

OPTIMIZATION OF MEDICAL ACCELERATORS

A Marie Skłodowska-Curie European Training Network

2nd Edition

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INTRODUCTION

Optimization of Medical Accelerators

The Optimization of Medical Accelerators (OMA) is the aim of this European training network. The project joins universities, research centers and ion beam treatment facilities together with leading industry partners, to address the challenges in cancer treatment facility design and optimization, numerical simulations for the development of advanced treatment schemes, beam imaging and treatment monitoring.

In the treatment of cancer, radiotherapy plays an essential role. Radiotherapy with hadrons (protons and light ions) offers several advantages over photons for specific cancer types. In particular, they penetrate the patient with minimal diffusion, deposit maximum energy at the end of their range, and can be shaped as narrow focused and scanned pencil beams of variable penetration depth. Continuing research into the optimization of medical accelerators is required to assure the best possible cancer treatment for patients.

The OMA network has been built around 15 early stage researchers working on dedicated projects to maximize the benefits of the use of particle beams for cancer treatment. The network consists of an international consortium of almost 40 partner organizations working in this field. It provides a cross-sector interdisciplinary environment for beyond state-of-the-art research, researcher training, and new collaborations.

The network's main scientific and technological objectives are split into three closely interlinked work packages.

Image © Kästenbauer/Ettl



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OMA Research

Beam Imaging and Diagnostics

Compared to conventional radiotherapy, proton therapy is still a developing technology. While the accelerator systems required to provide 200-400 MeV proton beams are a mature technology, many challenges, both clinical and technical, must be overcome before proton therapy has as sound clinical footing as e.g. X-ray radiotherapy. Amongst these challenges, effective imaging is of critical importance. All six projects in this area target the development of beyond state-of-the-art diagnostics that provide more detailed and complete information about the beam.

Treatment Optimization

By combining advanced computer simulations for dose delivery planning with novel treatment schemes and innovative patient scanning systems, OMA strives to further improve one of the most technologically advanced cancer treatment modalities. Five projects are carried out in this area.

Facility Design and Optimization

Crucial for optimum use of particle beam based cancer therapy are facilities providing beams over a wide range of energies adjustable to patient needs. This research area is optimizing existing and planned facilities. It incorporates the results from other OMA work packages into advanced designs and also develops new underpinning technologies that will help overcome existing limitations. Four projects within OMA are dedicated to this topic.

UNIVERSITY OF LIVERPOOL



A member of the Russell Group of major research-intensive universities in the UK, the University of Liverpool has an outstanding international reputation for innovative research. Currently more than 20,000 students are enrolled into more than 400 programs spanning 54 subject areas at its 3 faculties, including Health and Life Sciences; Humanities and Social Sciences; and Science and Engineering.

A rich variety of research is performed at Liverpool, including Particle Physics, Nuclear Physics and Condensed Matter Physics. Moreover, the University is a key partner in the Cockcroft Institute, an international center of excellence for accelerator science and technology. Embracing academia, government and industry, it is unique in providing the intellectual focus, educational infrastructure and the essential facilities in innovating tools for scientific discoveries and wealth generation.

The Liverpool Accelerator Physics Group develops, optimizes and exploits national and international scientific accelerator facilities and generates ideas towards future accelerators and beam diagnostic techniques that allow novel experimental studies and applications. Our strategy is developed in conjunction with the Cockcroft Institute and STFC in alignment with national priorities. It is focused on three thematic areas: frontier accelerators, novel accelerators, and accelerator applications. We have been the driving force behind large scale European networks in accelerator science and technology for many years. Through DITANET (beam diagnostics), oPAC (Optimization of Particle Accelerators) and LA³NET (Laser Applications at Accelerators) we have successfully trained more than 60 Fellows across Europe and have used the unique experiences gained during the implementation of OMA.

We have pioneered jet-based beam profile monitors, optical diagnostics for accelerators to measure beam profile, intensity, halo, position and emittance in least-destructive ways, as well as high resolution beam loss monitors for energy frontier accelerators and light sources using optical fibres. We have continued our close collaboration with the Clatterbridge Cancer Centre to pave the way for enhanced beam monitoring.

Project:

Halo-dose correlation in a medical accelerator

Supervisor: Prof Carsten P Welsch

Online beam monitoring in medical accelerators is an essential part of the patient's safety and also assuring the high quality and efficacy of cancer treatment. Charged particle beams interact with patient's tissue depositing their kinetic energy in many elastic and inelastic collisions demonstrating the highest energy transfer at the end of their path. Hence beam energy and energy spread; position and lateral profile of the beam as well as the beam current have to be precisely determined and recorded.

In clinical practice ionization chambers provide users with information on the dose rate. However, these interceptive devices degrade the beam and require multiple correction and calibration factors to convert the charge collected into dose. A new non-interceptive method of online beam monitoring would be highly desirable.

The LHCb VELO detector is a positionsensitive silicon detector which has been used for tracking vertices originating from collisions at the LHCb experiment at CERN. Its advantageous semi-circular design enables approaching the core of the beam without interfering with it. As such, it allows precise measurements of the surrounding beam 'halo' which can also provide information about the active delivery of the beam. The halo is associated with scattered particles which can result in additional and unwanted dose being delivered. In a clinical setting the beam passes through several components in the delivery system which shape and adapt the beam for the needs of the treatment. Accordingly, this excess beam is mostly collimated out. However, it is possible to utilize the detection of these peripheral particles with the VELO sensors to determine the parameters of the beam.

The stand alone operation of the VELO detector as an online monitor at the Clatterbridge Cancer Centre, UK (CCC) is being investigated. Correlation of the halo to the core of the beam will yield treatment

beam 'halo' maps, benchmarked against simulation studies. These maps are being developed into a database to retrieve beam information for different machine settings from beam monitor measurements. Accurate models are necessary to understand beam behavior and integrate the system, a full characterization of the CCC beamline and the validation of Monte Carlo simulations have been performed in collaboration with UCL, RHUL and CCC. This is expected to lead to a standard simulation model for future work at the beamline, as well as facilitate related studies into linear energy transfer, DNA damage, repair and radiobiological cell studies.

Researcher:

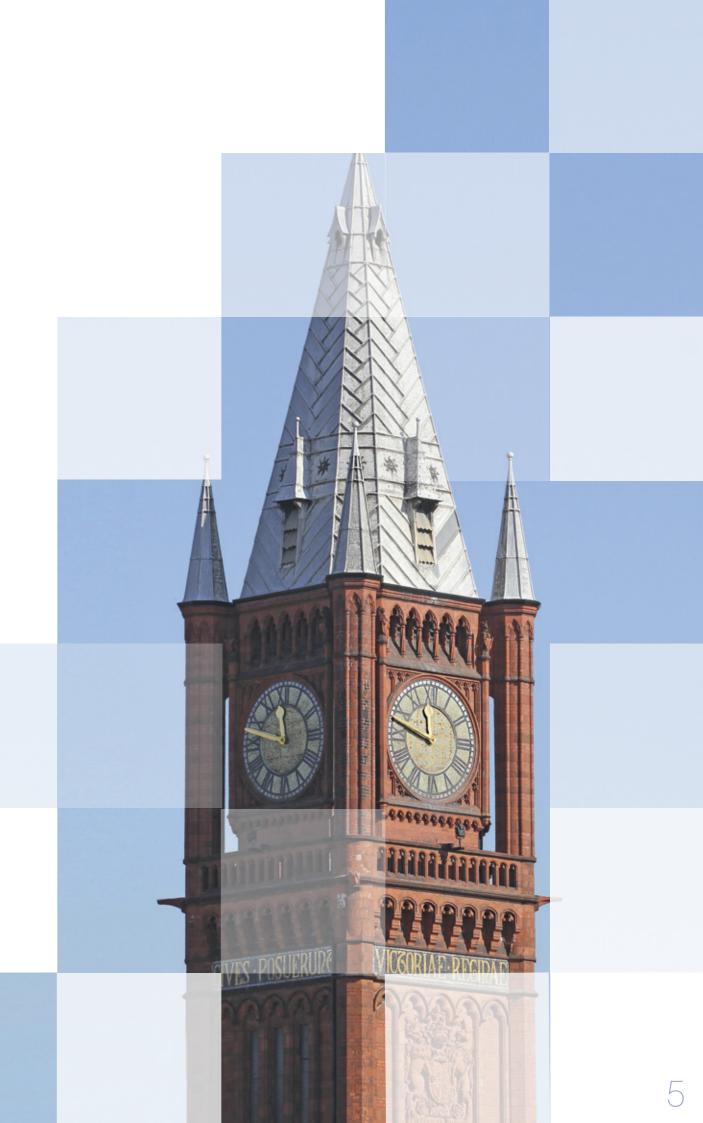
Jacinta Yap



Jacinta graduated with a Bachelor of Science majoring in Mechanical Engineering from the University of Western Australia in 2014. Thereafter, she pursued

a Masters in Medical Radiation Physics with the Centre for Medical Radiation Physics at the University of Wollongong. Her thesis was a study of the Relative Biological Effectiveness (RBE) in proton beam therapy by application of a novel silicon microdosimeter. RBE was derived given a microdosimetric approach where experimental data was evaluated alongside Monte Carlo simulations generated using Geant4. Throughout her study she engaged in short summer internships in the Medical Physics Research Department, Sir Charles Gairdner Hospital in Perth, Australia and at the National Cancer Centre, Singapore General Hospital in Singapore.

Jacinta was awarded her MSc with Distinction in July 2016 and following this, joined the OMA project where she has been working in parallel towards a PhD with the University of Liverpool. During her Fellowship Jacinta has both participated and presented at several schools, workshops and conferences, gaining additional international training in the accelerator and medical physics related fields. Her research with Clatterbridge and secondments undertaken at OMA partners have provided clinical and industry contact.



ASI – AMSTERDAM SCIENTIFIC INSTRUMENTS

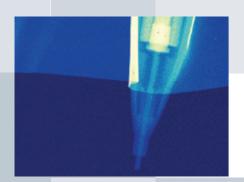


Amsterdam Scientific Instruments (ASI) is a hightech SME. The company was incorporated in 2011 and is co-located at the Amsterdam Science Park with FOM-Nikhef. its founding institute. Since its start, ASI has already gained early attention and traction with a product portfolio of next generation imaging detectors.

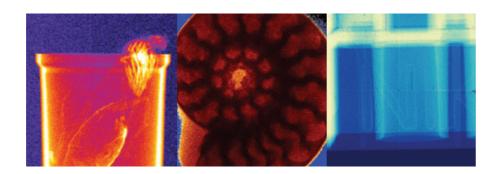
ASI is a global player in the scientific and industrial market for detector technology. It offers imaging solutions for various types of radiation. The team consists of members who have worked at several research institutes focused on various types of radiation sources and are experts on detector development and radiation imaging in their research application. This makes ASI products a reliable and out of the box solution in many fields of research.

The infrastructure of ASI consists of two fully equipped and operational laboratories that allow development and testing of its detection cameras for multiple applications like X-rays, mass spectrometry and electron microscopy. ASI's facilities also allow proof of principle experiments and end-to-end testing of new prototypes.

ASI's collaboration with Nikhef and AMOLF also allows access to other facilities present at the Amsterdam Science Park. Via Nikhef, ASI has access to clean rooms, cooling systems, laboratories, bonding machines and a test setup for the strip sensors. In addition, via its technology partners ASI has access to various testing facilities around the world.



Images taken with the Medipix3RX chip. Courtesv of ASI



Project: A versatile high-speed radiation detection platform

Supervisor: **Dr Dmitry Byelov**

ASI has unique expertise in the applications of the hybrid pixelated detector technology (Timepix, Timepix3 and Medipix3) developed by CERN and Nikhef. ASI is a spin-off startup from Nikhef, the Dutch subatomic and high energy physics institute. Within this project the Fellow has explored all levels of ASI's Medipix3 detectors, from the chip to the readout software, working very closely with Nikhef.

The Fellow has engaged in X-ray imaging and particle beam imaging for detector characterization and various novel applications. Via new collaborations such as the FleX-ray consortium the Fellow has studied new applications including spectral X-ray CT and proton beam quality assurance. This has included measurements with low flux protons and heavy ions at Heavy Ion Medical Accelerator in Chiba (HIMAC) in Japan and developing software and measurements with high flux protons at an ocular proton therapy centre, Clatterbridge Cancer Centre (CCC) in the UK.

Researcher: Navrit Bal



received a Physics MPhys degree from the University of Kent with a study abroad year at the University of California, Berkeley. At

Kent, his undergraduate Masters thesis was based on a series of computational material simulations entitled: Simulating the density of states, band structure, Fermi surface of cobalt and copper at 0-200 GPa. His final year modules included rocketry and human spaceflight, particle and quantum physics, magnetism and superconductivity and finally topics in functional materials. He also cofounded the Physics Society (PhySoc) and was Treasurer for 2 years.

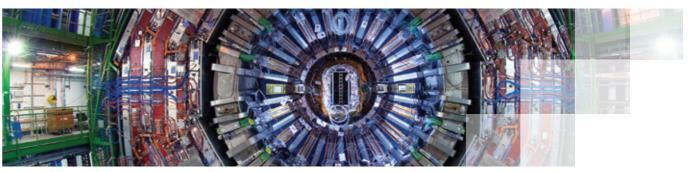
At Berkeley, mostly Physics and Nuclear Engineering classes were taken which led into a summer job within the RadWatch group at Lawrence Berkeley National Laboratory (LBNL). This is where he was the primary developer for the DoseNet project, a network of custom-made dosimeter devices, initially installed in schools in the San Francisco Bay Area and now at a number of sites around the world.

In September 2016 Navrit joined the OMA project at ASI (Amsterdam Scientific Instruments) working on Medipix3 detectors.

Characterization of the Medipix3 chip has been a significant part of the project, which included a secondment to CERN to collaborate with the chip designers at the Medipix group.

CERN – EUROPEAN ORGANIZATION FOR NUCLEAR RESFARCH

Image © CERN



CERN is the world's largest particle physics laboratory which acts as a focal point for European physics and technology collaborations.

CERN hosts each year a community of over 6,000 visitors from more than 300 external institutes around Europe, and from many non-CERN-Member States. CERN has world-class accelerator facilities, including the Isolde/PS/SPS/LHC complexes, a Technology Transfer Unit which enhances technology transfer and promotes communication and public education through press, publications, web pages, exhibitions and visits to the laboratory. CERN has a very strong track record as a European training center.

In recent years the volume of training given has been in the order of 11,000 person-days per year. Large fractions of these trainings are geared towards early stage researchers. CERN has great experience in tutoring and mentoring of ESRs as well as in the transmission of complementary skills.

Project: Improvements on FLUKA for medical applications

Supervisor: Dr Alfredo Ferrari

For efficient treatment planning and decision for optimum dose delivery schemes, Monte Carlo simulations are a key tool. The FLUKA code is de-facto standard in Europe for generation of physical input for carbon ion treatment planning systems, being used for this purpose by Siemens and RaySearch. The code is also used in three clinical facilities, CNAO (Italy), HIT (Germany) and MIT (Germany) for quality assurance, dose verification and as a research tool. The models embedded in the code for atomic and nuclear interactions have already demonstrated their accuracy for clinical applications in hadron therapy.

This project targeted further improvements in the modelling of the emission of secondary radiation. These improvements will allow better predictions of the primary particle fragmentation and its influence on the delivered dose during radiotherapy treatments. Moreover, the secondary radiation (including prompt gammas, positrons and other charged particles) can be used for in-vivo range verification.

Fragmentation of helium, lithium and carbon ion beams are analysed in different materials, and the results from the FLUKA simulations are validated against experimental data.

In collaboration with CNAO and INFN, analysis of the (biological) delivered dose and productions of the secondary radiation has been performed. This research has been applied to realistic treatment scenarios.



Finally, different radiobiological models for different regions of interest, e.g. healthy tissue vs tumor tissue, in the voxel description of the patient will be investigated. More efficient radiotherapy treatments and reduced side effects could be achieved.

Researcher:

Giulia Aricò



Giulia carried out her Master's degree in **Biological and Medical** Physics at the University of Trento in 2012. She developed her Master's thesis at the Paul

Scherrer Institute (Switzerland), in the field of proton therapy.

In the years 2013-2016 she performed doctoral research at the Heidelberg University Hospital, in collaboration with DKFZ (Germany). She investigated the fragmentation of carbon and helium ion beams in different materials of interest for medical purposes. Fixed target experiments were performed at the HIT facility. and the Timepix detectors, developed at CERN, were used for particle identification and tracking. She also performed measurements at the HIMAC facility (Japan) to investigate the response of the Timepix detectors to heavy ions, like neon and argon.

In 2016 Giulia joined the OMA project at CERN to work on improvements of the FLUKA code for medical applications. She has been contributing to the development of the nuclear interaction models for carbon and helium ions. She has also worked on collecting benchmarking data for ion interactions at low and intermediate energy ranges. Significant improvements in the FLUKA dose calculations, especially concerning helium ion beams, have been achieved.

Her expertise includes hadron therapy, ion-ion collisions, Monte Carlo simulations and solid state detectors.

CNAO – CENTRO NAZIONALE DI ADROTERAPIA ONCOLOGICA



Centro Nazionale di Androtreapia Oncologica (CNAO) in Pavia is one of the five centers worldwide in which hadron therapy is administered with both protons and carbon ions. The center has been established and funded by the Italian Ministry of Health and the Lombardy Region to use hadron therapy for cancer treatment. To date more than 2,200 patients received treatment at CNAO.

CNAO provides unique beams for medical applications and has pioneered many of the most advanced patient treatment schemes. The CNAO Foundation is also a center of research and development, whose activities range from clinical and radiobiological research to translational research with the objective of providing continual improvements in the capacity to cure.

The main CNAO accelerator is a synchrotron, the design of which resulted from research in high energy physics by the collaboration of Istituto Nazionale di Fisica Nucleare (INFN), CERN (Switzerland), GSI (Germany), LPSC (France) and the University of Pavia (Italy). It is a circular accelerator with a 25 m diameter along which carbon ions and protons beams are accelerated up to 400 MeV/u and 250 MeV, respectively.

Outside the main ring there are five extraction lines, about 50 m each, leading the extracted beam into three treatment rooms and in an experimental room. Each of the two side treatment rooms features a horizontal beam line, while the central hall has both, a horizontal and a vertical beam line. An experimental line, dedicated exclusively to research, is under commissioning. In 2018, more than 200 hours of beam time have been devoted to external researchers, during some week end and night shifts.

Although the center is mainly dedicated to clinical irradiation, it also provides great opportunities to perform research for scientific and industrial activities related to radiation biophysics, radiobiology, space research and detector development. For researchers a dedicated experimental irradiation room will be available, using the CNAO beams, in time slots not

Images courtesy of CNAO Centro Nazionale di Adroterapia Oncologica

impacting on patient treatment. Research is undertaken in parasitic modality during daily treatments, for the experiments in which the duration is not important and the measurement itself can be "paused" for an indefinite time.

Project:

Tumor tracking in particle therapy

Supervisor:

Prof Guido Baroni

Hadron therapy is an effective method to deal with radio-resistant tumors, which cannot be treated with photon radiotherapy. The method has higher precision and better efficacy in eradicating the tumor cells than photon radiotherapy. The irradiation technique is called active scanning (or pencil) beam, due to the advantage that it can be calibrated to hit the tumor region with specific energy and penetration depth. Despite the advantages of the procedure. a main problem arises from the interplay of the dynamic motion of the beam and the tumor motion, which may cause problems in delivering the predefined radiation dosage on the tumor cells and may potentially be harmful to the healthy tissue surrounding the area.

CT represents the clinical standard for treatment planning in both conventional and particle-based radiation therapy, with time-resolved (4D) CT being the current approach for moving organs. However, there is a growing development in the use of Magnetic Resonance Imaging (MRI) to support the clinical procedure. This is due to the advantages provided by MRI with

respect to CT, such as: (i) better soft tissue contrast, which allows to improve organs delineation, (ii) absence of ionizing radiation, which allows repeated image acquisition without delivering additional dose to the patient and (iii) MR acquisition in dynamic modality, which allows to acquire internal anatomo-pathological motion over different respiratory cycles.

Within this project, the Fellow applies motion modelling strategies to MRI data for organ motion quantification in abdominal regions of patients treated with particle therapy.



Specifically, acquired sagittal/coronal 2D cine MRI data have been exploited to quantify intra- and inter-fractional variations of patients' respiratory motion. The project explored deformable registration methods such as Optical Flow Algorithm to track the movement of the region of interest (ROI). This allowed for the planning of treatment margins based on the motion quantified by cine MRI data, which will be compared with conventional margins defined on the 4DCT dataset. Both, geometrical and dosimetrical comparisons have been performed. The approach will be validated relying on phantom simulations or by exploiting clinical data provided by experts. Additional motion modelling techniques have been evaluated for the possibility of updating the planning CT with the motion provided by MRI data.

Researcher: Charalampos Kalantzopoulos



Engineering at KU Leuven in Belgium. Through the Master degree, he collaborated with other institutes and industries such as imec, KU Leuven, UZ Leuven, Qaelum NV and icometrix

Project: Light ion therapy software for data exchange

Supervisor: Prof Luigi Casalegno

This project is focused on creating a common software bus that enables present and future packages of the configuration and support environment of the control system to easily interconnect in a complex and widely distributed hadron therapy facility.

An integral part of the project is the specification of protocols to be used in the facility's control system configuration and support environment. These protocols should allow for data exchange, assurance of security and privacy, and discovery of devices.

In order to support the development of new applications of the configuration and support environment, a product line architecture has been designed. The architecture specifies the scope of applications, general layout, and variation points. Additionally, a wizard generator has been developed to create customized base applications in accordance to the product-line architecture.

One of the major concerns in the medical environment is the assurance that programs and components are functioning as per specification. The Fellow has also approached the research topic of certification of the medical software, aiming at improving the certification of applications created for this project.

Novel control systems for a medical accelerator facility demand the increase of the monitoring via specification of tools

Charalampos obtained a 5-year diploma in Mechanical Engineering from Technical University of Crete, Greece. He then completed an MSc in Biomedical

He completed his master thesis in collaboration with icometrix, a Leuvenbased company specializing on medical imaging processing and biomarkers. His topic was on 3D MRI processing on patients suffering from Multiple Sclerosis, to extract biomarkers for the disease located on the upper cervical spinal cord.

Charalampos joined the OMA network in November 2018. He is working in close collaboration between CNAO in Pavia and Polytechnico di Milano.

that help with visualization and construction of workflows. To overcome this challenge, the next part of the Fellow's project includes the design and development of a graphical environment that enables the description of workflows composed of several medical accelerator activities. The graphical environment is to be backed by an XML based language, allowing for the description of the workflow states and events for each connected device.

Researcher: Carlos Afonso



Carlos Afonso graduated from University of Minho with a Bachelor's in Informatics Engineering in 2014. In the same vear he started his

Master's in Informatics Engineering at University of Minho, specializing in Applications Engineering, Distributed Systems, and Cryptography; having graduated in 2016. His Master's project was in the field of cloud computing, on the implementation and evaluation of elasticity strategies. During his Master's, he did an internship with the Iberian-International Nanotechnology Laboratory.

In October 2016 Carlos joined the OMA project, while also enrolling in the University of Pavia for his PhD. As part of the industrial research project, he has analyzed the software requirements for applications of the slow environment of CNAO's control system, and defined requirements for next generation applications in the slow environment with the aim of bringing technological updates and introducing mobile devices to the facility's software ecosystem.

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CSIC / IFIC -INSTITUTO DE FISICA CORPUSCULAR





The CSIC (Agencia Estatal Consejo Superior de Investigaciones Cientificas) is a Spanish laboratory having a long-standing reputation in theoretical and experimental physics. It has expertise in the design and construction of detectors and beam instrumentation for nuclear, medical and particle physics. CSIC is the largest public multidisciplinary research organization in Spain. It has 116 institutes or centers distributed throughout Spain. There is also a delegation in Brussels.

IFIC (Instituto de Física Corpuscular) is a nuclear and particle physics institute, where ongoing research activities include experimental and theoretical work with application in near-term and far-future projects. The institute has been participating in leading particle physics experiments since 1950 when it was founded.

Project: Application of high gradient RF technology for hadron therapy accelerators

Supervisor: Prof Juan Fuster Verdu

A new S-band High-Gradient (HG) RF lab is being constructed at IFIC, under a FEDERfunded collaboration agreement between the University of Valencia and the Spanish General Administration (MINECO) for the building integration and the equipment of scientific instrumentation. The main objective of the laboratory is the study of vacuum breakdown phenomenology of 3 GHz HG accelerating structures and development of normal-conducting RF technology, in particular for medical applications. The current activities of the IFIC HG-RF laboratory are developed in collaboration with CERN RF CLIC group within the framework of the knowledge transfer project 'High-power testing of a medical highgradient accelerating structure for proton therapy', for the design and testing of novel HG structures for compact and efficient proton beam facilities for cancer therapy.

The Fellow has contributed to testing and conditioning process, including breakdown studies of two novel high-power prototype 3 GHz accelerating structures commonly used in proton linacs. These accelerating structures are being designed and built at CERN to prove the principle of HG acceleration of low energy protons required for hadron therapy. The Fellow participated in the operation of the CERN X- and S-band testing facilities (Xboxes and Sbox). The first high gradient structure prototype for a medical proton linac has been tested using the high-power infrastructure from the CLIC experimental program. The Fellow has actively participated in testing and data analysis which has been used to improve the understanding of the physics of the breakdown phenomena and the limit in highImage courtesy of IFIC

gradient performances of normal conducting acceleration structures. The experience acquired in the running of the Xboxes will be used to contribute to the finalization of the implementation of the HG-RF lab constructed in IFIC. The test of the second proton linac structures at University of Valencia will complement this work.

The Fellow participated in studies of other low energy ion accelerators to be used as injector for hadron therapy linacs. Development of a compact and low-cost RFQ allows adapting the previous TERA design to modern technologies and building on the experience from the construction of CERN's Linac 4 RFQ.

Researcher:

Anna Vnuchenko



Anna Vnuchenko obtained her Master's degree in Physics from the University of Paris-Saclay, France in 2016. She completed a multidisciplinary program with a specialization in large facilities. Anna

also holds a degree from the department of physics and mathematics of the National Teachers' Training University in Ukraine. She has work experience from the department of nuclear and physical research in IAP-NASU, where she took an active part in design, installation and commissioning of an automated goniometer on nuclear recoil end-station of the accelerator-based facility, to study the radiation damage produced due to ion implantation. Apart from accelerator physics other areas of research included fundamental investigations of interaction processes of MeV ions with matter by means of HRBS and HERDA techniques.

Anna joined the OMA network to work on the application of high gradient RF technology for hadron therapy accelerators, a project hosted by CSIC/IFIC.

GSI – HELMHOLTZ CENTRE FOR HEAVY ION RESEARCH

GSI operates a world-wide unique accelerator facility for heavy ions comprising a linac, a synchrotron and a storage ring. The facility allows the production and acceleration of ions ranging from protons up to uranium. The high energy heavy ion beams are used to produce and separate rare isotope beams produced by projectile fragmentation. **Based on the experience with** the existing accelerators GSI has designed the accelerators of the new international Facility for **Antiproton and Ion Research** (FAIR) which is amongst Europe's largest accelerator projects presently pursued.



Image © A.Zschau, GSI

The research covers a broad range of fields extending from nuclear and atomic physics to plasma physics and is also engaged in materials research, biophysics and cancer treatment with heavy ion beams. GSI is most famous for the research of heavy elements culminating in the discovery of six new chemical elements.

GSI has also developed a new type of cancer treatment using carbon beams. This advanced technique is the basis for a new generation of dedicated medical accelerators which are built in industry and delivered to hospitals for patient treatment.

Project:

R&D into software solutions for a next generation dose delivery system

Supervisor: Dr Christian Graeff

Though scanned ion beams permit highly conformal treatment, and have shown successful in treatment outcomes at several tumor sites, producing the same treatment outcomes to moving tumors in the thorax and abdomen region remains a challenge. Interference between the target and beam motion as well as the changes to the beam range with the target movement has complicated exact dose delivery.

Advanced stage lung cancers and hepatic or pancreatic cancer patients could benefit tremendously from particle therapy if solutions for these challenges are found. A next generation dose delivery system is being developed, specifically aimed at the treatment of moving tumors and potentially other non-cancer targets of the thorax. Besides faster beam delivery, the dose delivery system integrates both motion detection and mitigation methods in its core functionality. The Fellow has implemented a preliminary motion mitigation strategy, where prior knowledge of the patient anatomy and tumor motion can be incorporated in treatment plan optimization, achieving optimal tissue sparing and conformal dose coverage.

The Fellow will continue to design and implement advanced motion mitigation strategies, which synchronize the delivery to the target motion for safe and conformal treatments. Experimental validation has been performed with 1D periodic motion phantoms and will be repeated with sophisticated moving phantoms to show the efficacy of the strategy and confirm the safety of the system

Researcher: Michelle Lis



Michelle obtained her Bachelor's degree in physics and molecular biology at Loyola University Chicago in 2014. During her studies, she performed research on quantifying image distortions and treatments planning errors in MRI scans due to patient motion, at Loyola University Medical Center in Maywood, Illinois. She continued her education at Louisiana State





University (LSU), a CAMPEP accredited university, where she was accepted into the Medical Physics graduate program in 2015. Her research focused on developing a physics-based model for low doses due to patient scatter and the risk on developing secondary cancers. In January 2017, Michelle joined the OMA project at GSI. Her research involves implementing a beam spot delivery which is synchronized to real-time detected respiratory motion.

Image © G.Otto, GSI



IBA – ION BEAM **APPLICATIONS**

Tha

IBA is the world leader in advanced cancer radiation therapy and diagnostic technologies. The company's special expertise lies in the development of innovative proton therapy technologies, supplying the oncological world with equipment of unequalled precision and benefiting from unrivaled experience in building more than 40 proton therapy centers worldwide.

Beside this, IBA develops and commercializes a full range of high-end monitoring equipment and software enabling hospitals to perform the necessary checks and calibration procedures of radiation therapy and radiology. Precision and control are essential in the delivery of radiation as treatment success and patient safety depend on it.

IBA has installed more than 400 accelerators worldwide. Most of these are used to produce radioisotopes in oncology (for cancer detection), and in neurology and cardiology. In addition to its medical activity, IBA leverages its scientific expertise in radiation to develop sterilization and ionization solutions for various industrial uses.

Research Highlight

Correction of Geometrical Effects of a Knife-Edge Slit Camera for Prompt Gamma-Based Range Verification in Proton Therapy

Instruments 2018, 2(4), 25

Project: Imaging solutions for a novel prompt gamma camera

Supervisor: Dr Julien Smeets

Ion therapy offers extremely high precision in beam delivery and hence demands very high accuracy to ensure that the maximum penetration depth coincides with the tumor. An online beam range verification is therefore highly desirable and would reduce the safety margins, which are currently applied in clinical practice. Prompt gamma rays are emitted along the particle track due to nuclear collisions between ions and patient tissue. Hence, they are an ideal probe to determine the particle range due to their correlation to the dose, the low attenuation inside the patient and their instantaneous emission.

The 'slit camera' of IBA measures the prompt gamma signal emitted by each pencil beam and allows therefore a range retrieval on a spot level. Two prototypes of the camera are used by clinical partners in the US and Europe. First patient measurements have been performed in 2015 and 2016 by the partner institutions showing the possibility to measure the proton range in patient treatment. The Fellow has developed and improved software tools to perform and test the various new treatment workflows made possible by the 'slit camera'.

Furthermore, the Fellow has supported clinical partners in their efforts to increase the number of treatment indications that can be monitored by the camera. In this context,

a trolley system was developed that enables positioning of the camera under the patient couch to allow for monitoring of abdominal and prostate treatments. The system further allows fast and highly reproducible positioning of the camera with respect to the patient and the room isocentre. This increases the quality of the measured prompt gamma data and improves the usage of the camera in the clinical workflow. The new trolley system has been used since the end of 2018 during patient treatment at OncoRay and has already proven its benefit for prompt gamma measurements.

Researcher: Johannes Petzoldt



Johannes Petzoldt studied Physics at the Technische Universität Dresden, Germany. He obtained his Diploma in March 2013, with a project on neutron and

proton activation of natural neodymium for the SNO+ experiment. Until September 2016, he worked as an assistant researcher on the topic "range verification for proton therapy" at OncoRay in Dresden, Germany. Johannes investigated scintillation materials, as well as beam characteristics at the proton therapy facility with respect to the novel Prompt Gamma Timing (PGT) method. Furthermore, he tested and characterized a PGT prototype system for the application in clinical practice. Johannes joined the OMA project to work at Ion Beam Applications (IBA) in Louvain-La-Neuve, Belgium. There, he will continue his research on range verification based on prompt gamma rays.

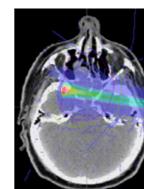
LMU – LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHFN

Ludwig-Maximilians-Universität München - the University in the heart of Munich. LMU is recognized as one of Europe's premier academic and research institutions. Since its founding in 1472, LMU has attracted inspired scholars and talented students from all over the world, keeping the University at the nexus of ideas that challenge and change our complex world.

The well-established Chair of Experimental Physics - Medical Physics in the Faculty for Physics of LMU aims to promote research and teaching in the field of medical physics. with special focus on advances in pre-clinical and clinical image-guided radiotherapy.

The R&D activities include new detector developments and novel approaches for dosimetry and in-vivo imaging, along with advanced computational methods, for application to a wide range of beam modalities, from established conventional sources of photons and hadrons up to laserbased systems.

The department offers a stimulating scientific environment, with a large multidisciplinary and international team and an excellent research infrastructure



Project: Advanced Monte Carlo and imaging methods

Supervisor: **Prof Katia Parodi**

Compared to analytical algorithms traditionally employed in Treatment Planning Systems (TPSs) for proton radiation therapy, Monte Carlo (MC) techniques show great potential for improving the accuracy of dose calculation

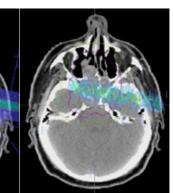
On the other hand, the precision of proton therapy is currently challenged by proton range uncertainties caused by e.g. anatomical changes or patient set-up uncertainties. To reduce such uncertainties, Prompt gamma (PG) is widely investigated to monitor proton range in-vivo by detecting energetic (~MeV) photons emitted by nuclear de-excitation processes in the beam path. However, the performance of PG monitoring is affected by tissue heterogeneities and counting statistics, which are not considered in conventional TPS. Hence, the goal of this project is to improve current TPS accounting for in-vivo proton range verification.

The initial phase of this project focused on guantifying the spot-by-spot conformities between PG (at the production level) and dose profiles and then selecting a few spots to provide reliable dose information, to be boosted above the statistics detection limit in the treatment plan. Relevant work has been published in Physics in Medicine and Biology.

Currently the project is focusing on further expanding the ability of this approach considering fractional anatomical changes. Also, the influence of the PG detection system will be taken into account in the near future.







Left: Dose distribution of a given pencil beam

Right: Prompt gamma emission distribution of this pencil beam.

Images courtesy of LMU

Researcher: Liheng Tian



Liheng Tian received his Bachelor's degree in Particle Physics and Nuclear Physics at the University of Science and Technology of China in 2013. During

his Bachelor's studies, he investigated the enhancement of radiation effects by nanogold for carbon radiation therapy at Institute of Modern Physics, Chinese Academy of Sciences.

In 2013, he started his Master's study at the University of Chinese Academy of Sciences in Beijing. From 2014 to 2016 his research focused on the use of radioactive ⁹C beam in radiotherapy. In his work, a Monte Carlo - based Local Effect Model (LEM) re-implementation was built for the evaluation of Relative Biological Effect (RBE) for radiation. Then, combining the LEM reimplementation and Geant4 MC simulation software, the RBE enhancement for ⁹C beam was simulated and investigated. The work about ⁹C was published in Medical Physics.

Liheng Tian joined the OMA network in 2016 at LMU Ludwig-Maximilians-Universität München in Germany.

Research Highlight

Toward a new treatment planning approach accounting for in vivo proton range verification.

Phys Med Biol, 2018. 63 (21)

MEDAUSTRON

Image © Kästenbauer/Ettl

MedAustron 🎴





MedAustron is one of the most advanced centers for ion beam therapy and research in Europe. The facility is designed to deliver proton and carbon beams to four different rooms: one reserved to non-clinical research and three dedicated to patient treatment, among which a combined horizontal-vertical beam line and a proton gantry.

Clinical operation with protons started in December 2016 and commissioning of carbon beam has recently started. Full operation is envisaged for 2021, when more than one thousand patients per year are expected to benefit from the world-class treatment offered by MedAustron. Currently the center treats around 270 patients per year while continuing commissioning and installation efforts. In order to reach the final patient throughput, intense upgrade work in various fields of the accelerator must be carried out.

Project:

Treatment facility optimization studies

Supervisor: Dr Claus Schmitzer

The Fellow has studied upgrade scenarios feasibility in term of beam dynamics,

accelerator technologies, safety and standards limitations. The effort will result in a cost/benefit analysis for the specific case of the MedAustron facility to reduce patient treatment time, allowing for a larger number of patients to be treated each year.

The possibilities to enhance the machine performance comprise:

a) Reduction of the cycle time of the synchrotron.

Presently, one of the most impacting factor is the reproduction of the magnet hysteresis in each cycle to assure reproducibility, which can be avoided through the development of a system for magnetic field regulation of the power converters for the synchrotron dipoles and quadrupoles. Other factors which affect the cycle time and need further optimization are the time needed for acceleration and extraction delay due to resonant extraction mechanism.

b) Active stabilization and control of the beam extracted from the synchrotron.

The intensity stabilization of the extracted beam on a sub-millisecond timescale would ease the irradiation process; the adaptation of the extracted particle rate to the amount of particles requested per raster point in the tumor region would significantly speed up the irradiation process.

c) Variable energy extraction.

Adapting the extraction energy of the synchrotron during one spill will allow irradiation of multiple energy layers in the tumor with one synchrotron filling, while the synchrotron is always filled with the maximum number of ions provided by the injector.

Researcher: Andrea De Franco



Andrea graduated from the University of Genova with a Master in Subatomic Physics in 2012. His thesis concerned the design and development of a novel neutron detector. He spent one year

in Japan in the framework of the Vulcanus project, studying Japanese for 4 months. He did an 8 months internship in the nuclear power plant system engineering department of Hitachi, performing safety system analysis for possible facility upgrade. Starting 2013 Andrea performed doctoral research in astrophysics of the University of Oxford for the Cherenkov Telescope Array project. His focus was on the development of a camera for ground based multi-Teraelectronvolt gamma-ray astrophysics.

In November 2016 Andrea joined the OMA project as a Fellow at the EBG MedAustron. He has actively participated in beam optics commissioning of not-yet-operational beam lines and led the slow extraction commissioning of the synchrotron for carbon and proton at 800 MeV which is so far only used for research purposes.

In 2018, he was appointed Project Leader of the RF-Knock Out extraction development and implementation project at MedAustron.

PSI – PAUL SCHERRER INSTITUT

The Paul Scherrer Institute is a research center for natural and engineering sciences, conducting cutting-edge research in the fields of matter and materials, energy and the environment and human health. By performing fundamental and applied research, PSI works on sustainable solutions for major challenges facing society, science and the conomy. PSI develops, constructs and operates complex large research facilities including SINQ neutron source, the Swiss Light Source (SLS) and the SµS muon source. The X-ray free electron laser SwissFEL started operation in 2017.

PSI operates a 590 MeV cyclotron, the world's most powerful proton accelerator, that delivers a 1.3 MW proton beam needed for the neutron and muon sources. PSI also developed and operates COMET, a superconducting cyclotron dedicated to the treatment of cancer patients. A third rotating gantry, GANTRY 3, was recently added to this treatment facility. A major upgrade of the SLS is currently under design. This upgrade will result in an increase of the brightness of the source by two orders of magnitude.

Research Highlight

Dielectric-Filled Reentrant Cavity Resonator as a Low-Intensity Proton Beam Diagnostic

Instruments 2018, 2(4), 24



of ultra-low charges

Supervisor: Dr Pierre-André Duperrex

Optimal patient treatment is one of the main goals of the Center for Proton Therapy, CPT. Another goal equally is continuous research and development of innovative treatment concepts. The achievement of these goals is facilitated by the unique position of CPT. embedded within the infrastructure of PSI

Beam diagnostics plays an important role at accelerator facilities. At PROSCAN, it helps optimize medical treatment schemes. For medical facilities, invasive diagnostics are predominantly used due to low intensities involved. This causes scattering issues and consequently reduces the beam quality delivered for patient treatment. Under OMA, a non-invasive monitor to measure beam current information has been developed. This monitor is built as a dielectric-filled reentrant cavity resonator with its fundamental resonance frequency as 145.7 MHz, the second harmonic of the PSI proton beam bunch repetition rate. Using the resonator, the beam intensity was measured to be lower than 100 pA for proton beam energies of 230 MeV, and 200 MeV. As the beam energy is lowered, the sensitivity of the reentrant cavity resonator is also reduced. For energies of 170 MeV and 140 MeV, the beam intensity is as low as 1nA.

We evolved the design of reentrant cavity to measure beam position information. For this, we built a Quadrated Dielectric Filled Reentrant Cavity Resonator tuned to the dipole mode of resonance as its working mode. The dipole mode resonance





frequency for this position monitor is matched to 145.7 MHz. Initial measurements of S-parameter i.e. transmission coefficient on the dedicated test-bench provided promising results in comparison to the simulated results.

The prototype was validated through beam line characterization in June 2019. The design will then be optimized taking into consideration the observations of the beam line tests.

Researcher: Sudharsan Srinivasan



Sudharsan graduated as a mechanical engineer from National Institute of Technology, Raipur, India in the year 2011. During his Bachelor's studies, he worked at Indira Gandhi

Centre for Atomic Research (IGCAR). India under Indian National Academy of Engineering (INAE) summer fellowship on artificial neural network modelling of welding joints.

After obtaining his Bachelor's degree, Sudharsan worked at Coal India Limited as an assistant manager for two years. In 2013. he started his Master's studies in nuclear applications at the University of Applied Science Aachen, Germany. His study focused on fundamentals of nuclear physics and detector technology with the emphasis on medical applications. He did his master's thesis at the Institute for Nuclear Physics, Forschungszentrum Jülich, Germany. The work was to design and construct an automated test bench to calibrate beam position monitors (BPMs) for the HESR in Darmstadt. In 2016, Sudharsan graduated with a Master's degree specialized in medical physics.

In January 2017, Sudharsan joined the OMA project at Paul Scherrer Institut. Sudharsan is enrolled at University of Groningen, Netherlands for his PhD.

Image courtesy of PSI

UNIVERSITY **COLLEGE LONDON**

≜UCL

UCL is one of the UK's premier universities and is consistently ranked in the world's top 25. It is a world-class research and teaching institution whose staff and former students have included 21 Nobel Prize winners.

Founded in 1826, it was the only university in England at that time which admitted students regardless of race or religion and the first to admit women on equal terms with men. It has an annual turnover (2011/12) of £871M and receives over £300M in research funding, the third largest in the UK. It has 29,000 students and 4,000 staff which includes the largest number of Professors of any HEI in the UK and the largest number of female professors. UCL has 74 academic departments organised into 10 faculties and is associated with several major teaching hospitals: UCLH, Great Ormond Street Hospital for Children, the Royal Free Hospital and Moorfields Eye Hospital.

Project:

Calorimeter for proton therapy and radiography

Supervisor:

Dr Simon Jolly

A key challenge in proton therapy is the measurement of the proton energy in the treatment room. The precise knowledge of proton energy is required for many applications in proton therapy, e.g. in proton Computed Tomography (proton CT) which is hoped to significantly reduce treatment planning uncertainties. In addition, an accurate energy measurement would also provide valuable quality assurance (QA) measurements of the treatment protons.

This project sought to adapt existing technology for the precise measurement of proton energy in a clinical setting. A calorimeter based on plastic scintillator was developed by the UCL High Energy Physics group for the SuperNEMO experiment. Preliminary calculations and early experimental measurements indicate that such a SuperNEMO calorimeter achieves an energy resolution in the region of 1% for clinical proton energies. Further measurements will be made to fully characterise the performance of the detector. This will form the basis of the energymeasurement stage for a proton CT system.

An advantage of the polystyrene scintillator is that it has a density similar to that of water. A system made of multiple stages of scintillator sheets and read out by a light sensor is able to directly measure the Water-Equivalent Path Length (WEPL) from the Bragg curve of the proton beam. The measurement of the proton range is crucial to ensure that the treatment is carried out safely. It is therefore part of a range of quality assurance procedures that are carried out each day before treatment starts. These range QA measurements take significant time to set up and adjust for different energies. The detector under development will also be used as the basis for a fast range QA system. This would allow several proton energy steps to be measured across the full energy range available at the nozzle within the time of delivery, significantly reducing the time taken to carry out the daily QA. Some tests are being planned in order to

explore the applicability of the detector to

light ion beams.

Researcher: Laurent Kelleter



Laurent obtained a Bachelor's degree in physics in 2013 from RWTH Aachen University. He graduated with a work on the set-up of a Silicon Photomultiplier

based scintillation detector prototype to measure atmospheric air showers. After spending a year abroad at the university of Montpellier, France, he obtained a Master's degree in experimental particle physics in March 2016 from RWTH Aachen. For his Master's thesis he worked on future online beam monitoring in ion therapy via prompt gamma radiation. The project included a two-week experimental beam test at the Heidelberger Ionenstrahl-Therapiezentrum (HIT). After completing his studies, he drew up a publication on the team's results in collaboration with the project partners from Jagiellonian University in Krakow, Poland.

In October 2016, Laurent joined the OMA network at University College London. His work focuses on the development of a scintillator-based detector for fast range verification in particle therapy. A prototype has been set up and tested in multiple European particle therapy centres. He is expected to complete his PhD at the Department of Physics and Astronomy in the autumn of 2019.

Image courtesy of UCL/MedAustron

UNIVERSITY **OF MANCHESTER**

The University of Manchester is one of the largest in the UK. It has an exceptional record of generating and sharing new ideas and innovations and is applying its expertise and knowledge to solving some of the major social, economic and environmental problems confronting mankind around the globe.

Manchester has the largest student community in the UK, with more than 28,000 undergraduates and 11,000 postgraduates. The University's four faculties include twenty academic schools and hundreds of specialist research groups undertaking pioneering multi-disciplinary teaching and research of worldwide significance in Engineering and Physical Sciences, Medical and Human Sciences, Life Sciences and Humanities

In the physics of particle accelerators, the University has international expertise in the dynamics of charged particles, RF accelerating structures and novel acceleration methods. It plays a key role in the luminosity upgrade of the Large Hadron Collider, and has a close collaboration with the Christie Hospital in a research programme focused around radiotherapy. Group members also work in a number of industrially-relevant projects utilizing particle accelerator technology.

Project: Gantry design for linac-boosted protons

Supervisor: Dr Hywel Owen

Proton computed tomography (pCT) is proposed to achieve a more precise dose delivery. Replacing conventional imaging techniques with pCT will reduce uncertainties of proton therapy planning. However, for an adult patient it requires a beam kinetic energy of approximately 330 MeV, compared to a maximum 230 MeV therapeutic beam. Due to the high energy (high rigidity) requirements and space limitations for a proton beam suitable for pCT, there is no design of a rotating beam delivery system for this application yet.

The overall goal of this project was to develop a detailed beam-optical and magnet design for a combined-function superconducting gantry for proton CT within the Research Beamline Room in Proton Therapy Centre at the Christie Hospital in the UK. The beam energy is proposed to be increased with a booster linear accelerator. The preliminary beam delivery system is a double achromat design with a pencil beam scanning system located downstream of the final bending section. An isocentric design is employed since it has been proven to be effective, flexible and is most widely used in proton centres. The gantry design consists of normal-conducting quadrupoles and superconducting, canted-cosine theta bending magnets.

Within this project, studies on the novel beam energy degrader will be carried out in collaboration with the Center for Proton Therapy at Paul Scherrer Institute, Switzerland. The current graphite degrader is to be replaced with boron carbide in order to improve the beam transmission from the cyclotron to the isocentre and to achieve a clinical beam with the best characteristics.



The University of Mancheste

Additionally, the beam energy degrader and high-gradient structures will be incorporated into the system and beam tracking studies of the delivery line including the complete magnetic design will be performed. The beam delivery system will also be amended such that beam diagnostics instruments, a cryogenic system or mechanical structures can be added into the arrangement.

Researcher: Ewa Oponowicz



Ewa studied biomedical engineering and physics at the Warsaw University of Technology. Poland. She obtained her Bachelor's degree in 2013 in cooperation

with National Centre for Nuclear Research in Poland where she worked on beam forming systems in medical electron accelerators.

She graduated in 2015 from the National School of Engineering in Nantes, France. Her Master's degree was carried out at CERN, where she was part of the Beam Instrumentation group. Her work focused on software development for the beam position and intensity measurement systems in the Antiproton Decelerator.

In 2016 Ewa joined the OMA project, as part of the Accelerator Group in the School of Physics and Manchester University where she is also enrolled for PhD studies. She is based at the Cockcroft Institute at the Daresbury Science and Innovation Campus.

UNIVERSIDAD DE SEVILLA / **CENTRO NACIONAL DE** ACELERADORES



CNA (Centro Nacional de Aceleradores) is a mixed centre of the University of Seville, Junta de Andalucía and the Spanish research council (CSIC). It is recognized as a national singular infrastructure (ICTS) for particle accelerator based interdisciplinary research and carries out fundamental and applied research. The center's main facilities are: a 3MV tandem van de Graaff; a 18 MeV proton (9 MeV deuteron) cyclotron; 1 MV tandem Cockcroft-Walton for accelerator mass spectrometry: a compact accelerator for ¹⁴C dating (MICADAS); a ⁶⁰Co photon irradiator; and a PET/CT scanner for humans and large animals.

Beside these instruments, the center has sample preparation laboratories, as well as an installation for radiopharmaceutical production. A small positron emission tomograph (PET) for animal studies completes the cyclotron laboratory. The tandem has seven independent beam lines, equipped for Ion Beam Analysis techniques and nuclear physcis experiments. The cyclotron has ports for PET isotope production, and an external beam line.

CNA has been involved in the 6th and 7th European framework program, as well as in Horizon 2020 and has a strong track record of training early stage researchers. It is also supported by Spanish national and regional grants. CNA has contracts and agreements with companies and institutions which provide a large fraction of its budget. Around 60 people work at CNA, from which approximately 50% have PhDs. 19 PhD theses have been defended at CNA between 2011 and 2018

Research Highlight

Feasibility Study of a Proton Irradiation Facility for Radiobiological Measurements at an 18 MeV Cyclotron

Instruments 2018, 2(4), 26

Project: Radiobiological effectiveness of protons

Supervisors: Prof José M Espino, Dr Miguel A Cortés-Giraldo

Particle therapy is one of the most promising techniques in the fight against cancer, with a growing number of dedicated accelerators being constructed and installed in hospitalbased clinical centers. Proton therapy is the most widely used particle therapy technique and is gaining an increasing interest in the medical community.

Proton beams are generally assumed to be 10% more biologically effective than photon beams in clinical practice, and a constant Relative Biological Effectiveness (RBE) value of 1.1 is currently used in proton therapy treatment planning. Research suggests that proton RBE varies towards the distal edge of the Bragg curve, increasing with proton Linear Energy Transfer (LET), leading to possible toxicity in the healthy tissue. Therefore, studies of proton RBE at low energies, typically found at the Bragg peak region of clinical beams are highly relevant. The beam lines available at two of the accelerator facilities at the National Centre of Accelerators (CNA) in Seville, the 3 MV tandem and the 18 MeV proton cyclotron, are suitable to perform such studies. These beamlines offer the advantage of providing proton beams with nominal energies in the region of interest, minimizing straggling due to passive degradation. A setup for the irradiation of biological samples was already designed and mounted at the 3 MV tandem facility.

This project aims to create a similar system at the 18 MeV proton cyclotron facility, to extend the energy range available for proton RBE studies. A comprehensive characterization of the beam line and beam properties has been completed, both with direct measurements of the dose profiles and with Monte Carlo simulations. Multiple solutions have been proposed to reach a good degree of dose homogeneity at the position of the biological samples and within the whole area of the samples. The set up proposed will allow irradiation of mono-layer cell cultures. The first experiments involving the irradiation of cell samples at the cyclotron facility are foreseen in the next future.

Preliminary measurements with 3D-microdetectors and Monte Carlo simulations have also been used to characterize radiation quality from a microdosimetric point of view. A Monte Carlo application, based on Geant4-DNA, has been developed for the computation of microdosimetric quantities in spherical sites for protons in liquid water which is intended to be included among the official examples of Geant4.

Researcher: Anna Baratto Roldán



Anna Baratto Roldán studied Physics at the University of Trieste in Italy. Following the completion of her Bachelor's degree in 2013. she enrolled in

the MSc course of Nuclear and Subnuclear physics at the University of Trieste, studying medical physics. During her studies she developed a keen interest in the fields of charged particle therapy and radiobiology.

Anna carried out her Master's thesis within a cooperation program between the University of Trieste and the INFN Section of Milan, and obtained her Master's degree in March 2016. For her thesis project, she worked on the measurement and analysis of charged secondary particles emitted by oxygen beams impinging on a PMMA target. The project was part of a larger experiment, held at the Heidelberg Ion Beam Therapy centre, which aimed to develop new real-time monitoring techniques for Charged Particle Therapy.

In November 2016, Anna joined the OMA, where she worked on the realization of a system for the irradiation of mono-layer cell samples at the cyclotron experimental beam line installed at the CNA. Part of Anna's training took place at the GSI Helmholtz Centre for Heavy Ion Research, where she joined the Biophysics group and performed some radiobiology experiments with Carbon and Iron beams at the UNILAC low energy facility X6, in the frame of FAIR Phase-0.

Finally. Anna enrolled in a PhD program at the University of Seville, and the work carried out within the OMA project will become part of her thesis.

ViALUX

ViALUX GmbH is a privately held company with a worldwide network of representatives. The ViALUX team has long-term experience in optics, image processing, and optoelectronics.

Knowledge and skills of a highly gualified team of engineers is the source of product innovations at the cutting edge of technology. A network of distributors covers the industrial areas in Asia, America, and Europe providing local service. Exporting more than 80% of its annual production ViALUX is proud to serve customers worldwide.

ViALUX develops, produces, and distributes electro-optical components and optical measurement systems for 3D-shape and deformation analysis. ViALUX products are successfully sold into different markets: automotive industry, steel industry, machinevision industry, life science, medicine, and research & development. ViALUX is an authorized DLP® Design House of Texas Instruments supporting customers in various high-performance industrial applications of the DLP micro-mirror device. One of such DLP applications is 3D scanning where ViALUX itself has developed high competence for specific medical 3D applications.

ViALUX engineers work on sustained product development along customer needs. Combining advanced optoelectronics with outstanding metrology software forms the core competence and is the key to company's success.

Project:

Optimization of high-performance 3D/4D surface scanning technology for patient monitoring in radiotherapy environment

Supervisor: **Dr Roland Höfling**

the task

Patient movement monitoring takes advantage of high-precision, high-resolution 3D surface scanning technology. DLP micro- mirror technology was adopted to implement state-of-the-art solutions in terms of accuracy, speed, and data density. For ultra-high-speed 3D/4D scanning, it would be ideal to use the 10-20 kHz switching rate of DLP pattern generator combined with an equivalent area imaging device. New sensor concepts are under development to overcome the speed barrier of conventional machine vision cameras and a new level of electronics integration is promising to solve

Within this project, the Fellow has conducted a systematic study of the performance of that new generation of 3D/4D sensors and contributed to the optimization of the system used over an extended time with radiation exposure. In general, this project is focused on optimizing the long-term availability and reliability of new 3D/4D scanning sensors made by ViALUX.

The theoretical background of radiation interaction with electronic devices has been systematically studied and experimental work performed benefiting from the extensive OMA partner network for gaining real-world data and application knowledge.



VAILIX

Researcher: Samuele Cotta



Samuele received his Bachelor's degree in Physics in 2013 from the University of Insubria in Como (Italy). He undertook his Master's studies at the University

of Insubria, focusing on medical physics. Samuele obtained his Master's degree in Physics in March 2016 with a thesis about the characterization of an active detector for neutron flux measurements. During his thesis work he assembled and tested a detector based on a CsI crystal, which was then used to measure the neutron contamination flux in a radiotherapy treatment room. The results were also obtained through Monte Carlo simulations.

In 2017 he joined the OMA project at ViALUX in Chemnitz, Germany. Samuele investigated the radiation hardness of the ViALUX 3D scanners which will be used in radiotherapy for patient positioning and monitoring. Samuele established a collaboration with the RADSAGA European Training Network. During his project, he tested the ViALUX devices in the radiotherapy treatment rooms in collaboration with the Stadtisches Klinikum in Dresden and GSI and at the FRM Il nuclear reactor in Munich.

3D/4D scanning sensor made by ViALUX. Image courtesy of Vialux

TRAINING PROGRAM

The OMA Fellows receive extensive research-based training within a unique international partnership. Since project start they have gained a broad insight into both, academic and industrial aspects associated with medical accelerators, with opportunities to undertake specific training and secondments within the network. The OMA partners cover a very broad, yet closely interconnected, program that combines many different fields. These range from biomedicine, oncology, Monte Carlo studies, electronics and imaging systems to accelerator science and technology. The contribution of industry partners ensures that the transfer of industry-relevant skills is an integral part of all individual projects.

This has created a truly collaborative network within a strong interdisciplinary environment that provides an excellent basis for the training of researchers. The fundamental core of the training consists of dedicated cutting-edge research projects for each Fellow at their host institution. To complement this, the network provides opportunities for cross-sector secondments for all Fellows. The secondment scheme enables them to spend time working at other institutions within the network, receiving hands-on training in specific techniques and a broader experience in different sectors. Another important aspect of the training is a series of network-wide events comprising several schools, topical workshops and an international conference, which are all open to the wider scientific community.

INTERNATIONAL SCHOOLS

Three OMA Schools have been organized during the life time of the project. Each School was one week in duration and participation was also open to researchers from outside the consortium. All talks given at the Schools are available via the respective event website.

1st OMA School – Medical Accelerators

The OMA School on Medical Accelerators covered topics including beam generation, transport and delivery to the patient, as well as treatment schemes, beam extraction and clinical assessment of effectiveness. Challenges related to beam diagnostics, imaging and patient issues were also be discussed. The School was held at CNAO in Pavia, Italy in June 2017.

2nd OMA School – Monte Carlo Simulations

This School covered geometry definition, material assignment, analysis, dose calculations, different solvers and post processors, as well as data visualization tools. The School was held at LMU in Munich, Germany in November 2017.

3rd OMA School – Particle Therapy

The 3rd OMA School took place in April 2019 at TU Vienna and MedAustron in Vienna, Austria. It covered advanced and combined treatment techniques which included for example real time beam monitoring, variable energy and intensity beam delivery for 3D tumor 'painting', as well as online beam and patient imaging.

TOPICAL WORKSHOPS

The network organized a series of two-day Topical Workshops covering all important research areas of the OMA project, and were open to external participants.

1st OMA Topical Workshop –

Facility Design Optimization for Treatment

2nd OMA Topical Workshop – Diagnostics for Beam and Patient Monitoring

3rd OMA Topical Workshop – Accelerator Design and Diagnostics

The OMA Fellows have also participated in a COSYLAB Academy, an interactive workshop in which they learned about the development and implementation of accelerator control systems.

VIEICIAIUS

COMPLEMENTARY SKILLS TRAINING

To give them a smooth start into their individual research projects and provide them with a skills that makes them highly competitive on the global job market, all OMA Fellows received training in researcher skills through an established guality School developed and implemented by the University of Liverpool. This Skills School model has been recognized by the European Commission as 'best practice' for providing future generations of scientists and engineers with highly relevant skills. Through this training the Fellows develop the non-technical skills that are invaluable for their future careers, whether that be in academia or industry.

Building on this School, training on Technology Transfer and Advanced Researcher Skills was organized at the University of Liverpool in 2019. It familiarized all Fellows with important topics such as research commercialization, grant writing and entrepreneurship. They also received training in skills useful in the labor market, such as CV writing and job interviews, and were made aware of different career pathways available to them.



FINAL CONFERENCE AND OUTREACH SYMPOSIUM

An outreach symposium took place in June 2019 at the Arena and Convention Centre in Liverpool and served as a culmination of the outreach activities undertaken during the course of the network. The Symposium presented the main research findings to the general public, emphasizing applications of the technologies concerned. All talks were live-streamed and on display at OMA partner organization across Europe. The network also organized a Final Conference in September 2019. This major event summarized and promoted the scientific results of the project and discussed remaining challenges and future collaboration. The conference was hosted by CNA in Seville, Spain."



DISSEMINATION & COMMUNICATION

The research results of the project have been disseminated via scientific journals, international events, and via the project website www.oma-project.eu. This is complemented by targeted social media campaigns about cancer therapy and a quarterly newsletter, the OMA Express, which can be accessed via the website.

The consortium as a whole and the Fellows individually have actively communicated the project to the general public. The Fellows have participated in a number of primary and secondary school visits, open days and science festivals to share their passion for science. Each OMA event featured a public lecture by a renowned scientist in the local language where the event was held. The network has also organized a major outreach Symposium in June 2019 which presented OMA research and its importance for science and society to the general public. Pan-European outreach events with a global reach, such as Marie Curie Day 2017, further boosted the impact.



Images courtesy of University of Liverpool



MARIE CURIE DAY

7 November 2017 marked the 150th anniversary of the birth of Marie Skłodowska Curie. In order to celebrate her life and achievements, as well as the EU funding program that bears her name, researchers from three OMA partner institutions organized a simultaneous and connected event at the University of Liverpool, CERN in Geneva, and Ludwig Maximilians University in Munich. Hundreds of school children, students and researchers participated across the three sites, and the initiative reached more than half a million people via internet and social media.

MANAGEMENT STEERING COMMITTEE

The Steering Committee is responsible for the overall network strategy and takes all decisions concerning the network. It consists of the following elected members:

Dr Miguel A. Cortés-Giraldo is an Associate Professor at the University of Seville. Spain. His main research is related with the development and use of Monte Carlo codes for radiobiology with protons.

Dr Christian Graeff, leader of the Medical Physics group of the GSI Biophysics department in Darmstadt, Germany. His main research interests are the treatment of moving targets with scanned ion beams, including treatment planning strategies and their experimental validation.

Dr Monica Necchi, Research Grants Manager at Fondazione CNAO in Pavia, Italy. Her main research interests deal with application of physics into the biomedical field and interactions of radiation with matter.

Dr Julien Smeets, Research Project Manager at Ion Beam Applications SA in Louvain-La-Neuve, Belgium. His research focuses on prompt gamma imaging and its development for proton therapy.

Prof Dr Carsten P Welsch, Head of the Physics Department of the University of Liverpool and scientific coordinator of the OMA network. His research covers frontier accelerators, novel acceleration schemes, as well as accelerator applications.

Michelle Lis, GSI was elected as Fellow representative in the Steering Committee.



Dr Monica Necchi



Dr Julien Smeets



SUPERVISORY BOARD

the job market.

of events.

PROJECT T.E.A.M.

Each beneficiary partner of the network is represented on the Supervisory Board. The board meets annually to monitor progress and ensure that the training is of the highest standard and remains relevant, also in relation to industry and

Day to day project management is carried out by the Project T.E.A.M. from the University of Liverpool based at the Cockcroft Institute in Daresbury, UK. The T.E.A.M. supports Professor Welsch in coordinating large scale research projects and is responsible for project management, monitoring, communication, and organization

Dr Miguel A. Cortés-Giraldo





Dr Christian Graeff



Prof Dr Carsten P Welsch

ASSOCIATED AND **ADJUNCT PARTNERS**



Adaptix Ltd.

Adaptix is transforming planar X-ray - the diagnostic imaging modality most widely used in healthcare worldwide. We are adding low-dose 3D capability - digital tomosynthesis - to planar X-ray while making it more affordable and truly portable so radiology can more easily travel to the patient. This transformation will enhance patient's access to the world's most important imaging technologies and likely increases the diagnostic accuracy for many high incidence conditions such as cardiovascular and pulmonary diseases, lung cancer and osteoporosis. Adaptix will replace tube-based Victorian-

era technology with an innovative Flat Panel X-ray Source made in a semiconductor foundry that will reduce costs to manufacture, deploy and maintain.



Added Value Solutions

Added Value Industrial Engineering Solutions S.L.U. is an international company which provides technology-based services to innovative and challenging projects. mainly for Big Science projects in the field of Nuclear Fusion, Accelerators, High Power Lasers, Space, Neutron Sources and Astrophysics. Strongly focused on the development of outstanding devices, instruments, mechanisms and structures. our expertise covers design, manufacture, assembly, tests and supply under ISO 9001 EN 9100, providing to our customers everything from conceptual design to turnkey solutions.

The Christie NHS Foundation Trust

The Christie

CHRISTIE Hospital is the largest singlesite cancer center in Europe, and treats around 40,000 patients per year (with over 130,000 radiotherapy treatments) with a dedicated oncology focus; since its foundation over 100 years ago The CHRISTIE and is associated research institutes have pioneered many new techniques in radiotherapy, including: leading early developments of dosimetry and fractionated treatment; first UK clinical use of multileaf collimation and intensitymodulated radiotherapy; first clinical use in the world of image-guided radiotherapy. The CHRISTIE presently has 16 networked linear accelerators and organizes chemotherapy delivery on 15 sites.

The Clatterbridge Cancer Centre NHS

Clatterbridge Cancer Centre

The Clatterbridge Cancer Centre is one of the largest networked cancer centres in the UK. From nine operating sites across Merseyside and Cheshire we treat over 9,000 new patients a year, offering pioneering chemotherapy, radiotherapy and proton therapy treatments. The National Eye Proton Therapy Centre, which has provided the UK's only proton therapy service since 1989, is the world's first hospital-based proton facility. We bring together high quality clinical services, research and academic excellence to drive forward the development of new leading edge drugs and therapies and provide the highest quality, specialist care for patients.



COSYLAB d.d.

Cosylab is developing next generation technologies for global niche markets and is a fast growing technological company, committed to creating innovative products and services intended for demanding markets and customers.

The company has started in a laboratory at the Jožef Stefan Institute , the largest Slovenian research institute and, due to first-hand experience of working in major accelerator facilities, has soon become the largest company specialized in developing control systems for particle accelerators. Amongst others, Cosylab is specialized in the field of control systems for particle accelerators and other large experimental physics facilities. We cover hardware and software products and accompanying services such as customization and integration of already existing solutions, custom development, consulting and tutoring.

C-RAD

C-RAD

C-RAD was founded in 2004 by researchers from Karolinska Institutet and the Roval Institute of Technology in Stockholm, clinics at Karolinska Hospital in Solna and people with extensive industrial experience in the field of radiation therapy.

C-RAD develops innovative solutions for use in advanced radiation therapy. The C-RAD group offers products and solutions for patient positioning, tumor localization and radiation treatment systems.

In 2015, C-RAD has acquired the Franco-Belgian Cyrpa group. Cyrpa develops innovative laser solutions for patient positioning and virtual simulation within radiation therapy.



Danfysik

Danfysik is one of the world's leading companies within the development and manufacturing of high quality equipment for particle accelerator laboratories, healthcare and industry, and employs some of the most skilled, experienced and dedicated engineers and technicians. Danfysik has customers and partners all over the world and our business is accelerating like our technology.

Major past projects include 3 complete injector synchrotrons for synchrotron light sources (ANKA, CLS, ASP), a complete synchrotron based particle therapy accelerator system, as well as state-ofthe-art insertion devices for synchrotron light sources. Our products our renowned around the world and we are recognized for example through King Frederik IX's Award for Excellence in Export.

leti

DTBS Healthcare department of CEA-LETI

A subsidiary of the Commissariat à l'Energie Atomique et aux Energies Alternatives (CEA) France's nuclear and renewable energy commission, Leti was established in 1967 in Grenoble. Today, the CEA-Leti is granted over 286 patents a year and handles a portfolio of more than 2,200 patented inventions. It has extensive facilities for micro- and nanotechnology research, and laboratories and equipment that provide first-class nanoscale characterization. chemistry and biology, photonics, design and upstream research capabilities.

The Detector Laboratory Department of micro Technology for Biology and Health of CEA-LETI works on integration of technologies in systems using X-ray or gamma-ray for medical imaging, security, NDT and environment for industrials partners.



Fistral Training and Consultancy Ltd

Fistral Training and Consultancy Ltd has been providing highly successful practical training courses and consultancy to organisations globally since 1991. Fistral deliver training courses in areas such as Project Management, Risk Management, Team Working, Communication, Collaboration, Influencing, Personal Effectiveness and Leadership

Fistral has wide-ranging experience in knowledge-intensive sectors in both academia and industry. We support research staff from first-entry to board-level in worldclass organisations, institutions and research centers. Instructors are active practitioners in their field ensuring training is applicable and focused on techniques and skills used in real life. This experience underpins the training we deliver and ensures it remains current and relevant



Holdsworth Associates

Holdsworth Associates is an award-winning public relations consultancy with a creative approach to communications. We support an exciting range of clients with innovative, cost-effective campaigns that achieve results

In 2013 we were voted 'Best PR Agency' in the Business Weekly New Year Honours Award and received an 'Outstanding Small Consultancy' silver award from the Chartered Institute of Public Relations (CIPR) PRide Awards. We have specialist knowledge in science and technology and offer a wide range of public relations services including engagement with the media, content creation, preparing press releases, publication of technical articles, social media and online communications.

Imperial College London

Centre for the Clinical **Applications of Particles**

The Centre for the Clinical Application of Particles (CCAP) at Imperial College London is an interdisciplinary collaboration that brings together staff from the Faculty of Medicine, the Imperial Academic Health Science Centre, the Department of Physics, the Imperial CRUK Cancer Centre, the Institute of Cancer Research, the John Adams Institute and the Oxford Institute for Radiation Oncology. Its principal objective is to develop the technologies, systems, techniques and capabilities necessary to deliver a paradigm shift in the clinical exploitation of particles.



INFN

INFN is the Italian research public institution devoted to nuclear physics, particle and astro-particle physics and their applications. INFN runs 4 national laboratories. Three of them are running and developing accelerators. Amongst others, there are specific projects for hadron therapy. INFN also runs laboratories for the development of detection techniques. INFN has unique and certainly largely sufficient infrastructure, specialized equipment and experienced personnel for training young researchers. INFN activity is deeply connected to that of Italian Universities and other academic Institutions. This ensures that the young researchers have the possibility to gain diplomas or PhD theses and learn more about research methods before going out to industry, to other nuclear installations or to the health-related field.

ASSOCIATED AND ADJUNCT PARTNERS (continued)



Innovation Agency

The Innovation Agency is the Academic Health Science Network (AHSN) for the North West Coast, covering Cheshire, Lancashire, Merseyside and south Cumbria.

They are one of 15 AHSNs, funded by NHS England to improve health and generate economic growth by accelerating the spread and adoption of innovation.

They work through collaborations with individuals and organisations in the NHS, other AHSNs, academia, local government, businesses, patients and voluntary sector organisations.

They are led by a partnership Board comprising senior leaders from these different sectors, to address the health needs of the region's population.



Instrumentation Technologies d.d.

Instrumentation Technologies is a provider of comprehensive solutions for the instrumentation of particle accelerators. which it markets under the established and protected trademark Libera and around which it has established a global community based on collaboration, bringing together some of the most prominent experts, engineers and scientists from many of the wellregarded international scientific and research institutes. Libera state-of-the-art instrumentation systems are used for diagnostics and beam stabilization at the accelerator facilities around the world. Many instruments have been developed in close collaboration with experts from research institutes. Different Libera products are designed to work together, getting synergetic effects and enabling turnkey solutions for beam stabilization.



Inventya Ltd

Inventva is a leading innovation management consultancy providing proof-of-market research, product-service commercialization and market-oriented due diligence services for R&D-led organisations. Our services validate the commercial potential of new ideas, increase market penetration, reduce risk and optimize investment. Specialists in businessto-business market intelligence and commercialization services, Inventya works across all scientific and technology domains, and across global markets. We work with R&D-led growth firms, investors, universities and public research laboratories.



OncoRay - National Center for Radiation Research in Oncology

The Dresden Center OncoRay pools the strengths of its three operating partners: the University Hospital Carl Gustav Carus Dresden; the Faculty of Medicine at the Technische Universität (TU) Dresden: and the Helmholtz-Zentrum Dresden-Rossendorf (HZDR). Together with the Heidelberg-based HIRO/German Cancer Research Center (DKFZ), OncoRay is the National Center for Radiation Research in Oncology (NCRO).

Across its locations the Center has an outstanding infrastructure and expertise in radiation research - also by international comparison. About 80 scientists from all over the world work on multidisciplinary programs at OncoRay, with research focusing on the fields of medicine, physics, biology and information sciences. The objective is to achieve a decisive improvement in the treatment of cancer using biologically individualized, technologically optimized radiotherapy.



PTB - Physikalisch-Technische Bundesanstalt

The Physikalisch-Technische Bundesanstalt (PTB) is the National Metrology Institute of Germany with scientific and technical service tasks. PTB measures with the highest accuracy and reliability - metrology as the core competence.

For service and research in the field of dosimetry for external beam radiotherapy PTB operates the Metrological Electron Accelerator Facility (MELAF) in Braunschweig, Germany. Three accelerators, two clinical accelerators and a 50 MeV research electron accelerator, offer excellent experimental possibilities for investigations with high-energy photon and electron radiation: from fundamental research to applications in hospitals. The PTB offers access to its metrologically well characterized radiation fields also for external researchers with other research projects beyond dosimetry.



Research Instruments GmbH

Research Instruments is focusing on rf cavities and systems, linear accelerators, particle sources, beam lines and diagnostics. They develop and provide special products for physics and energy research as well as for medical applications. Through their company history of Interatom, Siemens, ACCEL and now as part of Bruker Corporation they are continuously developing turn-key accelerator systems and key components for large scale accelerator facilities. Many of these projects were carried out in partnership with Universities and research centres from around the world.



STFC

STFC is the UK organization responsible for providing large scale accelerator facilities within the UK, and UK involvement in international accelerator programs.

The Accelerator Science and Technology Centre (ASTeC) is a distinct department with STFC which has the remit to undertake advanced research and development activities that will allow STFC to provide or contribute to current and future accelerator projects, both with the UK and internationally. ASTeC was responsible for accelerator design work on Diamond, 4GLS and the New Light Source Project, and has contributed to many international projects such as the International Linear Collider and CLIC. ASTeC is a core member of the Cockcroft Institute for accelerator research.

23 Intellectual Property Office

UK Intellectual Property Office

The Intellectual Property Office is the UK Government's official body responsible for Intellectual Property (IP) rights in the United Kingdom. These rights include patents. designs, trademarks and copyright. We are an Executive Agency of the Department for Business Innovation and Skills (BIS) with the aim of promoting innovation by providing a clear, accessible and widely understood IP system. Ultimately, this enables the economy and society to benefit from knowledge and ideas.



University of Lancaster

University of Lancaster is one of only a handful of universities with a collegiate system which has helped to forge a strong sense of identity and loyalty, and continues to be a distinctive feature of student life at Lancaster. Students from one hundred countries make up a thriving community based around our nine colleges, creating a culturally diverse campus in a location that boasts the combination of city, coast and countryside.

Lancaster's community extends far beyond the campus with research, teaching and student exchange partnerships with leading universities and institutions in 24 countries around the world. Lancaster's iourney has been a remarkable one, and it is now amongst the top one per cent of universities in the world, with an ambitious strategic plan.



University of Pennsylvania School of Medicine

Penn Medicine is one of the world's leading academic medical centres, dedicated to the related missions of medical education, biomedical research, and excellence in patient care. Penn Medicine consists of the Baymond and Buth Perelman School of Medicine at the University of Pennsylvania (founded in 1765 as the nation's first medical school) and the University of Pennsylvania Health System, which together form a \$5.3 billion enterprise.

The Department of Radiation Oncology at Penn Medicine is one of the largest and most respected programs in the world. The comprehensive program provides patients access to nearly every option available to treat their cancer. The department has an outstanding research program that provides patients with access to clinical trials that expand their treatment options.



University of Salamanca

Founded in 1218, the University of Salamanca is a well-recognized Spanish academic institution. It offers a wide range of studies to about 35,000 students, 4000 of which are international students and it contracts 2,500 researchers and lecturers. The graduate and post-graduate programmes cover the diverse fields of knowledge, including Physics and Medical Science. The University is partner in a variety of international research projects, including several ITN Actions, and has collaborations with many institutions in Europe and all over the world.



University of Santiago de Compostela

Located in a World Heritage city, the University of Santiago de Compostela (USC) traces its roots back to 1495. This institution maintains one of the most important academic traditions in Europe, being today a modern university committed with societal progress through the highest quality standards in academic and research activities. The university ranks 5th in Spain's best universities ranking. The USC offers 48 official degrees, 71 master's degrees and a significant number of doctoral programs covering almost any branch of knowledge. It is made of around 30000 students, 350 professors, 1900 lecturers. 300 research groups and 12 research institutes generate a highly recognized research activity.



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