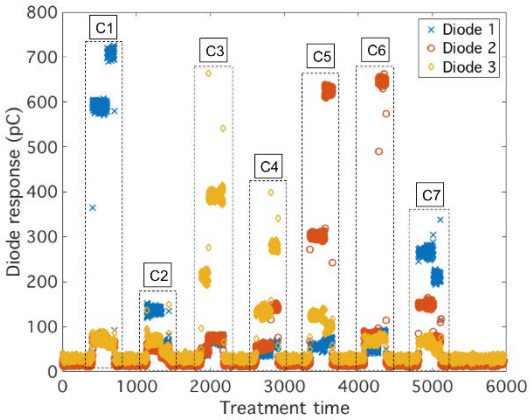


Figure 1. Response of all three diodes in the arbitrary HDR BT treatment.

Cath. #	Nom. L (mm)	Meas. L (mm)	Δ L (mm)	Nom. t (s)	Meas. t (s)	Δ t (s)
1	38	37.5	-0.5	10	9.6	0.4
	30.5	30.3	-0.2	5	4.6	0.4
2	29.5	29.0	-0.5	10	9.7	0.3
	34.5	34.9	-0.4	5	4.8	0.2
3	57	56.9	-0.1	10	9.8	0.2
	39.5	39.5	0.0	5	4.7	0.3
4	59.5	59.2	-0.3	10	9.7	0.3
	39.5	39.5	0.0	5	4.7	0.3
5	49.5	49.3	-0.2	10	9.5	0.5
	39.5	39.3	-0.2	5	4.4	0.6
6	57	56.4	-0.6	10	9.8	0.2
	44.5	44.2	-0.3	5	4.8	0.2
7	40.5	40.1	-0.4	10	9.8	0.2
	25.5	25.0	-0.5	5	4.7	0.3

Table 1. Results of the arbitrary BT treatment used to evaluate the proposed QA HDR BT applicator system. The discrepancy between the nominal and measured positions and dwell times by the diodes are reported as Δ L (mm) and Δ t (s), respectively.

Conclusion: The proposed intracavitary QA HDT BT applicator system has demonstrated the ability to simultaneously deliver and verify the BT treatment in real-time with sub-mm and sub-second accuracy. Treatment verification in the form of ^{192}Ir source dwell position tracking will serve as a safety net against various incidents and dose delivery inaccuracies. The setup requires minimal additional effort for the hospital staff in terms of operation and data analysis, allowing a smooth transition from a conventional multichannel applicator. New diodes will soon be implemented to increase the range of positional and dwell time sensitivity.

BRACHYTHERAPY UTILISING MINIATURISED X-RAY TUBES – AN EVOLVING TECHNOLOGY

Prabhakar Ramachanran[1]
[1] Peter MacCallum Cancer Centre, Melbourne, VIC, Australia, Ramachandran.Prabhakar@petermac.org

Electronic brachytherapy is an advanced radiation treatment technique specifically designed to deliver high doses of radiation inside or very close to the tumor-bearing tissues. Unlike the traditional radionuclide-based brachytherapy, electronic brachytherapy uses a miniaturised x-ray tube that can produce radiation when energised. Most of the electronic brachytherapy systems operate at 50 kVp and therefore posing less radiation exposure to both patients and staff compared to the standard Cobalt-60 or Iridium-192 based brachytherapy systems. Electronic brachytherapy systems have wider applications that include the treatment of skin, brain, breast, spinal metastasis, endometrium, and cervix. The Axxent Xoft brachytherapy system is a unique system which houses a miniature X-ray tube of 2.25 mm diameter at the tip of a flexible catheter. As a mobile unit, the Xoft system requires less shielding and can be operated in remote centres with minimal radiation shielding facilities. The dose fall-off characteristics mimic those of the low energy isotopes, yet the unit still maintains the high dose rate property of an Ir-192 source. This study details the implementation and commissioning aspects of the Axxent system for intra-operative radiotherapy in Breast Cancer and future applications. Electronic brachytherapy systems have the potential to replace conventional radionuclide-based brachytherapy sources and systems.

ON-LINE IMAGE-GUIDED HDR BRACHYTHERAPY (IGBT) FOR PROSTATE CANCER USING ULTRASOUND BASED REAL-TIME SOLUTION

Adam Yeo[1,2], Kurian George[1], Prem Krishnan[1], Sylvia Van Dyk[1], Keen Hun Tai[1], John Violet[1], Scott Williams[1], Sarat Chander[1], Tomas Kron[1,2,3]

[1] Department of Physical Sciences, Peter MacCallum Cancer Centre, Adam.Yeo@petermac.org
[2] School of Applied Sciences, RMIT University
[3] The Sir Peter MacCallum Department of Oncology, The University of Melbourne

Introduction: High dose rate (HDR) brachytherapy is a widely used for treating prostate cancer. An ultrasound image-guided HDR Real-time 'plan and treat' solution (Oncentra® Prostate, Nucletron) has been recently implemented in our department in order to administer more effective and efficient treatment procedures, compared to the existing CT-based HDR solution (Oncentra® Brachy, Nucletron). This work focuses on the clinical implementation of this new technique, including on-line HDR image-guided brachytherapy (HDR-IGBT) workflow.

Materials: A series of commissioning tests has been performed for ultrasound imaging, treatment planning as well as independent dose calculation system. A new optimisation algorithm (HIPO) was compared to the existing algorithm (IPSA) in the Oncentra® Brachy system. A seamless integration of real-time workflow has been designed and demonstrated. Tolerance for online image-guidance results were set based on 20 consecutive treatment fractions.

Results: Motorised ultrasound 3D-imaging could accurately reconstruct volumetric images within the uncertainty defined by slice thickness, providing good image contrast for target region as well as organs-at-risk with no radiation dose. A 'virtual catheter' can guide catheter insertion and real-time correction of catheter reconstruction is possible based on live image. Catheter reconstruction could be accurately performed for both plastic and stainless steel needles, based on ultrasound image within 1 mm measurable uncertainty based on methods described in Ref [1]. Figure 1 shows dosimetric comparison between CT-based planning with IPSA optimisation algorithm and US-based real-time planning with HIPO. Compared to the former technique, the newer technique showed reduction of $V_{150\%}$ and $V_{200\%}$ of the target volume by 24% and 13%, respectively, while $D_{30\%}$ and $D_{10\%}$ of urethra are kept within 5% change, which is still far less than tolerance dose. This implies more homogeneous dose distribution for efficient planning (i.e. DVH optimisation) with an appropriate set of user input (e.g. plan objective and constraints). Live ultrasound 2D-imaging during treatment could ensure accurate treatment delivery; its action level for immediate adaptation has been set as 3 mm for longer than 5 seconds for displacements of urethra and rectum from the planned positions , where rectum movement is only considered anteriorly towards catheters, see Figure 1. Post-treatment 3D-imaging could verify any possible deviation in patient geometry before and after the procedure. This retrospective study could pick up changes between planned and actually delivered in terms of dosimetry.

Table 1. Comparison of DVH parameters for target (prostate plus margin) as well as urethra between CT-based planning with IPSA and US-based real-time planning with HIPO.

	CT-based planning with IPSA	US-based real-time planning with HIPO
V_{target} (in cc)	37.3 (± 9.8) cc	36.8 (± 9.9) cc
$V_{150\%}$ (CTV)	31.9 (± 3.1) %	24.3 (± 2.4) %
$V_{200\%}$ (CTV)	12.6 (± 2.3) %	7.9 (± 1.0) %
$D_{30\%}$ (Urethra)	98.6 (± 3.1) %	104.8 (± 2.2) %
$D_{10\%}$ (Urethra)	103.1 (± 3.2) %	109.3 (± 2.8) %

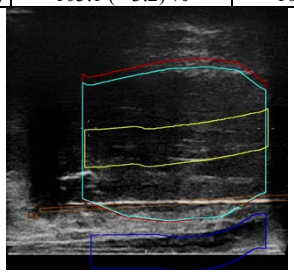


Figure 1. A snapshot of 2D live image on sagittal plane during treatment delivery with contours overlaid, showing that rectum movement caused catheter position out of planned reconstruction.

Conclusions: This new HDR solution enables single non-stop real-time adaptive procedures within an operation room, minimising patient movement and implant shift. More importantly, on-line IGBT could be effectively implemented for real-time treatment delivery verification and estimate the dose delivery to the insertion position with zero geometric uncertainty. There are some limitations including image artefacts and reproducibility of finding a same base-plane before/ after catheter insertion, which need to be addressed [2]. It is worth noting that total procedure time could be significantly reduced without compromising the quality of treatment procedure, aiming for 3-4 hours per procedure in the future, which will enable us to treat at least 2 patients/day.

References

15. Use of ultrasound in image-guided high-dose-rate brachytherapy: enumerations and arguments (S. Banerjee et al.), *J Contemp. Brachythrapy.* **9 (2)**, 146-150 (2017).
2. Imaging of implant needles for real-time HDR-brachytherapy prostate treatment using biplane ultrasound transducers (F. Siebert et al.), *Med. Phy.* **36 (8)**, 3406-3412 (2009).

Debate: SBRT vs Brachytherapy for localised prostate cancer

Tumour Board: Challenging Cases

Skin Brachytherapy

Partial Breast Brachytherapy

SAME DAY OPERATION AND INTRAOPERATIVE CATHETER PLACEMENT FOR PARTIAL BREAST IRRADIATION (SONIC-PBI)

Sean Park[1]

[1] Mayo Clinic, USA

Background: PBI is a treatment option for favorable early stage breast cancer. We initiated intraoperative brachytherapy catheter placement at breast conserving surgery to complete breast conserving therapy (BCT) within 10 consecutive days. Our goal was to improve patient compliance with adjuvant radiotherapy and decrease the total time for BCT.

Methods: 190 patients were prospectively evaluated and registered for intraoperative brachytherapy catheter placement from October 2012 to December 2016. Inclusion criteria included age ≥ 50 years, ≤ 2.5 cm, estrogen receptor positive invasive carcinoma or ductal carcinoma in-situ, and negative surgical margins and sentinel lymph node (SLN) on intraoperative pathology. Target volume was defined as 1 cm of breast tissue beyond the cavity excluding pectoralis, chest wall, and within 5 mm of skin surface. 3D CT planning was performed on the weekday after surgery and treatment was initiated on the following weekday. The cumulative incidence of recurrence was estimated considering death as a competing risk.

Results: 170 patients (89%) had intraoperative catheter placement. 19 patients were registered but did not have catheter placed due to intraoperative findings (11 positive SLN, 5 extensive disease, 2 failed SLN mapping, 1 no residual disease). One patient had delayed positive SLN on permanent pathology and catheter was used to boost the cavity prior to converting to whole breast radiation. Prescription doses were 34 Gy in 10 BID (57%), 32 Gy in 8 BID (14%), and 21 Gy in 3 daily (29%) fractions. Median age was 67 and 9% were premenopausal. Median tumor size was 0.9 cm, 18% were DCIS, and 6% were grade 3. BCT was completed in a median of 9 consecutive days. Three patients received adjuvant chemotherapy and 64% had adjuvant endocrine therapy. Median follow up is 1.7 years (39% with at least 2 years), and 2-year local recurrence rate is 2%.

Conclusions: Intraoperative pathology and brachytherapy catheter placement allows the initiation of PBI within 2 weekdays and the completion of BCT within 10 consecutive days in select patients with low short-term local recurrence rate. Long term follow up is planned for oncologic and cosmetic outcomes.

Advanced Heavy Ion and Proton Therapy Technology

RECENT PROGRESS AND FUTURE PLAN OF HEAVY-ION CANCER RADIOTHERAPY WITH HIMAC

Koji Noda[1]

[1] National Institute of Radiological Sciences, QST,
4-9-1 Anagawa, Inage-ku, Chiba 263-8555, Japan, noda.koji@qst.go.jp

Heavy-ion beams are very suitable for deeply-seated cancer treatment not only owing to their high dose localization around the Bragg peak, but also owing to the high biological effect there. NIRS, therefore, constructed HIMAC as the world's first heavy-ion accelerator facility dedicated to medical use. NIRS has conducted the cancer treatment with a carbon-ion beam with HIMAC since 1994, which results in the treated patient number of more than 10,000 during 22 years operation.

Since the carbon-ion radiotherapy with HIMAC was approved as an advanced medical technology in Japan in 2003, NIRS developed a compact carbon-ion radiotherapy facility in order to boost applications of the carbon-ion radiotherapy in Japan. As the fruits of this work, its pilot facility was constructed in the Gunma University, which has been successfully conducted since 2010.

Since 2006, further, NIRS has been engaged in a "new treatment research project" toward a new next generation research. One of the most important purposes is to realize the "adaptive cancer radiotherapy" to accurately treat tumor even with changing both the tumor size and shapes during a treatment period. Since both the static and moving tumors should be treated with HIMAC, the phase-controlled rescanning (PCR) method[1], based on a fast 3D scanning technology with a pencil-beam scanning, has been developed to move toward the goal of adaptive cancer radiotherapy. In order to verify the developed technology through the clinical study, the new treatment research project was conducted. The first patient was treated in May 2011. At the present, the NIRS scanning has adapted a full depth scanning with 201 energy steps of the HIMAC synchrotron. The moving-target treatment has been also carried out. A compact carbon-ion rotating gantry with superconducting technology was developed, and the clinical trial was already completed. From the next fisical year, thus, the treatment with the superconducting rotating gantry[2] will be started. Further, the intensity modulated carbon-ion RT combined with the 3D scanning will be developed, which will bring the more accurate and shorter-course treatments owing to the higher dose concentration.

We just start a new development plan, which called it "Quamtum Scalpel" project. Objectives of this project are to realize a higher performance radiotherapy and to construct a ultra-compact radiotherapy machine. As more sophisticated LET-painting technique, the multi-ions irradiation scheme has been being studied[3], which can diliver various LET distribution while keeping an uniform dose distribution, as shown in Fig. 1. For ultra-compact machine, the quamtum scalpel project will employ an ultra-compact heav-ion synchrotron, a heavy-ion rotating gantry with superconducting technology and a laser acceleration machine as an injector. Tha gola of the machine is shown in Fig. 2.

We report the development of HIMAC for the heavy-ion cancer radiotherapy.

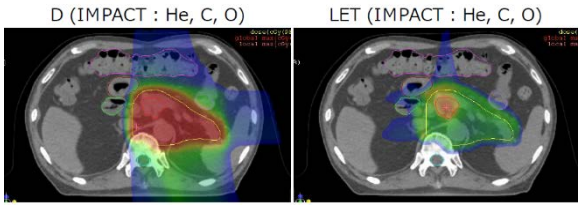


Fig. 1: Multi-ions irradiation with He, C and O. Dose distribution (Left) and LET distribution (Right).

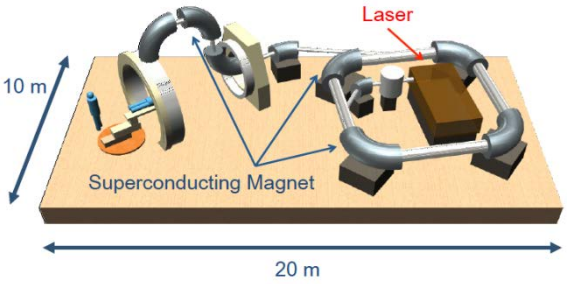


Fig. 2. The goal of an ultra-compact heavy-ions radiotherapy msachine.

References:

16. T. Furukawa, N, Saotome, T. Inaniwa, S. Sato, K. Noda, T. Kanai *Med. Phys.* **35** *2235-2242 (2008).*
2. Y. Iwata *et al.*, Phy. Rev. ST-AB 15, (2012) 044701
3. T. Inaniwa *et. al.*, Phys. Med. Biol. 62 (2017) 5180

RECENT DEVELOPMENTS AT THE UNIVERSITY OF PENNSYLVANIA'S ROBERTS PROTON THERAPY CENTER

Richard L. Maughan[1]

[1] Penn University, USA

The Roberts Proton Therapy Center treated its first patient on Australia Day 2010 with a double scattered proton beam. In 2012 the first patient was treated with pencil beam scanning and by that time patients were being treated in five treatment rooms. By March 2013 we were treating with PBS in three treatment rooms and double scattering in the other two. We currently treat about 100 patients per day in 4 treatment rooms, while one of our double scattering beam nozzles is being replaced with PBS. We treat 15 to 20 pediatric patients per day, many under general anesthetic. We treat a wide variety of indications in adult patients and all patients are registered on some form of clinical research protocol. We were the first proton center to have an operational CBCT system (September 2014). We have recently commissioned our research room incorporating a Small Animal Radiation Research Platform (SARRP) on one of the beam lines which can be used for both x-ray and proton irradiations to support our radiobiology research program. Areas of physics related research involve prompt gamma range monitoring, proto-acoustic range verification, the use of dual energy CT for better determining the HU vs. stopping power curve, microdosimetry and detector development. Aspects of this research and development program will be reviewed and discussed.

ITALIAN MEDICAL PHYSICISTS' AND RADIATION ONCOLOGISTS' VIEW ON HADRONTHERAPY

Mauro Carrara[1], Tommaso Giandini[1], Giulia Marvaso[2], Chiara Tenconi[1], Mario Ciocca[3], Stefania Russo[3], Federica Cattani[4], Delia Ciardo[2], Sara Morlino[5], Barbara Avuzzi[5], Nice Bedini[5], Sergio Villa[5], Paola Romanelli[2], Azusa Hasegawa[6], Barbara Vischioni[6], Francesca Valvo[6], Barbara A. Jereczek-Fossa[2,7], Roberto Orecchia[2,8], Riccardo Valdagni[5,7,9], Emanuele Pignoli[1]

[1]Medical Physics Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan – Italy, [2]Department of Radiotherapy, IEO European Institute of Oncology, Milan – Italy, [3]Medical Physics Division, CNAO National Center of Oncological Hadrontherapy, Pavia – Italy, [4]Department of Medical Physics, European Institute of Oncology, Milan – Italy, [5]Radiation Oncology 1, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan – Italy, [6]Clinical Division, CNAO National Center of Oncological Hadrontherapy, Pavia – Italy, [7]Department of Oncology and Hemato-oncology, Università degli Studi di Milano, Milan – Italy, [8]Scientific Directorate, European Institute of Oncology, Milan – Italy, [9]Prostate Cancer Program, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan - Italy

Introduction: The total number of patients treated with hadrontherapy (HT) has been growing exponentially in the last years. In Italy, HT started in 2002 with low-energy protons at the INFN-LNS (Istituto Nazionale di Fisica Nucleare - Laboratori Nazionali del Sud, Catania) for ophthalmic treatments. Nowadays, two hospital-based facilities are operative in the Country: the APSS (Azienda Provinciale per i Servizi Sanitari) in Trento, provided with proton scanning beams, and the National Center for Oncological Hadrontherapy (CNAO) in Pavia with both proton and carbon ion scanning beams.

In light of the increasing interest of the Italian Scientific Community, two similar surveys were conducted within all members of the Italian Association of Medical Physics (AIFM) and the Italian Association of Radiation Oncology (AIRO) to investigate their perception of HT.

Materials and Methods: The questionnaires were designed focusing on: (dis)advantages of HT, its current status and possible future improvements, and the need and opportunities for future investments in Italy and abroad. Information about professional qualification, main fields of clinical involvement, and specific competencies of the respondents were also collected. The complete list of submitted questions can be found elsewhere [1,2]. The anonymous responses of the participants were collected and administered through a web-based survey software (Google Forms).

Results: Valuable detailed information by both Radiation Oncologists (ROs) and Medical Physicists (MPs) emerged from the surveys. In general, potential reduction of toxicity to organs at risk and healthy tissues was perceived as the main advantage of proton therapy. In addition, efficiacy in the treatment of radioresistant tumors and hypoxic cells was indicated as an additional advantage peculiar of carbon ions. Pediatric tumors were perceived by ROs as particularly indicated for protontherapy.

On the contrary, start-up and maintenance costs of HT facilities are considered by MPs and ROs the main disadvantages. Moreover, the uncertainties related to organ motion were considered a weak point for HT. ROs also stressed the lack so far of level I clinical evidence.

Concerning the current status of radiotherapy technologies, HT is in general considered the technique with the great potential for improvement. In particular, protons and carbon ions ar considered the particles with the highest potential for the effective treatment of tumors, in particular those that poorly respond to conventional therapies (MPs) or those that are located in critical positions (ROs). Regarding educational needs in the field of HT, most respondents reported that they were motivated by personal interests rather than by daily professional needs.

Conclusions: In view of the continuous increase in the numer of HT centers worldwide, there is significant scientific, technological and clinical interest in the further development of particle therapy for effective cancer treatment. The majority of ROs and MPs are aware of the direction of future economical investments. Training and educational initiatives are currently perceived as necessary.

Acknowledgements: This study was partially supported by the research grant from Associazione Italiana per la Ricerca sul Cancro (AIRC): IG-14300. We thank the members of the Associazione Italiana di Fisica Medica (AIFM) and of the Associazione Italiana di Radioterapia Oncologica who took part in the survey.

References:

1. Giandini T, Tenconi C, Carrara M, et al. Physicists' views on hadrontherapy: a survey of members of the Italian Association of Medical Physics (AIFM). *Tumori* 103 (2017), 430-7.
2. Marvaso G, Vischioni B, Jereczek-Fossa BA, et al. Hadrontherapy from the Italian Radiation Oncologist point of view: face the reality. The Italian Society of Oncological Radiotherapy (AIRO) survey. *Radiol Med.* 122 (2017), 140-5.

QA in Proton Therapy and Treatment Optimisation

OUT-OF-FIELD DOSES ASSOCIATED WITH PROTON THERAPY

I. Gudowska[1,2], O. Ardenfors[1,2], Jan Lillhök[3], Linda Persson[3] and A. Dasu[4]

[1] Dept. of Physics, Stockholm University, Stockholm, Sweden, irena.gudowska@ki.se
[2] Medical Radiation Physics, Dept. of Oncology and Pathology, Karolinska Institutet, Sweden
[3] Swedish Radiation Safety Authority, Stockholm, Sweden
[4] The Skandion Clinic, Uppsala, Sweden

Introduction: Quantification of the radiation burden from secondary radiation produced in proton pencil-beam scanning (PBS) therapy is an important issue. Several epidemiological studies have indicated a higher risk of developing tumors among radiotherapy patients than in the general population. Furthermore, the number of radiation-induced second cancers is expected to increase since patients more frequently receive radiotherapy at a young age and have a prolonged long-term survival, especially after particle radiotherapy.
Several studies[1-3] have reported out-of-field doses produced in proton PBS therapy using a variety of experimental and numerical approaches.
Both experimental and numerical methods are associated with certain limitations and uncertainties, requiring careful analysis, especially when the doses are used for evaluating the risk of radiation-induced second malignancies.

Objectives: A review of measurement and calculation methods for evaluation of the out-of-field doses in proton therapy will be presented. Special focus will be given to uncertainties in determining secondary doses to the patient, to uncertainties in determining the energy spectra of secondary radiation in the treatment room, and to limitations of the measurement techniques and computation methods.
As an example, out-of-field doses from irradiating a whole-body phantom with a proton PBS brain tumor treatment plan are presented. Measurements of out-of-field doses using tissue-equivalent proportional counters (TEPC) placed at different positions outside the phantom and corresponding Monte Carlo simulations with MCNP6 are discussed. The results are presented in terms of absorbed dose to the detector and equivalent organ doses normalized to the absorbed dose delivered to the brain tumor. The uncertainties of the measured and calculated doses correspond to two standard deviations including both statistical and systematic uncertainty.
Additionally, the relevance of using radiation protection and operational dose quantities when reporting secondary doses in radiotherapy will be scrutinized. Their adequacy with regard to related radiation protection aspects and the evaluation of the risk of induction of second cancers will be debated.

Results: The measured out-of-field absorbed doses from the whole-body phantom irradiation with proton energies of 60-97 MeV, creating a Spread-Out-Bragg-Peak (SOBP) in the brain tumor, ranged between 0.4 and 9.9 $\mu Gy.Gy^{-1}$ for different detector positions close to the phantom. The uncertainties of the TEPC measurements were in the range of 10% taking into account uncertainties in detector operation parameters, detector positioning, counting statistics and the calibration procedure. The absorbed doses simulated with MCNP6 for the same positions ranged between 0.9 – 8.6 $\mu Gy.Gy^{-1}$ with uncertainties of roughly 20%. The uncertainties of the Monte Carlo simulation originates from uncertainties in statistics, experimental geometry, physics models and cross-section libraries used to sample the production of secondary particles.

Conclusions: Studies of secondary doses delivered to patients undergoing proton therapy are of special importance due to the large complexity in the secondary radiation field and secondary doses that can be delivered to normal tissues both close to and relatively far from the treated volume.

A careful determination of secondary doses in proton therapy and accurate determination of the uncertainties of the evaluated doses will support further studies regarding the secondary effects including the risk of second cancer after radiation treatment.

References:

1. Kry et al., *Med. Phys*. 44 (10), e391-e429 (2017).
2. Newhauser and Durante *Nature reviews. Cancer*, 11(6), pp.438–48 (2011).
3. Gudowska et al. *Radiation Protection Dosimetry*, 161(1), 357–362 (2014).

4D ROBUST OPTIMIZATION IN PENCIL BEAM SCANNING PROTON THERAPY FOR HEPATOCELLULAR CARCINOMA

T. Pfeiler[1,2], D. Ahmad Khalil[1], C. Bäumer[1], O. Blanck[3,4], M. Chan[3,5], E. Engwall[6], D. Geismar[1], S. Peters[1], S. Plaude[1], B. Spaan[2], J. Wulff[1], B. Timmermann[1]

[1] West German Proton Therapy Centre Essen, Essen, Germany, tina.pfeiler@uk-essen.de
[2] TU Dortmund University, *Experimental Physics* 5, Dortmund, Germany
[3] University Clinic Schleswig-Holstein, Department of Radiation Oncology, Kiel, Germany
[4] Saphir Radiosurgery Center, Güstrow and Frankfurt, Frankfurt, Germany
[5] Imperial College London Healthcare Trust, Department of Radiation Physics, London, United Kingdom
[6] RaySearch Laboratories AB, Stockholm, Sweden

Introduction: Pencil beam scanning proton therapy (PBS) enables high-precision treatment for malignant tumors due to its steep dose gradients in beam direction. The utilization of the distinctive dose profile of protons in an intensity modulated approach allows sparing of organs at risk (OARs) even for complex anatomies. However, it is exactly this concept that makes PBS particularly susceptible to range uncertainties and organ motion. The interplay of organ motion and beam scanning may cause relevant distortions of the intended dose distribution. In order to exploit the full potential of proton therapy also for moving targets, motion mitigation techniques like robust optimization and modelling of interplay effects become crucial components for motion management in PBS [1]. This study investigates the impact of 4D robust optimization on interplay effects and sparing of OARs compared to the conventional margin concept for hepatocellular carcinoma (HCC).

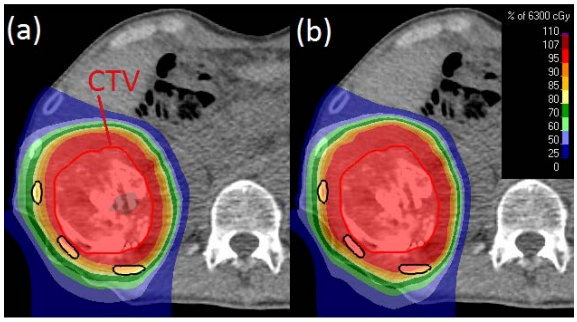


Figure 1. 4DD of a robust (a) and non-robust optimized plan (b).

Materials and Methods: Two-field PBS treatment plans were generated in a research version of RayStation 6 for 5 HCC patients using 4D robust optimization. A dose of 63 Gy_{RBE} (D_{pres}) was prescribed to the CTV in 15 fractions according to [2]. The robust optimization settings were chosen to achieve plan robustness against 2 mm setup error, 5% range uncertainty and morphological changes in 10 respiratory phases. For comparison purposes, corresponding non-robust optimized PBS plans were created based on beam-specific PTVs. The uncertainty parameters above were used as margins in this case, whereby the internal margin (accounting for target motion) was derived from the respiratory phases. Since the treatment planning system has no direct access to the time structure of the field delivery, a customized and experimentally validated interplay effect routine [3] was developed for 4D dose computations of irradiations with an IBA Proteus®Plus proton therapy system. It computes 4D dynamic accumulated doses (4DDs) based on an empirical beam-time model, 4D CT data sets and deformable image registrations. DVH metrics, such as the percentage over- ($V_{107\%}$) and underdosage (100-$V_{95\%}$) and the homogeneity index $HI = (D_{5\%} - D_{95\%})/D_{pres}$, served as evaluation criteria.

Results: The 4DDs revealed over- and underdosage ($V_{107,95}$) of up to 10% of D_{pres} for robust optimized plans per fraction. $V_{107,95}$ was approximately 1 to 3% less for the non-robust optimized plans. Accumulating all 15 fractions, it approached 0% for both treatment techniques. The HI ranged around 10% for a single fraction with slightly better results for the non-robust plans which already exhibited smaller HI values in the static case. Simulating the whole treatment course over all fractions, the HI decreased to less than 5%. OARs close to the target, such as ribs and the normal liver volume, could be better spared when using robust optimization (see Fig. 1). For example, V_{42Gy} and V_{33Gy} were about 0.5 to 2.5% smaller for the normal liver tissue (related to the normal liver volume).

Conclusions: Using the specified uncertainty criteria, robust optimization was not found to be superior to the conventional margin concept (non-robust optimized plans) in terms of reducing interplay effects for HCC patients. For a single fraction, HI and $V_{107,95}$ were even slightly smaller for the non-robust plans. But this advantage disappeared when regarding the whole treatment of 15 fractions. It could be demonstrated that dose inhomogeneities were averaged out for the applied fractionation scheme. Moreover, robust optimization reduced the 4DD to closeby OARs slightly which can be of importance for critical cases.

References:

17. Chang *et al.*, Int J Radiat Oncol Biol Phys 99:41-50 (2017).
2. Bush *et al.*, Cancer 117, 3053–9 (2011).
3. Pfeiler *et al.*, Z Med Phys, in press (2017). https://doi.org/10.1016/j.zemedi.2017.07.005

EFFICIENT PATIENT-SPECIFIC QA FOR SPOT-SCANNED PROTON THERAPY USING NOZZLE-INTEGRATED DETECTORS AND FAST MONTE CARLO DOSE CALCULATIONS

J E Johnson[1], C Beltran[2], H Wan Chan Tseung[2], D W Mundy[2], T J Whitaker[2], J J Kruse[2], M G Herman[2], K M Furutani[2]

[1] Department of Radiation Oncology, Mayo Clinic, Rochester, MN, USA, Johnson.Jedediah@mayo.edu
[2] Department of Radiation Oncology, Mayo Clinic, Rochester, MN, USA

Introduction: We have developed an end-to-end patient-specific QA technique in our spot scanning proton center which is more sensitive and efficient than traditional compartmentalized approaches.

Materials and Methods: The patient-specific methodology relies on independently verifying the accuracy of the delivered proton fluence and the dose calculation in the heterogeneous patient volume. Once a dose distribution has been approved for treatment, a DICOM export of the plan is performed from the treatment planning system. This plan is then imported into a fast, Monte Carlo second check system, which performs a full volumetric calculation of dose to material on the patient's CT image set for comparison against the originally planned dose[1]. The plan is concurrently prepared for treatment, after which it is delivered and measurements are performed using two detector systems which are dynamically integral to normal patient delivery. The two detectors are a spot position monitor (SPM) and a dose monitor (DM). The SPM and DM data are recorded by the Treatment Delivery System for every spot and are extracted for offline analysis following treatment. The measured data are compared to the expected delivery patterns using quantitative metrics.

It is critical to the safety of this approach that the holistic integration of patient-specific and patient-independent QA be maintained. The beam properties measured during initial system commissioning, which are input into the treatment planning system, must be re-verified regularly as is the standard approach in 3D and IMRT photon practice. To this end, the SPM and DM detectors are rigorously and independently validated for accuracy in daily, monthly, and annual QA intervals. These QA tests are performed using independent detectors such as reference class, ADCL-calibrated ion chambers (DM) as well as radiochromic film and ion chamber array detectors (SPM).

Results: Deviations in delivered vs. planned MU per spot are reported in a histogram. The absolute maximum deviation must be less than a predetermined threshold (0.002 MU), which if exceeded, will lead to immediate termination of the delivery. Spot position discrepancies in x and y (orthogonal to beamlet direction) are analyzed as a function of spot number (Figure 1). Systematic deviations, which are represented by the intra-energy-layer running average of the difference between planned and delivered spot positions (black dots), must fall within the systematic deviation threshold (blue lines). Similarly, the individual spot position deviations (green circles), must fall within the red dotted threshold lines, which represent the tolerance for random deviations from the intra-energy-layer running average deviation. All these action thresholds are linked to accuracy of the commissioned delivery system[2]. Even when plan delivery is acceptable, the Monte Carlo second check system has identified dose calculation issues which would not have been caught using traditional, phantom-based measurement techniques.

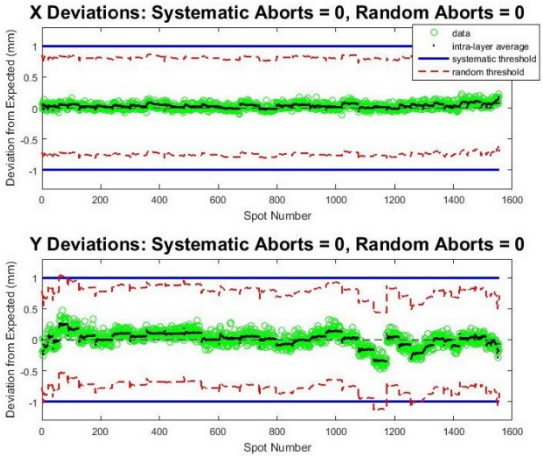


Figure 1: Spot position deviation analysis. Both the random and systematic components of spot position deviations are computed and compared to predefined action thresholds.

Conclusions: The efficiency and sensitivity of our patient-specific QA program has been improved by implementing a procedure which independently verifies both patient dose calculation accuracy and plan delivery fidelity. Such an approach to QA requires a holistic integration and maintenance of patient-specific and patient-independent QA.

References:

1. H. Wan Chan Tseung et al, *Med. Phys.* **42**, 2967 (2015).
2. J. Yu et al., *Med. Phys.* **41**, 081706 (2014).

TEST OF INNOVATIVE SILICON DETECTORS FOR THE MONITORING OF A THERAPEUTIC PROTON BEAM

Roberto Sacchi[1,3], Zahra Ahmadi Ganjeh[5], Roberta Arcidiacono[3,7], Andrea Attili[3], Nicolò Cartiglia[3], Marco Donetti[6], Federico Fausti[3,4], Marco Ferrero[3], Simona Giordanengo[3], Omar Hammad Ali[2,3], Marco Mandurrino[3], Lorenzo Manganaro[2,3], Giovanni Mazza[3], Vincenzo Monaco[2,3], Valentina Sola[3], Amedeo Staiano[3], Anna Vignati[3], Roberto Cirio[2,3]

[1] Dipartimento di Fisica, Università di Torino, via P. Giuria,1, 10125 Torino, Italy, email roberto.sacchi@unito.it
[2] Dipartimento di Fisica, Università di Torino, via P. Giuria,1, 10125 Torino, Italy
[3] Istituto Nazionale di Fisica Nucleare, sez. di Torino, via P. Giuria,1, 10125 Torino, Italy
[4] Dipartimento di Elettronica e Telecomunicazioni, Politecnico di Torino, Corso Duca degli Abruzzi, 24, 10129 Torino, Italy
[5] Faculty of Physics, Yazd University, Yazd, Iran
[6] Fondazione CNAO, Strada Campeggi 53, 27100 Pavia, Italy
[7] Università del Piemonte Orientale, Largo Dobegani 2/3, 28100 Novara, Italy

Introduction: In order to fully exploit the high selectivity of the dose deposition achieved with active proton beam scanning, the delivery system needs fast and accurate beam monitoring detectors. Recent developments in thin silicon detectors with moderate internal gain, optimized for timing applications (Ultra Fast Silicon Detectors, UFSD), offer a favourable technological option to conventional ionization chambers. Thanks to their fast collection time (1 ns in 50 μm thickness) and good signal-to-noise ratio, properly segmented sensors could allow discriminating and counting single protons up to the high fluxes of a therapeutic beam. Moreover, the excellent time resolution suggests using time-of-flight techniques for measuring the proton beam energy.

The MoVeIt project of the Italian National Institute for Nuclear Physics aims at developing two devices based on UFSD, one for particle counting and one for beam energy measurement, to characterize a therapeutic beam in radiobiological applications. We report here the progresses on the design of the detectors and front-end electronics and the results with the first detector prototypes.

Materials and Methods: Several 50 μm thick UFSD detector prototypes, both with single pads and segmented in strips, were fully characterized in our laboratory and tested on the clinical proton beam of the CNAO particle therapy facility, up to fluxes of 10^9 p/s. Different doping options of the sensors were also attempted and compared in order to increase the resistance to the radiation damage. A fully custom front-end readout, designed to provide single particle counting at high rate, is also in an advanced development stage and will be briefly described.

Results: Figure 1 shows a portion of waveform acquired from a 1,2x1,2 mm^2 UFSD pad exposed to the beam of CNAO. Thanks to the internal gain, the signal of protons can be easily discriminated from the noise background, while the limited thickness of the sensors causes a very short signal duration, less than 2 ns, as required at high measurement rates.

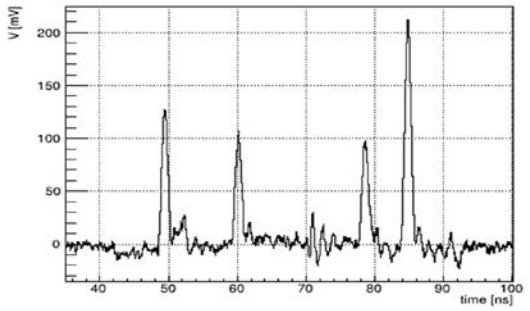


Figure 1. Signal waveform showing the crossing signal of protons on a UFSD pad.

Several quantities such as signal-to-noise ratio, pileup probability, internal gain and gain degradation with fluence were determined from the offline analysis of the collected waveforms and compared, whenever possible, to the laboratory measurements. Signal pileup, inducing deviation from linearity, was observed at a channel average frequency above 5 MHz and was traced to the highly non-uniform time distribution of the CNAO beam. This suggests that a suitable detector segmentation will be essential for counting rates at the GHz level.

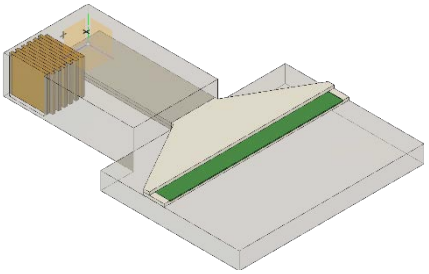
In addition, from the coincidence of two detectors aligned along the beam, the timing properties were studied. A crossing time resolution of less than 50ps was obtained, thus allowing precise beam energy measurements within few μs of irradiation by using the timing difference between two sensors at a mutual distance smaller than 1m.

Conclusions: UFSDs are found to be a viable option for improving the qualification and the monitoring of a therapeutic proton beams. However, a careful design is necessary to avoid large pileup inefficiencies and early performance degradation. Based on these results, the design and expected performance of the two devices will be presented and discussed.

References:

18. H.F.-W. Sadrozinski et al. *Nucl. Instrum. Meth. Phys. Res.* A **831**, 18-23 (2016).

Thursday 8th of February 11:30



DEVELOPMENT OF THE DOSE MAGNIFYING GLASS FOR CLINICAL PROTON RANGE MEASUREMENT

A.H. Merchant[1] , D.W. Mundy[2], C. Beltran[2], S. Guatelli[1,3], M. Petasecca[1,3], M. Lerch[1,3] , V. Perevertaylo[4] , M. Jackson[5] and A. B. Rosenfeld[1,3]

[1] Center for Medical Radiation Physics, University of Wollongong, Wollongong, 2522, Australia
[2] Department of Radiation Oncology, Mayo Clinic, Rochester, MN, USA
[3] Illawarra Health Medical Research Institute, University of Wollongong, Wollongong, 2522, Australia
[4] SPA BIT, Kiev, Ukraine
[5] Department of Radiation Oncology, Prince of Wales Hospital, Sydney, 2031, Australia

Introduction: The Dose Magnifying Glass (DMG) developed at the University of Wollongong has been shown in previous generations of the detector to be an accurate tool for proton range measurement[1], but requires further platform development in order to be used efficiently in the clinic for energy verification quality assurance or measurement of device water-equivalent-thickness (WET). Here we present the first steps and future plans for development of the DMG into a clinical tool.

Materials and Methods: The DMG is a miniature silicon strip detector comprised of an array of 256 individual silicon diodes. Each strip provides a sensitive area of 20 µm x 2000 µm, separated by a pitch of 200 µm. The diodes are embedded in a silicon chip, 51.4 mm x 4 mm mounted on a Kapton carrier board and housed in a PMMA phantom.

In order to be used efficiently in the clinic, a platform must be built around the DMG to enable fast measurements of an arbitrary range. Due to the limited scan range inherent to the device (~5.1 cm depth in silicon, or ~5.6 cm WET), incremental range shifters must be employed to shift the Bragg peak into the detectable range. In this first iteration of the platform, shown in Figure 1, an acrylic base was designed for positioning of the DMG as well as a series of ten brass plates, each machined to a thickness of 5 mm (2.85 cm WET). By sequentially adding brass plates until the measured proton range is within the sensitive volume, the DMG can be used to measure arbitrary proton ranges to a minimum of approximately 1.25 cm WET, the thickness of the device housing.

Development and verification is taking place at the Mayo Clinic proton facility in Rochester, MN using the Hitachi ProBeat-V spot-scanning proton therapy system. Clinical energies range from 71 MeV to 229 MeV. Preliminary testing has focused on baseline range measurements and determination of the WET of an object via range measurement. Measurements were compared with those of a Hitachi multi-layer ion chamber.

Results: At low energy (71.3 MeV), the Bragg peak in silicon is well resolved and the range of the distal 80% dose (R_{80}) was measured to be 39.90 mm, which is consistent with the MLIC measurement of 39.99 mm. At high energies (228.8 MeV), the silicon

Bragg peak is convolved with a broad peak introduced by proton scatter in the protective acylic case (Figure 2). The convolution makes measurement of

Figure 1. Model of the DMG housed in the platform. Brass sheets of 5 mm thickness are also indicated in front of the DMG axis of detection.

the R_{80} impossible. Efforts are ongoing to address this issue.

Another set of measurements were acquired to determine the WET of a brass plate. Measurements were taken without the plate in front of the detector and with, and the difference in measured range (WET) divided by the thickness of the brass to determine the RSP. Using the MLIC, the RSP was measured to be 5.77 vs 5.78 using the DMG R_{100}.

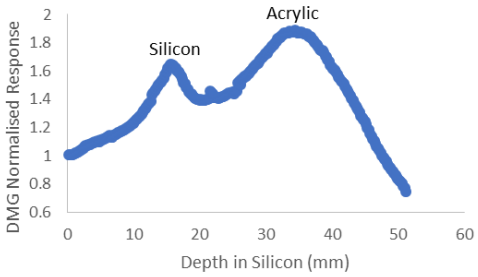


Figure 2. DMG response to a 228.8 MeV proton beam.

Conclusions: The DMG has the potential to significantly reduce the time required for accucrate proton range measurements. Efforts to improve the detector response and clinical applicability are ongoing.

Acknowledgements: The authors wish to thank the Prince of Wales Hospital Radiation Oncology Trust Fund for financial support of this project. This research has been conducted with the support of the Australian Government Research Training Program Scholarship.

References:

19. A. H. Merchant et al., *Rad. Meas.* V. **106**, 378-384 (2017)

GEM DETECTORS FOR USE IN PARTICLE THERAPY

Johannes Leidner[1,2], Fabrizio Murtas[2,3], Marco Silari[1]

[1] CERN, 1211 Geneva 23, Switzerland
[2] RWTH Aachen, Templergraben 55, 52056 Aachen, Germany
[3] INFN LNF, Via E. Fermi 40, 00044 Frascati (Rome), Italy

GEM (Gas Electron Multipliers) originally developed for high-energy physics have progressively found use for a number of other applications, e.g. for determining the amount of ^{55}Fe, a weak photon emitter that cannot be measured by gamma-spectrometry, in metallic radioactive materials. Here we will present some results of the use of two types of these detectors for monitoring in particle therapy: a triple-GEM detector and GEMPix, a novel gas detector with highly pixelated readout obtained by coupling a triple-GEM with the Timepix readout chip.

The triple-GEM was employed for measuring the beam spot dimensions and the homogeneity of a scanned irradiation field, which are daily QA tasks commonly performed using radiochromic films. The results show that the detector is able to monitor the 2D beam image on-line with a pad granularity of 2 mm and a response proportional to the number of delivered particles. The dose homogeneity was in good agreement with that obtained with radiochromic films.

The use of GEMPix to measure the energy deposition by protons and carbon ions in a water phantom is currently under study with a dedicated system consisting of a water phantom, a GEMPix inserted in the phantom with remote-controlled 3D movement, a PTW reference ion chamber, dedicated hardware and software. The Bragg curve, 2D images of the beam and a 3D reconstruction are obtained from a single depth scan performed in approximately 15 minutes. Discrepancies with results obtained with the PTW Peakfinder are being investigated.

The ultimate application of the GEMPix is for microdosimetry of particle beams. The GEMPix has been used as a small Time Projection Chamber (TPC) already and can be filled with a tissue equivalent gas. The aim is to exploit the tracking capabilities and the particle discrimination properties of the detector to measure the energy distribution along single particle tracks. Different volumes inside the detector can be defined simultaneously during a measurement (e.g. emulating a bunch of cells), with the potential to evaluate by-stander effects.

INSTALLATION OF A COMPACT, COMPREHENSIVE PROTON THERAPY UNIT VIA AN ELEVATOR SHAFT INTO AN EXISTING, STANDARD RADIOTHERAPY CENTER

Ben Clasie[1] and Greg Sharp[1]

[1] Massachusetts General Hospital & Harvard Medical School, Boston, USA

Introduction: Massachusetts General Hospital (MGH) is adding a new proton therapy unit within the Lunder Building located on the main campus. The new treatment room will expand the capacity for proton therapy services at MGH and is an optimal location for the clinical staff, but it also presents a challenge in installing a comprehensive proton equipment suite in an existing, treating and conventional radiotherapy clinic. The location is three floors underground and is located below emergency and operating rooms.

Materials and Methods: The proton therapy unit includes a 330 MeV accelerator, robotic patient positioner, half gantry, scanning nozzle, 2D and CBCT 3D volumetric imaging, associated power supplies, service platforms and translation slide. The proton equipment, 3rd party supplier coordination, scheduling, installation and equipment commissioning is provided by U.S.-based, ProTom International.

Results: The proton therapy unit, including the accelerator, gantry, treatment area, shielding, magnet power supplies, and equipment control racks, has the footprint of two conventional linac vaults with a recess dug for the gantry. Delivery, via the Lunder building elevator shaft, construction, and installation is complete. Technical commissioning is underway.

Conclusions: The presentation will discuss the unique challenges and opportunities of the environment and demonstrate how proton therapy can be implemented in locations alongside standard, existing radiotherapy centers.

Imaging with Protons and Ions

Thursday 8th of February 13:30

IONOACOUSTICS FOR RANGE MONITORING OF PROTON THERAPY

Katia Parodi[1], Sebastian Lehrack[1], Walter Assmann[1]
[1] Ludwig-Maximilians-Universität München, Faculty of Physics, Department of Medical Physics, Munich, Germany; Email: Katia.Parodi@lmu.de

Introduction: Proton therapy is an emerging treatment modality aiming to exploit the favourable interaction properties of swift ion beams in matter. Along with advanced beam scanning delivery methods, proton therapy can enable very good targeting of the dose to the tumour volume with excellent sparing of surrounding healthy tissue and critical structures in comparison to widely established external photon beam therapy. However, full clinical exploitation of the promised advantanges in the clinical practice is still hampered by the main issue of range uncertainties, i.e., uncertainties in the position of the well localized dose deposition of individual pencil beams in the so called Bragg peak. To this end, most of the currently investigated techniques aim at exploiting secondary emissions from nuclear interactions less obviously correlated to the dose deposition. Here, we present investigations on an alternative approach exploiting acoustic emissions originating from ion interaction in tissue, hence called "ionoacoustics".

Material and methods: When penetrating a medium protons mainly lose energy in electronic collisions, resulting in localized heating and a thermal expansion which generates thermoacoustic emissions detectable with acoustic transducers. Being the thermoacoustic emission naturally enhanced at the Bragg peak, time-of-flight (TOF) measurements in combination with the knowledge of the speed of sound in the traversed medium can enable recovery of the ion range, provided that sufficient signal can be detected. Since the ionoacoustic signal strength and shape have a complex dependence on the spatial distribution and temporal structure of the dose deposition, we performed a large series of measurements of ionoacoustic emissions in water at pulsed proton beams (~ns for pre-clinical energies, ~µs for clinical energies). Acoustic waves were recorded by transducers sensitive in corresponding frequency ranges, aligned along the beam direction distal to the Bragg peak.

Results: Systematic TOF measurements revealed the potential of (sub)millimetre accuracy and precision for range monitoring (figure 1), provided that sufficient signal is collected, eg., by averaging over more proton pulses for total doses up to 10 Gy (1). While the considered very low beam energies of ~20 MeV generate high frequency acoustic waves detectable with typical ultrasound transducers operating in the MHz range, clinical beam energies up to 227 MeV delivered by a compact, intrinsically pulsed synchrocyclotron demand the usage of broadband, low-frequency (kHz) hydrophones. This finding is consistent with earlier reported works at artificially pulsed clinical synchrotrons (2) and cyclotrons (3).

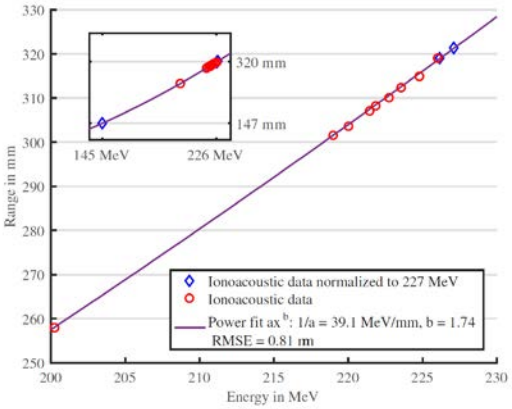


Figure 1. Compilation of ionoacoustic-deduced range in water, compared to a fit of reference measurements at the same clinical synchrocyclotron-based facility in Nice, France (ref (1), https://doi.org/10.1088/1361-6560/aa81f8. © Institute of Physics and Engineering in Medicine. Reproduced by permission of IOP Publishing. All rights reserved).

Conclusions: Although millimetre range monitoring based on ionoacoustics still demands relatively high fraction doses of a few Gy and is challenged by increased absorption and scattering in patient-like heterogenous tissue compared to water, the reported results encourage ongoing efforts of several groups to improve the detection efficiency and to account for tissue heterogeneities with proper simulation and image reconstruction methods. Ultimately, ionoacoustics could offer a compact and cost-effective modality for real-time in-vivo verification of the beam range (and possibly also anatomy with additional co-registered ultrasound imaging), at least for suitable clinical tumour indications of easy sonic access such as prostate, breast, liver.

Acknowledgement: The authors acknowledge the support of several collaborators from the Munich Military University (G. Dollinger), the Technical University Munich (V. Ntziachristos, S. Kellnberger and co-workers), the Center Antoine Lacassagne (J. Herault, M. Vidal and co-workers), S. Reinhardt, P. Thirolf as well as several BSc and MSc students at LMU (A. Edlich, A. Maaß, A.S. Duque, J. Stolberg, L. Sommer, J. Rudolf). This work was funded by the German Research Foundation, Cluster of Excellence Munich Center for Advanced Photonics

References:

20. Lehrack et al, *Phys. Med. Biol.* **62**, L20-L30 (2017).
2. Hayakawa et al, *Radiat. Oncol. Invest.* **3**, 42–5 (1995).
3. Jones et al, *Med. Phys.* **42**, 7090–7 (2015).

IN-BEAM OPENPET IMAGING FOR RI BEAMS

Taiga Yamaya[1]

[1]National Institute of Radiological Sciences (NIRS), National Institutes for Quantum and Radiological Science and Technology (QST), Japan, yamaya.taiga@qst.go.jp

OpenPET is our original idea to realize an open-type 3D PET scanner for PET-image guided particle therapy such as *in situ* dose verification and direct tumor tracking. The principal of dose verification for particle therapy is based on the measurement of positron emitters which are produced through fragmentation reactions caused by proton or carbon ion irradiation. Even with a full-ring geometry, the OpenPET has an open gap through which the treatment beam passes, while conventional positron cameras applied to particle therapy imaging have been basically limited to planner imaging. The key technology which has enabled OpenPET is our original, 4-layered DOI detector. In this presentation, we propose the use of positron emitter beams for direct visualization of the beam stopping position. In addition to a C-11 beam, an O-15 beam has been also demonstrated.

PROMPT GAMMA RANGE MONITORING OF PROTON THERAPY: STATUS AND PERSPECTIVES

Katia Parodi[1]

[1] Ludwig-Maximilians-Universität München, Faculty of Physics, Department of Medical Physics, Munich, Germany; Email: Katia.Parodi@lmu.de

Introduction: Proton beams exhibit favourable interaction properties in matter, which enable delivering a highly conformal dose to the tumour while better sparing surrounding healthy tissue and critical structures in comparison to widely established photon beams. However, the improved ballistic selectivity of protons comes at the expense of increased sensitivity to treatment planning and delivery uncertainties. A major yet unsolved limitation to full clinical expoitation of these advantages is related to the issue of range uncertainties, i.e. uncertainties in the stopping position of protons in tissue, determining the so called Bragg peak, where protons release most of their energy. Hence, several approaches are currently investigated to enable an in-vivo, ideally real-time verification of the proton beam range in the patient. Currently, one of the most promising methods already entering clinical testing is related to the detection of the energetic (several MeVs) prompt gamma emitted in the de-excitation stage of tissue nuclei after nuclear interaction induced by the passage of protons through matter.

Material and methods: Following the first characterization of prompt gamma as a background signal to the at that time widely investigated in-beam positron emission tomography (PET) [1], almost 10 years ago prompt gamma were shown to be a promising nuclear-induced radiative emission enabling an indirect verification of the proton range in tissue [2]. Owing to the characteristic (sub)ns time scale of the relevant nuclear de-excitation processes, prompt gamma offer a signal almost simultaneous to the beam delivery, thereby eliminating known shortcoming of PET-based treatment verification such as sensitivity to washout processes. However, the energy range in the MeV region prevents application of off-the-shelf detector technologies widely adopted in medical imaging. Hence, several years of detector development were needed in order to build and translate into the clinical testing first prototypes able to collimate and detect the energetic prompt gamma perpendicular to the beam direction. Moreover, additional detector concepts exploiting different physical features (e.g., energy, time, scattering) of the prompt gamma emissions and interactions are under development, along with several computational studies to investigate the clinical relevance and to support possible future clinical workflows based on the comparison of measured and predicted signals.

Discussion: This presentation will discuss the rationale for prompt gamma monitoring, reviewing the main detector concepts and computational efforts for introduction into the clinical workflow. Special emphasis will be given to the reported first clinical testing with a mechanically collimated prototype camera in Europe [3] and USA [4], along with ongoing investigations at our own institution.

Conclusions: Prompt gamma detection and imaging offer a promising and versatile approach for real-time in-vivo monitoring of proton therapy. Despite the need of further optimization, the first reported clinical experience supports the promise of millimetre range verification of individual pencil-beams, provided that enough statistics is collected. Moreover, several efforts are ongoing at our as well as other institutions to propose alternative detection concepts and improve computational models for optimal exploitation of this nuclear-induced photon emission.

Acknowledgement: The author acknowledges several fruitful discussions with the groups at Oncoray Dresden and University of Pennsilvania, who pioneered clinical testing of prompt gamma monitoring, as well as her team at LMU Munich, particularly PD Dr. Peter Thirolf, Dr. Georgios Dedes, Dr. Guillaume Landry and Dr. Marco Pinto.

References:

21. Parodi et al, *Nucl. Instrum. Med. A* **545**, 446-58 (2014)
2. Min et al, *App. Phys. Lett.* **89**, 183517 (2006)
3. Richter et al, *Radioth. Oncol.* **118**, 232–7 (2016)
4. Xie et al, *Int. J. Rad. Biol. Phys.* **99**, 210–8 (2017).

IN-VIVO RANGE VERIFI CATION IN HADRONTHERAPY USING PROMPT GAMMA RAYS: A GEANT4 SIMULATION STUDY

Melek Zarifi[1], Susanna Guatelli[1], Yujin Qi[1], David Bolst[1], Dale Prokopovich[2], Anatoly Rosenfeld[1]

[1] Centre for Medical Radiation Physics, University of Wollongong, Wollongong NSW Australia, mz659@uowmail.edu.au
[2] Australian Nuclear Science and Technology Organisation, Lucas Heights NSW Australia

Introduction: Prompt gamma (PG) rays have been proposed for *in-vivo* beam range verification during treatment delivery. As a secondary by-product emitted almost instantly upon ion-nuclear interaction, PG rays offer real-time tracking of the Bragg peak (BP). However their detection is challenging since they have a broad energy spectrum with intereference from other gamma rays, such as the ones generated by secondary neutrons. Numerous approaches have been proposed to utilise PG for *in-vivo* BP monitoring [1-3]. In this work, Geant4 Monte Carlo [4] (MC) simulations were used to study the spectral, spatial, temporal and angular distribution characteristics of PG emission and detection from hadron radiation fields of varying energy. The study will provide valuable information for the development of clinically suitable PG detector systems.

Materials and Methods: The Geant4 MC toolkit has been adopted to characterise PG emission and detection from hadron irradiation of a homogeneous water (H_2O, density of 1.0 g/cm^3) phantom. Pencil beams of proton and ^{4}He (62-250 MeV/u) and ^{12}C (120-490 MeV/u) were simulated. The phantom was cylinder in shape (ϕ40 cm x 40 cm). The transit time of PG production is the time interval between particle incidence on the phantom to PG emission. An ideal detecting sphere (ϕ100 cm) surrounding the phantom registers PG rays that reach its surface once emitted from the phantom. The TOF is the interval of time from the particle incidence on the phantom to the detection of the secondary (gamma ray and neutron) at the detecting sphere. The Geant4 physics included electromagnetic (standard_opt3 physics list) and hadronic physics (QGSP_BIC_HP for protons, neutrons and pions, Binary Ion Cascade models for ions). HP data libraries are adopted to model neutron interactions up to 20 MeV. The production threshold of secondary particles was fixed to 0.05 mm.

Results: Gamma energy spectra generated in the water phantom show characteristic PG peaks at 4.44 MeV (^{12}C*), 5.21 MeV (^{15}O*) and 6.13 MeV (^{16}O*). A strong correlation between PG production and the dose profile was seen. The range and corresponding PG spatial and temporal properties for proton beams are given in Table 1. Total gamma and PG between 3-7 MeV were also studied, but the threshold of 1 MeV offers similar suitability for BP tracking as the window with the advantage of higher statistics.

The PG spatial distribution on the ideal detecting sphere showed isotropically azimuthal emission but non-isotropically axial emission. PG are preferably emitted normal to the BP, with the emission from proton slightly backward, while neutrons are mainly emitted forward. As the beam energy increases, the PG transit time and TOF mean also increase. The TOF peak width/integral also increase which is attributed to the greater distance of travel by the ions. Neutrons are seen to be emitted at longer TOF values relative to PG, which could suggest a means of discriminating PG from the background and hence improve the signal-to-noise ratio of PG detection.

Table 1. Proton beam range and the corresponding PG (≥1 MeV) longitudinal distal fall-off, transit time and TOF peak mean.

Beam Energy (MeV)		62	150	200	250
Range (±0.1mm)	Proton	31.9	155.5	256.3	374.7
	PG	27.0	150.3	251.1	369.2
PG Time (±0.1ns)	Transit Time	0.3	1.2	1.9	2.5
	TOF Mean	2.0	2.7	2.9	3.0

Range/transit time are taken at 80% fall-off.

Conclusion: The emission and detection characteristics of PG rays from hadron irradiations of a water phantom were studied. Our results show that the higher energy PG rays (≥1 MeV) offer improved information for range verification. A preferential axial angular position for PG detection lies at a normal/slightly backward direction relative to the BP. The PG TOF spectra was seen to change with varying beam energy, and hence beam range, suggesting a potentially better technique of beam range verification using PG. A recent paper from Krimmer et al. [3] showed a simple method of BP monitoring using the PG TOF peak mean and integral. Further investigations into this technique for hadrontherapy range verification are underway.

Acknowledgments: We would like to thank the University of Wollongong Information Management & Technology Services (IMTS) for computing time on the UOW High Performance Computing Cluster.

References:

22. CH. Min et al., *Appl. Phys. Lett.* **89**, 183517, 2006.
2. C. Golnik et al., *Phys. Med. Biol.* **59**, 5399-5422, 2014.
3. J. Krimmer et al., *Appl. Phys. Lett.* **110**, 154102, 2017.

SIMULATION STUDY ON IMAGING OF A MONOCHROMATIC CARBON BEAM BY MEASURING SECONDARY ELECTRON BREMSSTRAHLUNG

Mitsutaka Yamaguchi[1], Yuto Nagao[1], Koki Ando[2], Seiichi Yamamoto[2], Makoto Sakai[3], Raj Kumar Parajuli[3], Kazuo Arakawa[1,3], Naoki Kawachi[1]

[1] Takasaki Advanced Radiation Research Institute, National Institutes for Quantum and Radiological Science and Technology (QST), Takasaki, Gunma, Japan, E-mail: yamaguchi.mitsutaka@qst.go.jp
[2] Department of Radiological and Medical Laboratory Sciences, Nagoya University Graduate School of Medicine, Nagoya, Aichi, Japan
[3] Gunma University Heavy Ion Medical Center, Gunma University, Maebashi, Gunma, Japan

Introduction: Monitoring methods for therapeutic carbon-ion beams are studied worldwide. Recently, a beam-imaging technique by measuring secondary electron bremsstrahlung (SEB) using a pinhole X-ray camera was proposed for therapeutic proton beams [1, 2]. In this work, we performed a simulation study on the imaging of a therapeutic carbon-ion beam with a pinhole camera by measuring SEB.

Methods: Monte Carlo simulations were performed to evaluate the image acquired by a pinhole camera for X-ray using the simulation code PHITS [3]. Figure 1 shows a 3-D view of a part of the geometrical setup, which was symmetrical to the *yz*-plane. A water phantom was placed at the origin of the coordinate, which comprised a container (polymethyl methacrylate) with water inside. A pinhole camera was placed 98 cm apart from the phantom. It was composed of a tungsten shield having a pinhole collimator and a board of cerium-doped gadolinium aluminum gallium garnet (GAGG). The field of view of the pinhole camera on the *xy*-plane corresponded to the area where $|x|$ and $|y|$ were smaller than 14.65 cm and was divided into 32 × 32 pixels. A 278-MeV/u carbon beam were injected to the phantom along the *x*-axis. Distribution of energy deposition in the GAGG owing to the SEB photons (SEB component) was recorded. In addition, the background component, which means energy depositions owing to secondary particles other than the SEB, was also recorded by a separate simulation with the same geometrical setup.

Results: Figure 2(a) and (b) represent the acquired images for the SEB and background component, respectively. Figure 2(c) represents the sum of the two components. For (a) and (c), beam trajectories were clearly imaged and the right edges of the regions having high pixel values seem to coincide with the expected Bragg-peak position (x = 4.87 cm), calculated by a separate PHITS simulation. In contrast, figure 2(b) had flatter distribution and did not become the shape of the trajectory. Figure 2(d) shows the image acquired in an experiment with almost the same condition as the simulation study. The experimental image was very similar to figure 2(b), although the ratio of the background component to the SEB component was two to three times larger than that in the experimental result.

Conclusion: The image acquired by a pinhole camera was evaluated by performing the Monte Carlo simulations. The SEB component clearly represented the beam trajectory while the background one did not. The sum of the SEB and background component well reproduced the experimental result, although the ratio of the background component to the SEB component was two to three times larger than that in the experimental result.

References:

23. M. Yamaguchi et al., *Nucl. Instrum. Methods Phys. Res.* A **833** 199 (2016).
2. K. Ando et al., *Phys. Med. Biol.* **62** 5006 (2017).
3. T. Sato et al., *J. Nucl. Sci. Technol.* **50** 913 (2013).

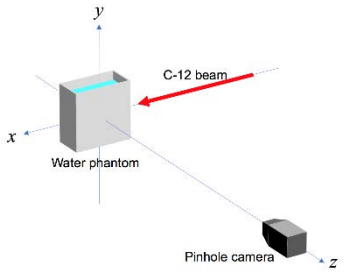


Figure 1. A 3-D view of the geometrical setup.

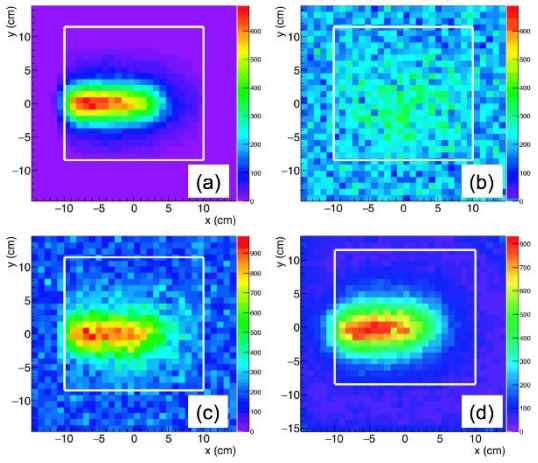


Figure 2. Resultant images for the (a) SEB component, (b) background component, (c) sum of the two components in the simula-

tions and (d) experimental result. The white rectangles in the images represent the edges of the water phantom.

THE BERGEN PROTON CT PROJECT – PROTON TRACKING IN A HIGH-GRANULARITY DIGITAL TRACKING CALORIMETER

D. Roehrich[1]
for the Bergen pCT project

[1] Institute of Physics and Technology, University of Bergen, Bergen, Norway; Dieter.Rohrich@ift.uib.no

Introduction: Particle therapy, a non-invasive technique for treating cancer using protons and light ions, has become more and more common, e.g. Norway has decided to build two particle treatment facilities, one of which will be located in Bergen. Being able to position the Bragg peak accurately is a major advantage of protons and light ions, but incomplete knowledge about the tissue properties and their relative position limits the precision. Range uncertainties of several millimetres may arise, mainly due to the - not one-to-one - conversion of photon attenuation maps from computed tomography (CT) scans into relative stopping power. A proton/alpha CT scanner provides direct information about the stopping power and has the potential to reduce range uncertainties from current values of 3-10 mm to about 1 mm.

Proton CT: For a proton CT scan the particles – typically protons or alpha particles - are energetic enough to traverse the patient completely, and the Bragg peak is positioned in a calorimeter. The trajectories of every single incoming proton and outgoing proton, as well as the residual energy/range is measured. The calculation of the proton trajectory inside the target region and the measured residual proton energy/range provide a 3D-map of the relative stopping power. During a scan, the patient needs to be rotated to obtain projection data from a set of angles. Prototypes of pCTs have been built and tested in beams (see e.g. [1,2]); however, readout rates are currently limited to several MHz. In order to use a pCT in a clinical environment, the total scanning time has to be reduced to the order of seconds or minutes.

Digital tracking calorimeter prototype: A prototype of an extremely high-granularity digitial tracking calorimeter has been designed and constructed. The prototype is a silicon/absorber sandwich calorimeter (4cm x 4cm x 10cm total volume) with 24 sensitive layers of Monolithic Active Pixel Sensors (MAPS): MIMOSA23 pixel sensors (30μm x 30μm pixel size).

This first prototype, designed as an electromagnetic calorimeter with tungsten as absorber, was tested in hadron and electron beams [4]. The feasibility of this detector as a proof-of-concept tracking calorimeter for proton CT has been demonstrated through proton beam tests at KVI-CART in Groningen, NL, and Monte Carlo simulations with the GATE framework [5]. Traversing protons are recorded and their tracks are reconstructed. The MIMOSA23 sensor chips give a 1-bit response per pixel. The energy loss must be modelled from the measured size of the charge diffused pixel clusters around a proton track hit. By applying track reconstruction algorithms and calculations of residual ranges through model fits of the Bragg Curve, we obtain the WEPL of each proton as well as its vector on the detector front face.

The second prototype, which has been optimised for pCT, has been designed and simulated with aluminium as absorber layer. The latest developments in MAPS technology allow the fabrication of extremely-high granularity, low material budget and large area silicon detectors with integration times of microseconds and sparsification/zero-suppression of the data on the sensor itself (see e.g. [3]). Since the detector is realized with commercially available CMOS technology, many layers of large area sensors necessary for a pCT scanner are feasible. The construction of an optimized (pre-)clinical prototype is under way. The sensor layers consist of MAPS chips originally developed for the upgrade of the inner tracking system of the ALICE experiment at the LHC (CERN). The rate of protons that can be handled by the optimized prototype and the range resolution are expected to increase markedly compared to the first prototype. Simulations, design and first test results of sensor layers will be presented.

References:

1. M. Bruzzi et al., Prototype tracking studies for proton CT, IEEE Transactions on Nuclear Science, vol. 54, no. 1, pp. 140-145, 2007.
2. Sadrozinski, H.F. et al., Development of a Head Scanner for Proton CT. Nucl Instrum Methods Phys Res A, 699, pp. 205-210, 2013.
3. M. Mager et al., Ultra low-power, CSA-based MAPS for ALICE Upgrade, FEE2014, 19-23 May 2014, Argonne National Lab.
4. G.-J. Nooren and E. Rocco, First results of beam tests of a MAPS based ElectroMagnetic calorimeter, 11th Intern. Conf. on Large Scale Applications and Radiation Hardness of Semiconductor Detectors, 3-5 July 2013, Florence, Italy.
5. Pettersen, H.E.S. et al., Proton tracking in a high-granularity Digital Tracking Calorimeter for proton CT purposes, Nucl. Instrum. Methods Phys. Res. Sect. Accel. Spectrometers Detect. Assoc. Equip. 860, 51–61, 2017; doi:10.1016/j.nima.2017.02.007

Australian Proton Therapy Project

AUSTRALIAN PROTON THERAPY PROJECT

a.prof michael penniment

director of raditation oncology rah, director australian bragg centre for proton therapy and research (ABC).
Dept of medicine Adelaide university

Introduction: Building will commence this year on the ABC. The project planning began in earnest 5 years ago, including centre design, research and training and service modelling

Project Outline:

ABC will occupy 3 floors of the proposed 13 story building in the health campus next to SAHMRI and the University of Adelaide Medical school

From commencement of build to patient treatment is expected to take 2y

A second facility is proposed as the Asia Pacific training , service and maintenance centre for Protom accelerators. This is likely to be built and opened in 2019

In parallel with the above, we have begun staff training, and continue to provide comparative planning solutions for clinicians with patients who may benefit from proton therapy.

Research partnerships should and are being formed in key areas:

- clinical indications
- radiobiology
- big data
- imaging
- robotics and industrial design
- particle therapy physics

Conclusions

Beyond the treatment facility with its specific patient focus, there is an immediate need to form key collaborations to undertake focussed projects. The first target should be the ACRF grant opening in march this year.

As details of the “Tonsley park” facility become available the scope of opportunity beyond the ABC will become clear.

DUAL-ENERGY γCBCT FOR ADAPTIVE PROTON THERAPY: A FEASIBILITY STUDY

Scott Penfold[1,2], Jiahua Zhu[2]
[1] Department of Medical Physics, Royal Adelaide Hospital, Adelaide, SA 5000, scott.penfold@sa.gov.au
[2] Department of Physics, University of Adelaide, Adelaide, SA 5005

Introduction: Online adaptive particle therapy may prove to be an important tool in reducing dose delivery uncertainty in certain tumor sites. This has the potential to reduce the margins needed for particle therapy and thereby increase healthy tissue sparing. Current in-room cone beam computed tomography (CBCT) systems consist of an X-ray tube and an integrating flat panel detector. Due to the uncertainties associated with converting CBCT Hounsfield Units (HUs) to relative stopping powers (RSPs) with this imaging solution, deformable image registration of the planning CT to the CBCT is required for dose of the day calculations. This is a computationally intensive process and brings with it uncertainties in soft tissue deformation due to the limited contrast resolution achievable with existing CBCT systems. A more favorable approach would involve an in-room imaging solution that provides accurate RSP information on which dose could be directly calculated. A novel CBCT imaging system consisting of a radioactive Eu-155 source opposing a pixelated solid-state detector is proposed to meet the needs for online adaptive proton therapy.

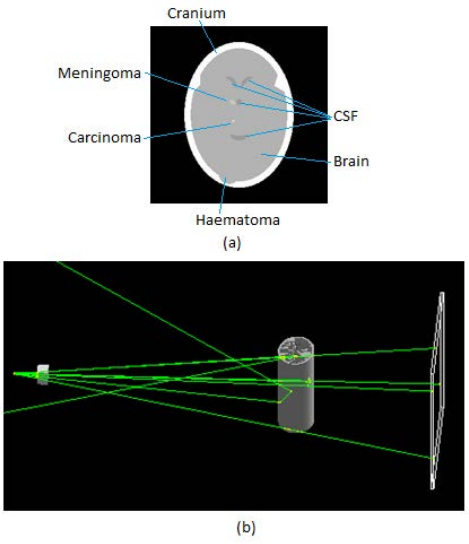


Figure 1. (a) Cross-section of the head phantom used in the Geant4 study. (b) Geometry of the Geant4 simulation showing some example gamma rays.

Materials and methods: The physical properties of Eu-155 were used to calculate a required source diameter for image acquisition in a clinically realistic time frame. The source and pixelated cadmium-zinc-telluride (CZT) flat panel detector were constructed in Geant4. A Monte Carlo simulation (Fig. 1(b)) was performed to model the proposed imaging system. A head phantom (Fig. 1(a)) was imaged with both the novel imaging concept as well as a conventional X-ray tube system. Both data sets were reconstructed with an advanced iterative image reconstruction algorithm known as total variation superiorization with diagonally relaxed orthogonal projections (TVS-DROP). The new imaging concept allows for dual-energy CT image reconstruction and therefore more direct relative stopping power calculation. Accuracy of reconstructed relative stopping powers with the new imaging concept were compared to an X-ray tube based method and the simulation ground truth.

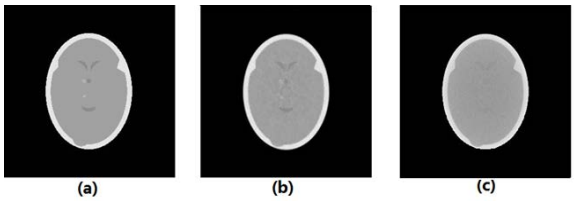


Figure 2. (a) Reference head phantom. (b) Reconstruction of dual-energy γCBCT. (c) Conventional CBCT image reconstruction. All wondow widths and levels are equal.

Results: Calibration of the proposed imaging system for reconstruction of relative stopping power was successfully performed. Qualitatively, the dual-energy γCBCT reconstructed images showed superior soft tissue resolution than images produced with the conventional X-rtay tube based CBCT (Fig. 2). Quantitatively, more accurate RSP pixel values were obtained with dual-energy γCBCT in comparison to conventional CBCT.

Conclusions: Eu-155 has many properties that make it attractive as a radiation source for in-room pretreatment imaging. The dual-energy emissions make monochromatic DECT possible, improving the accuracy of RSP reconstruction. A Monte Carlo simulation comparison of a CBCT system based on Eu-155 and a CZT detector panel with a conventional CBCT imaging model were performed. Improved image quality and quantitative image reconstruction values were obtained.

Fundamental Physics of Ions Interaction and New Accelerator Technology in Particle Therapy

COMPREHENSIVE APPROACH TO HADRON INTERACTIONS WITH MATTER

J. J. Bailey, I. B. Abdurakhmanov, Sh. U. Alladustov, A. S. Kadyrov and I. Bray
Department of Physics, Astronomy and Medical Radiation Science,
Curtin University, Perth, Australia

Introduction. One of the primary benefits of hadron therapy is a large ratio of the radiation dose at the Bragg peak to that in the plateau region before the peak. From the physics point of view three factors must be considered that may potentially enhance or undermine this benefit.

(i) In order to reach deep-seated tumour cells therapeutic ion beams should have energies from a hundred up to a few hundreds of MeV per a.m.u. At such high energies, energy losses due to ionisation are small. The main channels of energy losses here are nuclear collisions which may lead to fragmentation of nuclei of the target, and of the incident beam particles if the latter is a heavy ion like $^{12}_{6}$C. These also result in emission of neutrons. In the plateau region, the nuclear fragments and emitted neutrons can cause side effects, including new tumour cells. In addition, the nuclear fragmentation processes may disperse the beam and substantially affect the composition of the beam reaching the Bragg peak region. This complicates radiation dose localization simulations, which usually assume the initial beam composition. Due to complexity of nuclear interactions, there is no unified theory capable of their description. Interaction models are generally anchored to experimental data, which in some areas are far from complete [1].

(ii) As the residual beam particles approach the Bragg peak region, their energy reduces significantly. When the energy falls below tens of MeV, energy losses due to excitation and ionisation of the target atoms and molecules become dominant. It is often stated that the theory of these processes is well developed. However, this is not quite correct. Currently available Monte Carlo simulation packages for modelling of biological damage induced by hadrons rely on the Bethe-Bloch (BB) theory of energy losses. However, the BB theory and its numerous improvements cannot meet accuracy requirements. There are a number of reasons for this. First, the BB-type theories do not include electron capture channels. Second, they are perturbative and their applicability is limited to projectile energies higher than several MeV. Furthermore, they are based on the so-called dipole approximation to the first Born approximation. Third, the BB-type theories do not include coupling between various reaction channels. When hadrons approach the Bragg peak region, their energy diminishes considerably. In this energy region, the probability of electron capture becomes dominant and coupling between the channels becomes significant. In fact, when the energy falls below 100 keV per a.m.u., further energy losses are purely due to electron capture. Hence, accurate simulations of ion beam passage through matter at the micro- and nanoscale require inclusion of the electron capture channels in addition to ionisation [2].

(iii) In the Bragg peak region, the probability of target ionisation by the incident hadrons reaches its maximum. This leads to production of a copious number of electrons. These so-called δ-electrons have energies sufficient to further ionise the target and, as a result of multiple scattering, are capable of causing DNA double-strand breaks. It is estimated that among all the double strand breaks of DNA molecules of tissue treated by ion therapy, about 70% are produced by the δ-electrons [2]. Therefore, it is necessary to understand interactions of the produced δ-electrons in combination with interactions of the beam ions.

Convergent close-coupling approach to hadron collisions. We have been working on a comprehensive approach to modelling hadron interactions with matter known as the convergent close-coupling (CCC) method, which is capable of addressing all the three factors mentioned above. So far, we have developed the CCC approach to proton and heavy-ion collisions with atomic and molecular targets [3,4]. The approach accounts for all possible reaction channels including ionisation and electron capture, and is capable of providing the most detailed information about the collision process. It can be used to calculate stopping powers [5] including electron capture. Previously, we developed the CCC approach to electron-impact ionisation of atomic and molecular targets (see review [6] and references therein) which can be applied to δ-electrons. In addition, work is in progress on developing CCC approach to nuclear breakup reactions. Current progress in applications of the CCC method to collisions of protons and $^{12}_{6}$C ions with one- and two-electron targets will be reviewed.

Acknowledgments: This work is supported by the Australian Research Council.

References:

1. C. Zeitlin and C. La Tessa, Front. Oncol. **6**, 65 (2016).
2. D. Belkic, J. Math. Chem. **47**, 1366 (2010).
3. I.B. Abdurakhmanov, A.S. Kadyrov, S.K. Avazbaev and I. Bray, J. Phys. B: At. Mol. Opt. Phys. **49** 115203 (2016).
4. I.B. Abdurakhmanov, J.J. Bailey, A.S. Kadyrov and I. Bray, Phys. Rev. A, submitted (2017).
5. J.J. Bailey, A.S. Kadyrov, I.B. Abdurakhmanov, and I. Bray, J. Phys: Conf. Ser. **777** 012010 (2017).
6. I. Bray *et al*, J. Phys. B: At. Mol. Opt. Phys. **50** 202001 (2017).

NUCLEAR REACTION CROSS SECTIONS FOR HADRON THERAPY

Edward Simpson[1]

[1]Department of Nuclear Physics, Research School of Physics and Engineering,
The Australian National University, Canberra ACT 2601, Australia, edward.simpson@anu.edu.au

Introduction: Hadron therapy encompasses a new class of treatments for cancer, where a beam of highly energetic protons or heavier ions are used to kill tumour cells. In contrast to the photons used in conventional radiotherapy, charged particles deposit the majority of their energy at the end of their track, making them much more effective at killing tumours whilst causing less damage to healthy tissue. Currently protons and carbon ions are used. Heavy ions such as carbon carry more charge than protons and create more ionisation at the end of the track, increasing the biological efficiency of the dose. The use of even heavier beams such as ^{16}O, ^{28}Si, ^{48}Ti and ^{58}Fe is currently being explored.

One significant complication of beams of hadrons are the nuclear reactions that can occur en route to the tumour. Indeed at the highest energies used for carbon beam therapy, 70% of the beam particles undergo some nuclear reaction [1]. Planning hadron therapy treatments using Monte Carlo techniques therefore requires total nuclear reaction cross sections for a variety of interacting systems and over a wide range of energies. Current empirical models are tuned to reproduce measured cross sections for stable isotopes, but in some cases overestimate these measurements by 20% (see e.g., [2,3]).

Methods: Here we discuss an alternative approach: the optical limit of Glauber theory [4], which describes existing measurements better and offers more reliable predictions for the many systems where there is no experimental information. The essential inputs into the model are the density distributions of the projectile and target, taken from Hartree-Fock calculations, and a parameterization of the nucleon-nucleon interaction. We also suggest how existing implementations of empirical models within GEANT4 could be improved [2].

Results: Sample results for ^{12}C+^{12}C collisions are shown in Figure 1. In general, the optical limit calculations are significantly better than the existing empirical models [3]. The implementation of these empirical models within GEANT4 can (and should) be improved. Results for ^{1}H, ^{9}Be and ^{27}Al targets will also be presented.

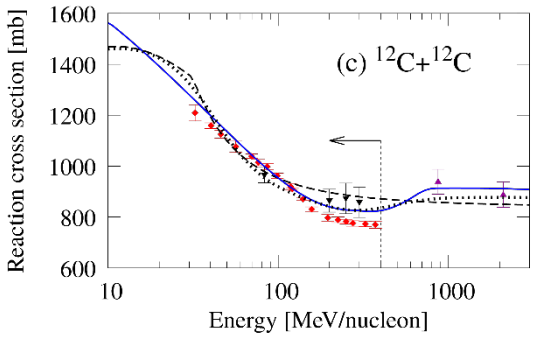


Figure 1. Calculated reaction cross sections for ^{12}C+^{12}C. The black dashed and dotted lines are empirical model calculations [3], and the blue line is from the present optical limit of Glauber theory calculations. The data points are from [5] (red diamonds), [6] (black triangles) and [7] (purple triangles).

Conclusions: The optical limit of Glauber theory and density folding models offer a significant improvement over conventional empirical models for reaction cross sections. Further improvements to the present calculations can be made, to include an energy dependent range of the nucleon-nucleon interaction, Fermi motion effects, and Pauli blocking. Ultimately, these calculations should contribute to improvements in planning of hadron therapy treatments, and provide the basis for a more reliable empirical model.

Acknowledgements: Support from the Australian Research Council under grants Nos. FT120100760 and DP170102423 is gratefully acknowledged. This research was undertaken with the assistance of resources and services from the National Computational Infrastructure (NCI), which is supported by the Australian Government.

References:

1. E. Haettner, *Physics in Medicine and Biology* **58** 8265 (2013)
2. Geant4 Physics Reference Manual
3. W. Shen et al., *Nuclear Physics* **A491** 130 (1989)
4. R. J. Glauber, *Lectures in Theoretical Physics vol 1* (Interscience, New York) p 315 (1959)
5. M. Takechi et al., *Physical Review C* **79** 061601 (2009)
6. S. Kox et al., *Physical Review C* **35**, 1678 (1987).
7. J. Jaros et al., *Physical Review C* **18** 2273 (1978)

CAN NOVEL ACCELERATOR TECHNOLOGY IMPROVE PROTON/ION THERAPY?

Suzanna Sheehy[1]

[1]Oxford University, UK

The idea of treating patients with charged particles emerged as soon as accelerators were available to provide sufficient energy to the beams. While small changes have been made to the details of cyclotrons and synchrotrons for this application, their intrinsic limitations remain. Cyclotrons have limited energy reach and single energy output, so require degrader systems before the patient, while synchrotrons are relatively large and cannot vary energy as rapidly as desired. In this talk, I will overview other options for accelerator technology which may be available in the near future. I will also discuss how innovations in accelerator technology motivate a start-to-end consideration of the facility, including treatment gantries, in order to deliver the flexibility and precision required to fully utilise this therapy option.

ITRO 2018

Mantra Mooloolaba-Beach, Queensland Australia, February 10th-11th 2018

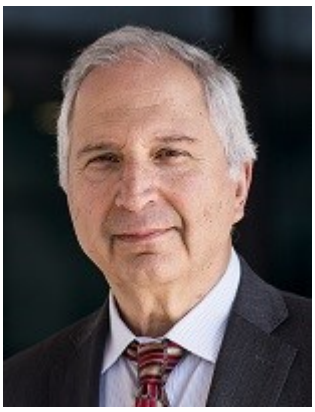
mmnditro2018.com

CENTRE FOR MEDICAL RADIATION PHYSICS

UNIVERSITY OF WOLLONGONG

cmrp@uow.edu.au

Welcome from the Chairs



Distinguished Professor

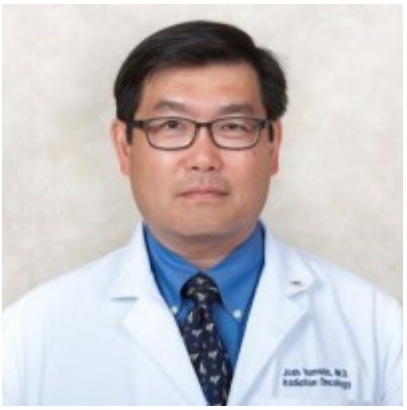
Anatoly Rozenfeld, PhD

Doctor

Josh Yamada, MD

Innovative Technologies in Radiation Oncology (ITRO) is devoted to clinical implementation of new technologies in X-ray therapy, brachytherapy and particle therapy. A special focus of ITRO 2018, to be held on the 10th to 11th February, will be Integrating Biology and Technology (Immunotherapy and SBRT, Hypofractination and Particle Therapy, SRS, Integration of multiparametric MRI into Radiotherapy and other approaches on the way to personalised treatments).

ITRO—International Faculty



Doctor Josh Yamada, MD

Dr. Yamada is an Associate Attending Radiation Oncologist and member of the brachytherapy service in the Department of Radiation Oncology at Memorial Sloan Kettering Cancer Center. He is a graduate of the Faculty of Medicine at the University of Alberta and completed residency training in Radiation Oncology at the Princess Margaret Hospital at the University of Toronto. He completed a fellowship in brachytherapy at Memorial Sloan Kettering Cancer Center and has been a faculty member in the Department of Radiation Oncology at Memorial Sloan Kettering Cancer Center for over 15 years. He has an academic interest in prostate cancer, brachytherapy, and spine radiosurgery, and has published widely on these topics. He has been invited to lecture on these topics both nationally and internationally. He and his wife Susy are the proud parents of five children. He as a special place in his heart for Australia!

Professor Laura Dawson, MD, FRCPC, FASRO

Dr Laura Dawson is a radiation oncologist at the Princess Margaret Cancer Centre, and a Professor the Department of Radiation Oncology, University of Toronto. She completed her medical school and radiation oncology residency at the University of Toronto and a fellowship in high precision radiation therapy at the University of Michigan, where she stayed on as a faculty member until 2003, at which time she returned to Canada to develop a hepatobiliary radiation therapy program at the Princess Margaret Cancer Centre. She is an internationally recognized leader in hepatobiliary and liver metastases radiation therapy and in the use of advanced radiation technologies, including stereotactic body radiation therapy (SBRT) and image guided radiation therapy (IGRT). She is the principal investigator of several phase III clinical trials, including RTOG1112, an international randomized trial of SBRT for locally advanced hepatocellular carcinoma and HE.1, a Canadian randomized trial of low dose whole liver radiation therapy to treat painful liver cancer, unsuitable for other treatment. She has published over 150 scientific papers. She was a recipient of an ASCO career development award, and her research has been funded by the NIH, CIHR, NCIC CTG, and the Canadian Cancer Society.

ITRO—International Faculty

Professor Karl Rossi, MD

Carl Rossi, MD, is a radiation oncologist specializing in proton beam therapy, specifically for prostate cancer and lymphomas. He is also the current medical director for the Scripps Proton Therapy Center, which will provide treatment to target tumors with high control and precision. In addition to treating a variety of cancers with radiation, it is also used to treat some non-cancerous conditions. Dr. Rossi has a research focus on the quality of life and cure rate in prostate cancer and lymphoma treated with proton beam radiation. He believes in treating his patients as equal partners throughout the treatment process. This involves open, honest communication, including what the treatment will entail and the pros and cons of the treatment course. With this information patients can make informed decisions. He also wants his patients to feel supported in whatever path they choose to take with regard to their treatment plan. When he is not caring for patients or conducting research at Scripps Proton Therapy Center, he enjoys running, cycling, travelling and flying.

Doctor Jimmy Caudell, MD, PhD

Having graduated from college with a degree in Genetics at age 20, Jimmy Caudell pursued a Ph.D. in Molecular Genetics at M.D. Anderson Cancer Center, receiving this for work identifying candidate oncogenes in prostate cancer. He then went to medical school at UT Houston, received an M.D., and then did residency training at University of Alabama at Birmingham for Radiation Oncology. He was recruited to Moffitt Cancer Center to lead the Head and Neck program in Radiation Oncology. Currently, Dr. Caudell is an Associate Member of Radiation Oncology at Moffitt Cancer Center and Research Institute. He is internationally known for head and neck treatment planning, toxicity, and outcomes research. Specifically, his work on treatment planning and dysphagia following radiation treatment has been internationally recognized and has been used to guide how radiation treatments are planned. Dr. Caudell has been a PI on a number of clinical trials, both investigator-initiated and co-operative groups. He serves on the National Comprehensive Cancer Network Head and Neck Guideline Panel which sets national guidelines for treatment of Head and Neck Cancer. Dr. Caudell is an author of 36 peer-reviewed papers, 7 book chapters, and numerous scientific presentations.

ITRO—International Faculty

Professor Mira Keyes, MD

Dr. Keyes is a Clinical Professor in Radiation Oncology, Division of Surgery University of British Columbia (UBC) Vancouver, BC Canada. She obtained her MD in 1986 from the University of Novi Sad, Yugoslavia. In 1996, she completed Radiation Oncology Residency Training Program at UBC. Dr. Keyes is one of the four founders of the British Columbia cancer Agency (BCCA) Prostate Brachytherapy Program, established in 1998. Dr. Keyes is past BCCA Brachytherapy Program Quality Assurance chair. Since 2006, she is a Provincial Brachytherapy Program Head. Dr. Keyes is a co-chair for the Royal College Brachytherapy Diploma Group development. She is a past elected board member and secretary for ABS (American Brachytherapy Society) and present ABS Chair of the Education and Schools Committee. She is a member of the editorial board for Brachytherapy Journal. Dr. Keyes is a former Residency Training Program Director in Radiation Oncology at UBC, and past Royal College examiner in Radiation Oncology. She is a recipient of serval UBC teaching awards including: 2017 AD McKenzie UBC Department of Surgery Clinical Teaching Award, 2016 Best Teacher Award and 2014 CanMeds of Excellence both UBC Radiation Oncology Residency Training Program Awards. In 2017 she was awarded ABS – Presidents Award for outstanding contribution to American Brachytherapy Society. Dr Keyes has been a keynote speaker at many national and international conferences; including ASTRO, ABS, Australian Brachytherapy Group annual meetings, Seattle Prostate Institute Annual Advanced Prostate Brachytherapy Courses, MD Anderson Brachytherapy Advanced Conferences and CARO. Dr Keyes is ASTRO and ABS course director for “hands on” prostate brachytherapy workshops and ABS prostate school. She is an author of over 60 peer reviewed manuscripts and recipient of many peer review grants including a CIHR grant in 2015 for translational research. She has a large clinical GU and breast cancer practice.

Professor John Fiveash, MD

Professor John Fiveash, MD, is a radiation oncologist with the Department of Radiation Oncology, University Hospital Birmingham, and has been the Medical Director of Radiation Oncology for UAB Highlands Gamma Knife. He has interests in CNS and prostate malignancies, conducting research in novel agents for CNS tumors and advanced radiation therapy planning.

ITRO—International Faculty

Professor Vladimir Feygelman, PhD

Vladimir M. Feygelman graduated from the Department of Physics at Rostov State University in the former U.S.S.R in 1982 with a degree in Laser Physics. In 1985 he was awarded a PhD in Physical Chemistry at the same university. Since 1990 Dr. Feygelman is involved in Medical Physics, first as a Post Doc at the University of Florida (Gainesville), and then as a clinical radiotherapy physicist in Canada and USA. In 2006 he joined the faculty of Moffitt Cancer Center. Currently he is a Senior Faculty Member at Moffitt and Professor at USF Department of Oncologic Sciences. Dr. Feygelman divides his time between clinical duties, research, and teaching physics PhD students and medical residents. As a senior physicist, he is responsible for implementation of all major technological developments at the Department of Radiation Oncology. His research interests are primarily focused on quality assurance of complex advanced treatments. Dr. Feygelman was a member of the AAPM Task Group 244 on commissioning of dose calculations. He was the principal writer of the IMRT/VMAT section. Currently he serves as a Co-Chair of the AAPM working group on reference dose specification in treatment planning systems. Dr. Feygelman is an author of over 50 peer-reviewed papers on Medical Physics and was an invited speaker at various national and international meetings such as AAPM, ESTRO, and IEEE.

Professor Hiroshi Tsuji, MD

Hiroshi Tsuji, MD, is Director of the research Program for Carbon Ion therapy and Diagnostic Imaging at National Institute of Radiological Sciences (NIRS), where he has been since 1997. He also currently serves as Head of Clinical Oncology section in the hospital of the same institute. He received a M.D. from Hokkaido University in 1982, and a Ph.D. from Tsukuba University in 1996 for his study on proton radiotherapy of hepatocellular carcinoma. He has had 30 years of experience in clinical research on radiation oncology, including 8 years in Proton therapy and 17 years in carbon ion radiotherapy. The NIRS has more than 8,000 patients experience of C-ion RT, including more than 2,000 prostate cancers. He has actually been in charge of the treatment for these patients and advancing hypofractionation based on the outcomes obtained. His current research centers on standardization and clarification of charged particle therapy, for which he works on clinical trials of hypofractionated C-ion RT for common cancers as well as establishing new treatments for radio-resistant tumors. Particularly, effective usage of newly developed scanning irradiation is a current main concern.

ITRO—International Faculty

Professor Wolfgang Tomé, PhD

Professor Tomé works at Montefiore Medical Center and the Albert Einstein College of Medicine in New York City. He is the Director of the Division of Therapeutic Medical Physics of Montefiore Medical Center and the Director of Medical Physics of the Institute for Onco-Physics at the Albert Einstein College of Medicine. In addition, he also holds appointments as Visiting Professor of Medical Physics at the Centre of Medical Radiation Physics at the University of Wollongong, Australia and the University of Wisconsin at Madison. He has over 200 peer-reviewed publications, 16 book chapters, 2 books, over 200 abstracts, 5 patents to his credit, and is a Fellow of the American Association of Medical Physics. His current research interests include: techniques to mitigate normal tissue injury; bio-effects of focused-ultrasound; biologically guided therapy, MR guided therapy, SBRT, as well as immunoadjuvant cancer therapies.

Doctor Chris Barker, MD

Dr. Barker is an Assistant Attending Member and Director of Clinical Investigation of the Department Radiation Oncology at Memorial Sloan Kettering Cancer Center in New York City. He earned his Doctor of Medicine degree from the University of Florida in Gainesville, and subsequently received post-graduate medical education in radiation oncology at Memorial Sloan Kettering. He was a Howard Hughes Medical Institute Research Scholar in the Radiation Oncology Branch at the National Cancer Institute. Dr. Barker is a clinical specialist in radiotherapy for skin and eye cancers, and represents the Department of Radiation Oncology at several weekly multidisciplinary group meetings which focus on the care of skin cancer patients, including the Melanoma Disease Management Team, the Multidisciplinary Skin Cancer Management Program, and the Head and Neck Disease Management Team. He serves as a member of the National Comprehensive Cancer Network Ocular Melanoma Sub-Committee. He serves as an associate editor and editorial board member for the journals Clinical Skin Cancer and Brachytherapy, respectively, and has published over 50 peer-reviewed articles in the biomedical literature. He has received research funding from federal, philanthropic and industry sources for studies of the biologic effects of radiation as well as methods to deliver radiotherapy more effectively. A significant component of his research program involves the integration of novel targeted and immunologic therapies with radiotherapy for the treatment of cancer.

ITRO—International Faculty

Professor Michael Zelefsky, MD

Professor Michael Zelefsky is a recognized international authority in the treatment of prostate cancer with radiotherapy. He is the Chief of the Brachytherapy Service at Memorial Sloan Kettering Cancer Center and Vice Chair of Clinical Research. He also serves as a leader of the Genito-urinary Disease Management Team at Memorial Sloan-Kettering and has been instrumental in the development of novel radiation techniques which have been adopted world-wide including IMRT, IGRT and intraoperative adaptive brachytherapy treatment planning. Professor Zelefsky has published over 350 publications as well as chapters and textbooks. He is currently exploring approaches using targeted biologic agents concurrent with hypofractionated stereotactic radiosurgery for high risk disease as well as implementing novel brachytherapy techniques to improve the precision for brachytherapy in the treatment of prostate cancers. Dr Zelefsky is the Editor in Chief of Brachytherapy, an international journal which represents the premier journal in the world for articles devoted to the use of brachytherapy in the treatment of cancer.

Doctor Antonio Damato, PhD

After obtaining a PhD in Nuclear Engineering at the Massachusetts Institute of Technology on medical and non-medical applications of phase contrast imaging, I trained as a post-doctoral fellow in therapeutic medical physics at Boston Medical Center. I focused on brachytherapy while an assistant professor at Harvard Medical School / Brigham and Women's Hospital and eventually moved to Memorial Sloan Kettering Cancer Center as brachytherapy physics division head in the Department of Medical Physics.

My clinical activities include leading the brachytherapy physics team in our mission of designing and delivering brachytherapy treatments, ensuring the quality of our clinical operations, developing new methods and techniques to further the scope of brachytherapy, and implementing new technologies in our clinic. My research has focused on the use of technological innovation to enhance quality assurance efficacy and efficiency, and the use of process analysis to improve the safety of the brachytherapy practice. Other areas of clinical and research focus have been image-guided brachytherapy using MR and CT and development of novel brachytherapy applicators and techniques.

ITRO—International Faculty

Doctor Michael R Folkert, MD, PhD

Dr. Michael R. Folkert is an Assistant Professor and Co-Director of the Brachytherapy Program and Director of the Intraoperative Radiation Therapy Program at UT Southwestern Medical Center in Dallas, TX, USA, and co-leads their multi-disciplinary Sarcoma and Gastrointestinal Malignancy programs. He originally trained as a medical physicist at the Massachusetts Institute of Technology and Massachusetts General Hospital, but then transitioned to medicine, training at Harvard Medical School and then Memorial Sloan Kettering Cancer Center with an emphasis on Brachytherapy. His clinical research focuses on novel brachytherapy applicators for all body sites, toxicity assessment and reduction techniques in brachytherapy and stereotactic body radiation therapy, and complex multiparametric image analysis for cancer outcomes prediction. Additionally, he has a professional interest in brachytherapy and procedural education for residents and practicing physicians. He has served as PI on Phase I and II clinical trials, has published over 40 peer-reviewed papers and authored 8 book chapters, and has received grant funding from industry, the American Cancer Society, NIH, and the Cancer Prevention and Research Institute of Texas.

Professor Chandan Guha, MD

Professor Chandan Guha obtained his MBBS from the University of Calcutta, India and his PhD in Immunology at Medical University of South Carolina, Charleston. He completed his residency training in Radiation Oncology at Washington University and the Albert Einstein College of Medicine, Bronx, NY. He is the founding Director of the Institute for Onco-Physics and Professor of Radiation Oncology, Urology and Pathology, Vice Chairman, and the Director of Translational Research of the Department of Radiation Oncology at Montefiore Medical Center, Albert Einstein College of Medicine, New York. His laboratory is investigating several approaches to combine immunotherapy with radiation therapy and has proposed that hypofractionated radiation of tumors could produce autologous in situ tumor vaccines. Besides immunotherapy, his laboratory is developing strategies for stem cell-based therapies to mitigate and treat radiation injury and to induce regeneration of irradiated organs, such as, liver, intestine and lung. His group discovered that hepatic irradiation could be used as a preparative regimen for liver cell transplantation to promote repopulation of stem cells and adult hepatocytes in host liver. Dr. Guha is funded by multiple grants from the National Institute of Health and has collaborations with several Industrial partners to develop novel applications of radiation and ultrasound for tumor immunotherapy and regenerative medicine.

MMND ITRO 2018
PROGRAM

Saturday 10th February 2018
ITRO Day 1

07:30 – 07:35	**Introduction/Welcome** **Anatoly Rozenfeld/Josh Yamada**
BrainLab Sponsored Stereotactic Session/CNS ***Session chairs:*** **John Fiveash/Josh Yamada**	
07:35– 08:00	**(Invited) John Fiveash** ***What's new in CNS Radiosurgery? – Cranial Integrating surgery and radiosurgery in the treatment of brain metastases*** **University of Alabama Birmingham USA**
08:00 – 08:25	**(Invited) Josh Yamada** ***What's new in CNS Radiosurgery: Radiosurgery for benign spine conditions*** **MSKCC, NY USA**
08:25 – 08:45	**(Invited) John Fiveash** ***How many is too many for radiosurgery alone*** **University of Alabama Birmingham USA**
08:45 – 09:05	**(Invited) Josh Yamada** ***The Impact of Dose in the Management of Spine Metastases with Radiosurgery: Update of the MSKCC Experience*** **MSKCC, NY USA**
09:05 – 09:25	**(Invited) John Fiveash/Josh Yamada/Matthew Foote** **Interesting/Challenging Case discussions** **University of Alabama Birmingham/MSKCC, NY USA/Princess Alexandra Hospital Qld**
09:25 – 09:40	**Morning Tea/Exhibits**
Skin ***Session chairs: Chris Barker/Jimmy Caudell***	
09:40 – 10:30	**Chris Barker/Jimmy Caudell** ***What's new in Skin Radiation Therapy (40 min with 10 min for questions/discussion)*** **MSKCC, NY/Moffitt Cancer Center, USA**
10:30 – 10.45	**Bryan Burmeister** ***(15 min including discussion/questions)*** **Radiation Oncology Centres (ROC), Fraser Coast and Redland Australia**
10:45 – 11:00	**Gerald Fogarty** ***(15 min including discussion/questions)*** **Genesis Cancer Care, Australia**
11:00 – 11:15	**Barker/Caudell/Local MDs** ***Interesting/Challenging Case discussions (15 min including discussion/questions)*** **MSKCC, NY/Moffit Cancer Center, USA**
11:15 – 11:30	**Break/Exhibits**

GI ***Session chairs: Laura Dawson/Michael Folkert***	
11:30 – 12:20	**Laura Dawson/Michael Folkert** ***What's new in GI RT*** ***(40 min with 10 min for questions/discussion)*** **Princess Margaret Cancer Centre, Canada/MSKCC, NY, USA**
12:20 – 12:37	**Laura Dawson** ***Topic of choice*** ***(12 min + 5 min discussion/questions)*** **Princess Margaret Cancer Centre, Canada**
12:37 – 12:54	**Michael Folkert** ***Topic of choice*** ***(12 min + 5 min discussion/questions)*** **MSKCC, NY, USA**
12:54 – 13:10	**Laura Dawson/Michael Folkert/Local MDs** ***Interesting/Challenging Case discussions*** **Princess Margaret Cancer Centre, Canada/MSKCC, NY, USA**
13:10 – 14:00	**Lunch**
Head and Neck ***Session chairs: Jimmy Caudell/Michael Barton***	
14:00 – 14:50	**Jimmy Caudell/Michael Barton** ***What's new in HN RT*** ***(40 min + 10 min discussion/questions)*** **Moffit Cancer Center, USA/ Ingham Institute for Medical Research , Australia**
14:50 – 15:07	**Jimmy Caudell** ***Conventional re-irradiation versus SBRT for locoregionally recurrent H&N Cancer.*** ***(12 min + 5min discussion/questions)*** **Moffit Cancer Center, USA**
15:07 – 15:24	**Michael Barton** ***Topic of choice*** ***(12 min + 5min discussion/questions)*** **Ingham Institute for Medical Research , Australia**
15:24 – 15:40	**Jimmy Caudell/Michael Barton/Michael Jackson** ***Interesting/Challenging Case Discussions*** **Moffit Cancer Center/Montefiore Medical Center, New York, USA/POWH Australia**
15:40 – 15:55	**Afternoon Tea/Exhibits**

GU *Session chairs: Mira Keyes/ Michael Folkert*	
15:55 – 16:45	**Mira Keyes/Michael Folkert** ***What's new in GU Radiation Therapy*** ***(40 min + 10 min discussion/questions)*** **University of British Columbia, Canada/MSKCC, NY, USA**
16:45 – 17:02	**Mira Keyes** ***Topic of choice*** ***(12 min + 5min discussion/questions)*** **University of British Columbia, Canada**
17:02 - 17:19	**Michael Folkert** ***Toxicity Reduction for SBRT and HDR Brachytherapy in Prostate Cancer - Spacers and Beyond*** ***(12 min + 5min discussion/questions)*** **MSKCC, NY, USA**
17:19 – 17:35	**Mira Keyes/Michael Folkert/Joseph Bucci** ***Interesting/Challenging Case discussions*** **University of British Columbia, Canada/MSKCC, NY, USA/STG CCC, Kogarah, Australia**
17:35	**Adjourn**
19:30	**ITRO Faculty Dinner**

MMND ITRO 2018
PROGRAM

Sunday 11th February 2018
ITRO Day 2

Particle Therapy ***Session chairs:*** **Verity Ahern/Michael Jackson**	
08:00– 08:25	**(Invited) Carl Rossi** ***What's new in charged particle therapy*** **Scripps Proton Therapy Center, USA**
08:25 – 08:50	**(Invited) Hiroshi Tsuji** ***What's new in charged particle therapy*** **National Institute for Quantum and Radiological Science and Technology, Japan**
08:50 – 09:05	**(Invited) Carl Rossi** ***Topic of choice*** **Scripps Proton Therapy Center, USA**
09:05 – 09:20	**(Invited) Hiroshi Tsuji** ***Topic of choice*** **National Institute for Quantum and Radiological Science and Technology, Japan**
09:20 – 09:35	**(Invited) Hiroshi Tsuji/Carl Rossi/Verity Ahearn** ***Interesting/Challenging Case discussions*** **NIRS Japan/Scripps Proton Therapy Center, USA/Crown Princess Mary Cancer Centre Australia**
09:35 – 09:50	**Morning Tea/Exhibits**
ITRO Physics/Applied Technology Session ***Session chairs: Lois Holloway/ Anatoly Rozenfeld;***	
09:50–10:10	**Wolfgang Tome** ***MRI-ONLY Radiation Therapy workflow for abdomen*** **AECM, USA**
10:10–10.30	**Vladimir Feygelman** ***Quality of Head and Neck plans-Where we are and does it matter*** **Moffitt CC, USA**
10:30–10:50	**Anatoly Rozenfeld** ***Innovations in QA for stereotactic radiotherapy: CMRP development and clinical implementation*** **CMRP UOW**
10:50–11:10	**Tomas Kron** ***SBRT in clinical trials: what QA is required and how can it be done?*** **Peter MacCallum CC**
11:10-11:30	**Paul Keall** ***MRI-Linac: overview of Australian program*** **RRL, University of Sydney**

11:30-11:50	**Peter Metcalfe** ***Bespoke dosimeters for MRI linac*** **CMRP UOW**
11:50 – 12:50	**Lunch**
Immunotherapy: A Primer ***Session chairs: Chris Barker/Chandan Guha***	
12:50 – 13:15	**Chandan Guha** ***RT and Immunotherapy*** **Montefiore Medical Center, NY, USA**
13:15 – 14:00	**Chris Barker** ***Combining Radiotherapy and Immunotherapy for Cutaneous Melanoma: Safety, Efficacy, Future Directions*** **MSKCC, NY, USA**
	RT Immunotherapy: toxicity and cautions: **MSKCC, NY, USA**
14:00 – 14:20	**Chris Barker/Chandan Guha** ***Interesting/Challenging Cases in RT Immunotherapy*** **MSKCC/Montefiore Medical Center, NY, USA**
Special Topic: Regeneration and RT ***Session chairs:***	
14:20 – 14:55	**Chandan Guha** ***Regeneration and RT*** **Montefiore Medical Center, NY, USA**
Closing Remarks / Adjourn **Anatoly Rozenfeld/Josh Yamada**	

BrainLab Sponsored Stereotactic Session/CNS

Skin

Gl

Head and Neck

GU

Particle Therapy

ITRO Physics/Applied Technology

MRI-ONLY RADIATION THERAPY WORKFLOW FOR ABDOMEN

Shu-Hui Hsu[1], Qi Peng[2], Madhur Garg[3], Wolfgang A. Tomé[4]
[1] Department of Radiation Oncology, Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, NY, 10461, USA; [2] Department of Radiology, Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, NY, 10461, USA; [3] Department of Radiation Oncology, Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, NY, 10461, USA; [4] Department of Radiation Oncology, Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, NY, 10461, USA,
wolfgang.tome@einstein.yu.edu

Introduction: MRI is increasingly being used in the radiation therapy workflow due to its superior soft tissue visualization, but it is not often used as a sole imaging modality in the planning process because of the lack of electron density information. The use of multi-imaging modalities requires an imaging registration step and therefore introduces uncertainties. The uncertainties are likely larger in the abdomen due to breathing and gastrointestinal motion. Thus, we propose a MRI-only radiation therapy workflow in the abdomen to support the delineation of targets and organs-at-risk (OARs) in the treatment planning, dose calculations using synthetic CT from MRI and treatment verification using synthetic CT or MRI.

Materials and Methods: First, to explore the feasibility of synthetizing CT from MRI, diagnostic MRI scans for one patients were analyzed. These image volumes included in-phase, fat and water images using a Dixon sequence, and T2-weighted images using a T2-turbo spin echo sequence. These images were corrected for their non-uniform intensity using N4itK algorithm. To separate air from bone, abdominal wall and spine area were automatically identified using intensity thresholding, morphological processing, and region growing methods. Fuzzy c-means clustering with a spatial constraint (FCM) was used to classify different tissue types, and attenuation properties were assigned to individual tissue classes to generate synthetic CT. Second, to investigate appropriate CT numbers assigned to individual tissue classes, a retrospective study on CT datasets was performed on 18 patients who received stereotactic body radiation therapy (SBRT) for liver or pancreas treatments using volumetric modulated arc therapy (VMAT). CT numbers on population CT datasets were collected for several OARs, and compared with CT number derived based on ICRU 46. In addition, dose accuracy was evaluated for CT numbers from population and ICRU against clinical CT.

Results: The synthetic CT from MRI is shown in Figure 1, and the quality is comparable to clinical CT. Our results demonstrate the feasibility of using MRI alone to support treatment planning and image guidance. When comparing CT numbers between the population and ICRU, the difference was less than 50 Hounsfield Units (HUs), except for gastrointestine (GI) with air pocket and bone (Figure 2). ICRU- and population-based HU plans for the all target volumes were close to the clinical CT plans with 0.7% and 0.1% difference on average. Heterogeneity-off plans presented 2.1% difference in PTV D99.9% for all subjects (Figure 3).

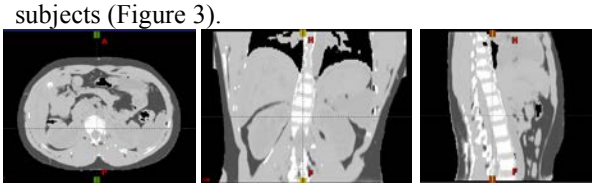


Figure 1. Synthetic CT generated from MRI in axial, coronal, and sagittal views.

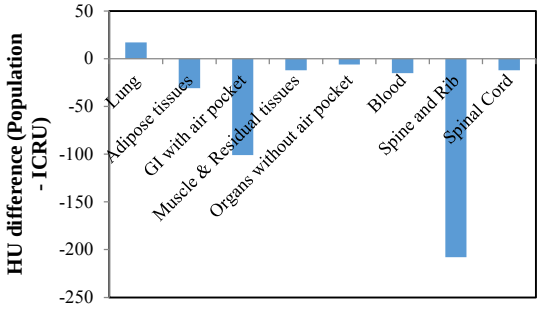


Figure 2. HU differences between population and ICRU for various tissue types.

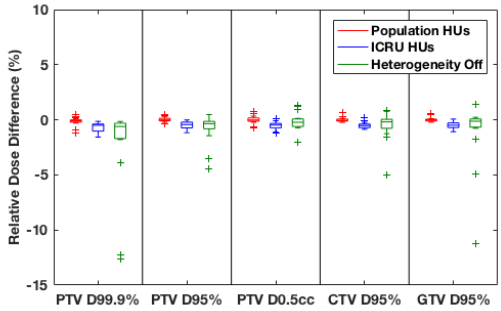


Figure 3. A box-and-whisker plot of relative dose difference (%) in the target volumes for population HU, ICRU HU and heterogeneity-off plans against clinical plans.

Conclusions: The proposed method allows automatic segmentation of tissue and generation of synthetic CT for the abdomen. Dose accuracy of ~1% was achievable by assigning appropriate CT numbers to individual tissue classes. We have demonstrated the feasibility of a MRI-only radiation therapy workflow for abdominal radiation therapy. Future work will include improving the quality of synthetic CT, evaluating its dosimetric accuracy, and exploring the workflow in treatment verification using synthetic CT or MRI.

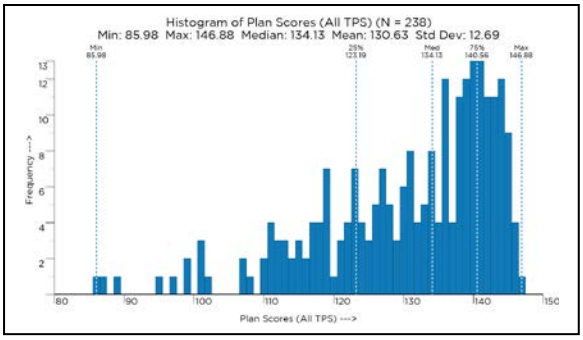
Acknowledgements: This work was supported by a research grant from Varian Medical Systems, Inc.

HEAD AND NECK PLAN QUALITY: WHERE WE ARE AND DOES IT MATTER?

V. Feygelman*[1] and B. Nelms[2]
[1] Moffitt Cancer Center, Tampa FL, USA. vladimir.feygelman@moffitt.org
[2] Canis Lupus LLC, Merrimac, WI, USA

Introduction: In this presentation, we review the state of affairs on a variety of topics pertinent to the quality of Head and Neck (HN) radiation treatment planning. We cover (1) the results of a recent, international study that collected and measured meric-based plan quality as well as dosimetric accuracy (measured vs. calculated) for a challenging case; (2) early experiences with planning automation; and (3) potential effects of target dose homogeneity on clinical complications.

1. HN Planning Study: A web-based platform (ProKnow) was used to run the study. A published HN patient CT was provided with pre-contoured targets and organs. Uploaded plans were scored in real-time and will full transparency using the objective, composite plan quality metrics (PQM) formalism [1]. A total of 21 metrics were extracted, scored function-wise, and summed for each plan (target dose coverage and homogeneity made up 63% of the total, with the rest for organ-at-risk sparing). The participants were free to choose the treatment planning system (TPS), treatment modality, beam energy, and planning techniques. This study was unique in that estimated delivery time was tallied (not scored) and pre-treatment dose QA results were requested.



A total of 238 plans were submitted from 34 countries, with 39% from the USA. In terms of treatment modalities, VMAT made up 73% of the submissions, followed by fixed gantry IMRT (18%), tomotherapy (6%), and protons (3%).

Over 95% of the reported (77) QA tests used either a true (65%) or single angle (31%) composite measurements. The results support setting aggressive goals in terms of TPS algorithm commissioning. The median 2%(local normalization)/2mm gamma-analysis passing rate was 90%, with the top quartile of performers showing passing rates over 95%.

The overall distribution of the composite PQM scores for all participants is shown in the Figure. There was no statistically significant difference in composite PQM scores between VMAT, IMRT, and helical tomotherapy. There was no correlation between plan quality and total number of MU. However, VMAT plans were significantly more efficient in terms of MU than both IMRT and tomotherapy.

All TPS studied were able to produce high quality plans: 6 of 6 TPS models had scores in the top 25%, and 4 of those in the top 10%. All TPS and modalities showed substantial variability in plan quality distribution, suggesting needs for planner training and/or automation.

2. Attempts at automation: There are three approaches to automated planning in commercially available systems. AutoPlanning (Philips Pinnacle) attempts to mimic a human planner's actions. Knowledge-Based Planning (Varian Eclipse RapidPlan) tries to reproduce the DVHs from previously accepted plans of similar geometry. RaySearch RayStation Multi-Criteria Optimization explores the pre-calculated Pareto front to quickly arrive at the dosimetric tradeoffs acceptable to the user. From the personal experience [2] and literature [3] it appears that the first two have not yet demonstrated the ability to produce good GTV/PTV dose coverage with high homogeneity (<105% single voxel hot spot), while the last one shows promise but requires further evaluation.

3. Does dose homogeneity matter? Compared to a pooled analysis [4] presumably carried out with RTOG-type dose homogeneity criteria, the study requiring tighter target dose homogeneity [5] appears to suggest lower incidence of gastrostomy tube placement following HN chemoradiation. This requires further investigation prior to focusing on more costly modalities as the way to reduce tube dependence.

References

1. Nelms, B.E., et al., Variation in external beam treatment plan quality: An inter-institutional study of planners and planning systems. Practical Radiation Oncology, 2012. 2(4): p. 296-305.
2. Gintz, D., et al., Initial evaluation of automated treatment planning software. J Appl Clin Med Phys, 2016. 17(3): p. 331-346.
3. Tol, J.P., et al., Evaluation of a knowledge-based planning solution for head and neck cancer. Int J Radiat Oncol Biol Phys, 2015. 91(3): p. 612-20.
4. Setton, J., et al., A multi-institution pooled analysis of gastrostomy tube dependence in patients with oropharyngeal cancer treated with definitive intensity-modulated radiotherapy. Cancer, 2015. 121(2): p. 294-301.
5. Strom, T., et al., RIsk factors for percutaneous endoscopic gastrostomy tube placement during chemoradiotherapy for oropharyngeal cancer. JAMA Otolaryngology–Head & Neck Surgery, 2013. 139(11): p. 1242-1246.

INNOVATIONS IN QA FOR STEREOTACTIC RADIOTHERAPY: CMRP DEVELOPMENT AND CLINICAL IMPLEMENTATION

M. Petasecca[1], M. K. Newall[1], M. Duncan[1], V. Caillet[2,3], B. James[1], J. T. Booth[2,3], P. Keall[4], M. L. F. Lerch[1], V. Perevertaylo[5], A. B. Rosenfeld[1]

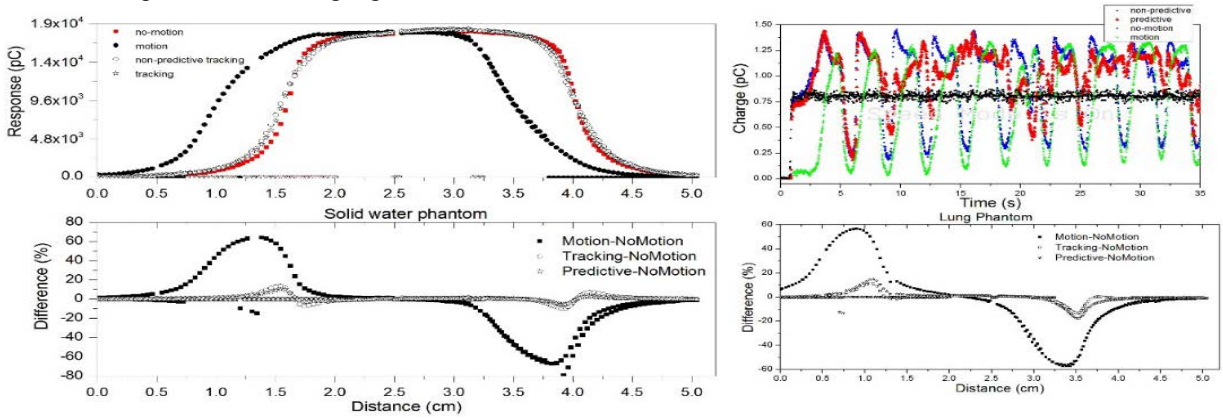
[1]Centre for Medical Radiation Physics, University of Wollongong, Wollongong, Australia
[2]Northern Sydney Cancer Centre, Royal North Shore Hospital, Australia
[3]Institute of Medical Physics, School of Physics, University of Sydney, Australia
[4]Radiation Physics Laboratory, School of Medicine, University of Sydney, Australia
[5] SPA-BIT, Kiev 02232 ,Ukraine

Introduction: Optimisation of treatment delivery based on patient-specific intra-fractional changes in anatomy is compulsory in organs affected by breathing or cardiac cycle. MLC tracking by using electromagnetic transponders implanted in the tumor is one strategy to adapt the beam shape and position in real-time. MLC tracking combined with highly conformal delivery modalities such as SRT has been shown to be feasible for lung and liver cancer treatment on a standard linac. QA for such treatments requires specialised tools with high spatial resolution for accurate measurement of sharp dose fall-off and high timing resolution for verification of the interplay of effects between organ motion and modulation of the irradiation fields. A dosimetry system for fast verification of the performance of MLC tracking in SRT is proposed.

Material and Methods: A monolithic 2D silicon detector, known as DUO, has been developed and comprises 512 pixels each with size 40x800 mm^2 and pitch 0.2mm arranged in two linear orthogonal arrays. The DUO is read out by a multichannel electrometer synchronised with the linac. For evaluation of the accuracy and effectiveness of MLC tracking in both soft tissue and lung, we placed DUO in a solid water phantom, homogeneous timber phantom and timber phantom with a solid water spherical hidden target of 1 cm diameter. We installed the phantoms on a moving platform supplied with a set of patient-specific motion patterns. The commercial Calypso system provides real-time position of the target to the MLC software which has been tested using a predictive and non-predictive tracking algorithm. We planned the target dose using 3DCRT (a 2 cm diameter field) and IMRT (with 5mm margins) treatments. Measurements performed by DUO are compared to EBT3 film for cases with and without motion, as well as motion with the MLC tracking algorithms enabled.

Results: Fig.1 shows the comparison of the SUP-INF 3DCRT static beam profile measured by DUO in the solid water phantom and the same beam delivered using a patient specific breathing motion pattern with and without MLC tracking. The predictive tracking has a lower discrepancy with respect to the static beam showing a reduction of the beam misplacement from ±70% to ±12% and ±58% to 20% in the solid water and timber phantom respectively. Discrepancies between DUO and EBT3 are within 2.4% overall. Temporal analysis shows the interplay effects between beam position and target motion with clear difference between predictive and non–predictive algorithms.

Conclusion: It is observed that motion distorts the planned dose profile in both solid water and lung phantom. MLC tracking reduces dose smearing significantly as demonstrated by the no-motion and motion-tracking results. The DUO detector has proven to be an effective tool for pre-treatment verification of real-time adaptive stereotactic deliveries with both high spatial resolution for dose profiling and high temporal resolution for pulse by pulse dose reconstruction.



Solid water phantom		DUO		EBT3	
Modality	*Profile direction*	*FWHM (cm)*	*RHS Penumbra (cm)*	*FWHM (cm)*	*RHS Penumbra (cm)*
no motion	inf-sup	2.43 ± 0.02	0.3 ± 0.02	2.49 ± 0.02	0.4 ± 0.02
motion	inf-sup	2.5 ± 0.02	0.66 ± 0.02	2.6 ± 0.02	0.69 ± 0.02
tracking	inf-sup	2.48 ± 0.02	0.42 ± 0.02	2.5 ± 0.02	0.43 ± 0.02
predictive tracking	inf-sup	2.46 ± 0.02	0.38 ± 0.02	2.5 ± 0.02	0.41 ± 0.02

BESPOKE DOSIMETERS FOR MRI-LINAC

P Metcalfe[1,2], M Gargett[1], S Alnaghy[1], T. Causer[1,3], E. Patterson[1], N. Roberts[1], D. Cutajar[1], G.P. Liney[1,2], L Holloway[1,2], J. Begg[2], U. Jelen[2], B Oborn[1,3], M Petasecca[1], A. Rosenfeld[1]

[1] Centre For Medical Radiation Physics, University of Wollongong, NSW, Australia
[2] Ingham Institute of Applied Medical Research and Liverpool CCC, Sydney, NSW, Australia
[3] Illawarra Cancer Care Centre, Wollongong, NSW, Australia

Introduction: Magnetic fields utilized in MRI-linacs generate a Lorenz force on secondary electrons produced. The Lorenz force impacts secondary electron paths. The electron return effect (ERE) for transverse designs and the electron focus effect (EFE) for some inline designs represent unique challeges for radiotherapy dosimetry [1,2].

Methods: The researchers at CMRP are developing a unique suite of dosimeters that are MR compatible and that can characterise dose in high dose gradaient regions with high spatial resolution. The MOS*kin* has been used to characterise the surface dose enhancement on the Ingham in line MRI linac. Various silicon array dosimeters have been developed to measure penumbral focusing for inline designs and asymmetric penumbra for transverse designs to within 0.2mm resolution. Two array dosimeters the magic plate (M512) and the dose magnifying glass (DMG) will be discussed. A small ceramic magnet which acts as a test bed for these devices will also be discussed.

Results: Part 1: The MOS*kin* has been used to measure a small electron focussing zone in the Ingham inline MRI linac and doses approaching 200% of dose (normalised to dose at 10mm depth) at surface have been measured as shown in figure 1. The results agree with our first published dosimetry results on this MRI-linac[3], note that a build up curve is re-established 4 cm off axis.

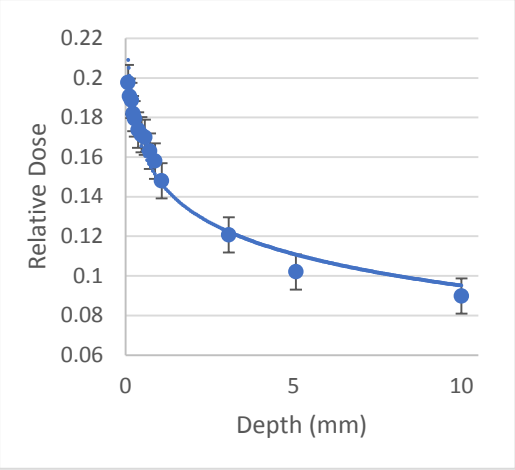


Figure 1. Surface dose measured for in line MRI linac (Courtesy E. Patterson)

Part 2: Our modelling and experimental results on the Ingham MRI linac show electron focusing does reduce the width of the beam penumbra in lung[4,5]. For transverse designs an electron return effect produces an asymmetric penumbra for transverse designs. Shown in figure 2 is a typical penumbra asymmetry modelled using Monte Carlo methods at 1T in transverse mode with the M512 array dosimeter.

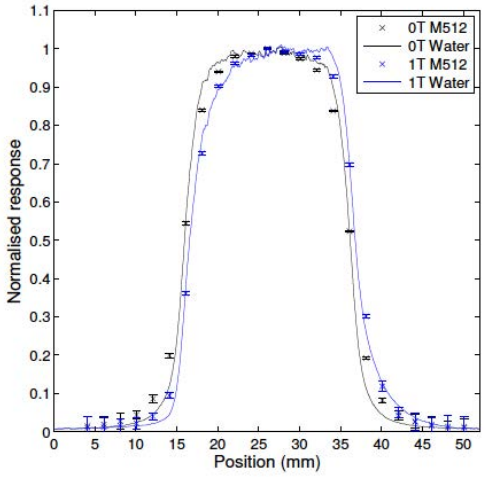


Figure 2. Dose profiles predicted using Monte Carlo Simulation for with M512 array dosimeter and dose in water: for a 6MV X-ray beam of 2cm x2cm in a 1Tesla B field
(Courtesy M. Gargett)

Conclusion: In this work the MOS*kin* and various array dosimeters are being developed for use with MRI-linac systems. The MOS*kin* is being used to characterise surface dose which is particularly important for "air core" in-line designs such as the Ingham Australian MRI linac, where it has been assessed for this type of measurement. The array dosimeters, specifically the M512 and the DMG, are being developed to measure penumbral focusing for inline designs and asymmetric penumbra for transverse designs to within 0.2mm resolution. A small ceramic magnet system acts as a test bed for these devices.

References:

24. Gargett M et al Medicl Physics 42, 856-865, 2015
2. Alnaghy S et al APESM journal 39,921-932, 2016
3. Liney GP Med Phys 43, 518-5194, 2016.
4. Oborn B et al Medical Physics 43, 368-377, 2016.
5. Alnaghy S et al Medical Physics, in print 2018

Immunotherapy: A Primer

Regeneration and RT