Welcome to the digital edition of the January/February 2018 issue of CERN Courier.

Proton therapy was first administered in a patient at Berkeley National Laboratory in September 1954, the same month CERN was founded. The breakthrough followed the invention of the cyclotron, and the relationship between high-energy physicists and oncologists has grown closer ever since. This issue of the Courier takes a look at some of the medical applications of accelerators, in particular for particle therapy. Hadron beams can allow tumours to be targeted more precisely than conventional radiotherapy and the number of centres is growing rapidly across Europe, for example thanks to efforts such as the TERA Foundation. A shift to more compact linac-driven treatment centres, meanwhile, promises to expand access to particle and radiotherapy in the challenging environments of low- and middle-income countries, where cancer rates are predicted to be highest in the coming decades. Accelerator technology is also bringing new opportunities in radioisotope production for theragnostics and advanced treatment modes, as exemplified by the recently completed MEDICIS research facility at CERN, while detector and computing technology from particle physics continue to have a major impact on medical imaging and treatment planning.

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Viewpoint

Strategic step for medical impact

Knowledge transfer for the benefit of medical applications is a thriving part of CERN’s programme.

By Frédérick Bordry

Innovative ideas and technologies from physics have contributed to great advances in medicine, in particular radiation-based medical diagnosis and treatment. Today, state-of-the-art techniques derived from particle physics research are routinely used in clinical practice and medical research centres: from technology for PET scanners and dedicated accelerators for cancer therapy (see p32), to simulation and data analysis tools.

Transferring CERN’s know-how to other fields is an integral part of its mission. Over the past 60 years, CERN has developed widely recognised expertise and unique competencies in particle accelerators, detectors and computing. While CERN’s core mission is basic research in particle physics, these “tools of the trade” have found applications in a variety of fields and can have an impact far beyond their initial expectations. An excellent recent example is the completion of CERN MEDICIS, which uses a proton beam to produce radioisotopes for medical research (see p29).

Knowledge transfer (KT) for the benefit of medical applications has become an established part of CERN’s programme, formalised within the KT group. CERN has further initiated numerous international and multidisciplinary collaborations, partially or entirely devoted to technologies with applications in the medical field, some of which have been funded by the European Commission (EC). Until recently, the transfer of knowledge and technology from physics to medicine at CERN has essentially been driven by enthusiastic individuals on an ad hoc basis. In light of significant growth in medical applications-related activities, in 2017 CERN published a formal medical applications strategy (approved by the Council in June).

Its aims are to ensure that medical applications-related knowledge transfer activities are carried out without affecting CERN’s core mission of fundamental research, are relevant to the medical community and delivered within a sustainable funding model.

The focus is on R&D projects using technologies and infrastructures that are uniquely available at CERN, seeking to minimise any duplication of efforts taking place in Member States and associate Member States. The most promising CERN technologies and infrastructure that are relevant to the medical domain shall be identified – and the results matched with the requirements of the medical research communities, in particular in CERN’s Member States and associate Member States. Projects shall then be identified, taking into account such things as: maximising the impact of CERN’s engagement; complementarities with work at other laboratories; and the existence of sufficient external funding and resources.

CERN’s medical applications-related activities are co-ordinated by the CERN KT medical applications section, which also negotiates the necessary agreements with project partners. A new KT thematic forum, meanwhile, brings together CERN and Member State representatives to exchange information and ideas about medical applications (see p46). The CERN Medical Applications Steering Committee (CMASC) selects, prioritises, approves and coordinates all proposed medical applications-related projects. The committee receives input from the Medical Applications Project Forum (MAPF), the CERN Medical Applications Advisory Committee (CMAAC) and various KT bodies.

Although CERN can provide a limited amount of seed funding for medical applications projects, external stakeholders must provide the funding needed to deliver their project. Additional funding may be obtained through the EC Framework Programmes, and the CERN & Society Foundation is another potential source.

The transfer of know-how and technologies from CERN to the medical community represents one of the natural vehicles for CERN to disseminate the results of its work to society as widely as possible. The publication of a formal strategy document represents an important evolution of CERN’s program and highlights its commitment to maximise the societal impact of its research and to transfer CERN’s know-how and technology to its Member States and associate Member States.
For the past 40 years, CERN’s accelerator complex has been served by a little-known linear accelerator called Linac2. Commissioned in 1978, the 50 MeV linac was constructed to provide a higher beam intensity to the newly built Proton Synchrotron Booster (PSB).

It superseded Linac1, which accelerated its first beam in 1958 and was the only supplier of protons to the CERN Proton Synchrotron (PS) for the following 20 years. Linac1 was sent into retirement in 1992, having spent 33 years accelerating protons as well as deuterons, alpha particles and oxygen and sulphur ions, and is now an exhibit in the CERN Microcosm. Linac3 took over CERN’s ion production in 1994, but today Linac2 is still injecting protons into the PS and SPS from where they end up in the Large Hadron Collider (LHC).

Although the construction of this workhorse of the CERN accelerator chain was an important step forward for CERN, and contributed to major physics discoveries, including the W, Z and Higgs bosons, Linac2’s relatively low energy and intensity are not compatible with the demanding requirements of the LHC luminosity upgrade (HL-LHC). Persistent vacuum problems in the accelerating vessels over the past years also raise major concerns for the performance of the LHC. For this reason, in 2007, it was decided to replace Linac2 with a more suitable injector for the LHC’s future.

A decade later, in spring 2017, the 160 MeV Linac4 was fully commissioned and entered a stand-alone operation run to assess and improve its reliability, prior to being connected to the CERN accelerator complex. The machine’s overall availability during this initial run reached 91 per cent – an amazing value for an accelerator whose beam commissioning was completed only a few months earlier. The Linac4 reliability run will continue well into 2018, sending the beam round-the-clock to a dump located at the end of the accelerating section under the supervision of the CERN Control Centre (CCC) operation team. After a consolidation phase to address any teething troubles identified during the reliability run, Linac4 will be connected to the next accelerator in the chain, the PSB, in 2019 at the beginning of the LHC Long Shutdown 2. Test beams will be made available to the PSB as soon as 2020, and from 2021 all protons at CERN will come from the new Linac4, marking the end of a 20 year-long journey of design and construction that has raised many challenges and inspired innovative solutions.

Linac4 has the privilege of being the only new accelerator built at CERN since the LHC. With an accelerating length of 86 m, plus 76 m of new transfer line, Linac4 is definitely the smallest accelerator in the LHC injection chain. Yet it plays a fundamental role in the preparation of the beam. The linac is where the beam...
density is generated under the influence of the strong defocusing forces coming from Coulomb repulsion (space charge), and where negative ions initially at rest (containing protons emerging from a bottle of hydrogen gas) are progressively brought close to the relativistic velocities required for acceleration in a synchrotron. This rapid increase in beam velocity requires the use of complex and differentiated mechanical designs to accelerate and focus the beam. Combined with the need for high accelerating gradients (the beam passes only once through the linac), particular demands were placed on Linac4 to achieve the high values of availability required by the first element of the acceleration chain.

The main improvements provided by Linac4 stem from the use of negative hydrogen ions instead of protons and from a higher injection energy into the PSB. Negative hydrogen ions – a proton with two electrons – are converted into protons by passing them through a thin carbon foil, after their injection into the PSB to strip them of electrons. This charge-exchange technique involves progressively injecting the negatively charged ions over the circulating proton beam to achieve a higher particle density. After injection, both beams pass through the stripping foil leaving only protons in the beam. This provides an extremely flexible way to load particles into a synchrotron, making the accumulation of many turns possible with a tight control of the beam density.

**Extensive modifications**

However, the use of hydrogen ions does not come without complications. It requires extensive modifications to the injection area of the synchrotron and a complex ion source in front of the linac. The other key element for generating the high-brightness beams required by the LHC upgrade is the increase of the injection energy in the PSB by more than a factor three with respect to the present Linac2, which reduces space-charge effects at the PSB injection and allows the accumulation of more intense beams.

On top of these crucial advantages for the HL-LHC, Linac4 is designed to be more flexible and more environmentally clean than Linac2. Modulation at low energy of the beam-pulse structure, the option of varying beam energy during injection and a useful margin in the peak beam current will help prepare the large variety of beams required by the injector complex, at the same time reducing beam loss and activation in the PSB. Linac4 is also designed for the long term. Having originated from studies at the end of the 1990s, the goal was to progressively replace the PS complex (Linac2, PSB and PS) with more modern accelerators capable of higher intensities for the future needs of the LHC and other non-LHC programmes. Alas, this ambitious staged approach was later discarded to give priority to the consolidation of CERN’s older synchrotrons, but Linac4 retains features related to the old staged programme that could be exploited to adapt the CERN injector complex to future physics programmes. Examples are the orientation of the Linac4 tunnel, which leaves space for future extensions to higher energies, and its pulse-repetition frequency. The latter is currently limited by the rise time of the PSB magnets to about 1 Hz, but this could be upgraded up to 50 Hz were the PSB to be replaced one day by another accelerator.

Last but not least, Linac4 is a model for the successful reuse of old equipment. All its accelerating structures operate at a frequency of 352 MHz, which is precisely that of the old Large Electron Positron (LEP) collider. Linac4 reuses a large quantity of LEP’s RF components, such as klystrons and waveguides, which were carefully stored and maintained following LEP’s closure in 2000. However, the LEP klystrons installed in Linac4 will gradually be replaced in pairs by modern klystrons with twice the power.

Reaching Linac4’s required performance and reliability posed several problems in the design and construction of the new linac. The first challenge was to build a reliable source of negative hydrogen ions, starting from a new design developed at CERN that profited from the experience of other laboratories such as DESY and Brookhaven National Laboratory. The ion source is a complex device that starts from a bottle of hydrogen similar to the one used...
in Linac2 and generates ions in a plasma heated by a high-frequency wave of several dozen kilowatts. Following some initial difficulties, the new ion source is now steadily providing the minimum beam intensity required by the LHC, while improvements are still ongoing.

**Accelerating elements**

After the ion source, the challenge for the main Linac4 accelerating section has been to integrate focusing and accelerating elements in the small linac cells, achieving a good power efficiency at the same time. These requirements motivated the use of four different types of accelerating structure: an RF quadrupole (RFQ) to take the energy to 3 MeV; a drift-tube linac (DTL) of the Alvarez type to 50 MeV; a cell-coupled drift-tube linac (CCDTL) to 102 MeV; and finally a Pi-mode structure (PIMS) to the final energy of 160 MeV. Most of these accelerating sections include important innovations. The CCDTL and PIMS structures are a world-first developed specifically for Linac4 and used for the first time to accelerate a beam. The DTL includes a novel patented mechanism to support and adjust the drift tubes and makes use for the first time at CERN of a long focusing section made of 108 permanent magnet quadrupoles. To these innovations we had to add a novel scheme to “chop” the beam pulse at low energy, a simplified RFQ mechanical design, and finally the flexible and upgradeable beam optics design.

In spite of a general trend towards superconducting accelerators, Linac4 is entirely normal-conducting. This is a logical choice for a low-energy linear accelerator injecting into a synchrotron and operating at low duty cycle. Linac4 is pulsed, and the short particle beam is in the linac only for a tiny fraction of time. Although as much as 24 MW of RF power are needed for acceleration during the beam pulse, the average power to the accelerating structures will be only 8 kW, out of which only about 6 kW are dissipated in the copper, the rest going to the beam. The power required to cool Linac4 to cryogenic temperatures would be much higher than the power lost into the copper structures.

The construction of Linac4 is a great example of international collaboration, expanding well beyond the boundaries of CERN. Already in the R&D phase between 2004–2008, Linac4 collected support from the European Commission and a group of Russian institutes supported by the ISTC international organisation. The construction of the accelerator received important contributions from a large number of collaborating institutes. These included CEA and CNRS in France, BINP and VNIITF in Russia, NCBJ in Poland, ESS Bilbao in Spain, INFN in Italy and RRCAT in India. Organising this wide network of collaborations was a great challenge, but the results were excellent both in terms of technical quality of the components and in terms of developing a common working culture.

Linac4 brought proton-linac technology back to Europe. Since the construction of Linac2 in 1978 and of the HERA injector at DESY a few years later, all new proton linac developments took place in the US and in Japan. The development effort coordinated by CERN for the construction of Linac4 allowed bringing back to Europe the latest developments in linac technology described above, with a strong involvement of European companies. A measure of the success of this endeavour is the fact that many technical solutions developed for Linac4 will be now adopted by the normal-conducting section of the new European Spallation Source linac under construction at Lund, Sweden.

The inauguration of Linac4 on 9 May 2017 marked the corona of a long project. The ground-breaking on so-called “Mount Citron” (made in the 1950s with the spoil from the construction of the PS ring) took place in October 2008 and the new linac building started to take shape. Construction extended over the mandate of three CERN Directors General. It’s expected that Linac4 will have a long life – at least as long as Linac2 – and play a vital role at the high-luminosity LHC and beyond.

**Résumé**

*Sur la route du Linac 4*

Après deux décennies de conception et de construction, l’accélérateur linéaire Linac 4 du CERN est sur le point d’être intégré à la chaîne d’injection du LHC. Cet accélérateur, qui jouera un rôle vital pour le LHC à haute luminosité, utilise, non pas des protons, mais des ions d’hydrogène négatifs, qu’il injecte, après avoir augmenté leur énergie, dans le Booster du PS.

*Maurizio Vretenar* and *Alessandra Lombardi*, CERN.
25 years of TERA

Therapeutic particles

The accelerator technology underpinning Europe’s first particle-therapy facilities, driven by the TERA Foundation during the past 25 years, is poised to unleash new treatment modes in more compact ways.

Last September the TERA Foundation – dedicated to the study and development of accelerators for particle therapy – celebrated its 25th anniversary. Led by visionary Italian physicist Ugo Amaldi, TERA gathered and trained hundreds of brilliant scientists who carried out research on accelerator physics. This culminated in the first carbon-ion facility for hadron therapy in Italy, and the second in Europe: the National Centre for Cancer Hadron Therapy (CNAO), located in Pavia, which treated its first patient in 2011.

The forerunner to CNAO was the Heidelberg Ion-Beam Therapy Centre (HIT) in Germany, which treated its first patient in 2009 following experience accumulated over 12 years in a pilot project at GSI near Darmstadt. After CNAO came the Marburg Ion-Beam Therapy Centre (MIT) in Germany, which has been operational since 2015, and MedAustron in Wiener Neustadt, Austria, which delivered its first treatment in December 2016.

While conventional radiotherapy based on beams of X-rays or electrons is already widespread worldwide, the treatment of cancer with charged particles has seen significant growth in recent years. The use of proton beams in radiation oncology was first proposed in 1946 by Robert Wilson, a student of Ernest Lawrence and founding director of Fermilab. The key advantage of proton beams over X-rays is that the absorption profile of protons in matter exhibits a sharp peak towards the end of their path, concentrating the dose on the tumour target while sparing healthy tissues. Following the first treatment of patients with protons at Lawrence Berkeley Laboratory in the US in 1954, treatment centres in the US, the former USSR and Japan gradually appeared. At the same time, interest arose around the idea of using heavier ions, which offer a higher radiobiological effectiveness and, causing more severe damage to DNA, can control the 3% of all tumours that are radioresistant both to X-rays and protons. It is expected that by 2020 there will be almost 100 centres delivering particle therapy around the world, with more than 30 of them in Europe (see p32).

Europe entered the hadron-therapy field in 1987, when the European Commission launched the European Light Ion Medical Accelerator (EULIMA) project to realise a particle-therapy centre. The facility was not built in the end, but interest in the topic continued to grow. In 1991, together with Italian medical physicist Giampiero Tosi, Amaldi wrote a report outlining the design of a hospital facility for therapy with light ions and protons to be built in Italy. One year later, the pair established the TERA Foundation to raise the necessary funding to employ students and researchers to work on the project. Within months, TERA could count on the work of about 100 physicists, engineers, medical doctors and radiobiologists, who joined forces to design a synchrotron for particle therapy and the beamlines and monitoring systems necessary for its operation.

Ten years of ups and downs followed, during which TERA scientists developed three designs for a proton-therapy facility initially to be built in Novara, then in the outskirts of Milan and finally in Pavia. Political, legislative and economic issues delayed the project until 2001 when, thanks to the support of Italian health minister and oncologist Umberto Veronesi, the CNAO Foundation was created. The construction of the actual facility began four years later. “We passed through hard times and we had to struggle, but we never gave up,” says Amaldi. “Besides, we kept ourselves busy with improving the design of our accelerator.”

Introducing PIMMS

Meanwhile, in Austria, experimental physicist Meinhard Regler had launched a project called Austron – a sort of precursor to
the European Spallation Source. In 1995, together with the head designer — accelerator physicist Phil Bryant — he proposed the addition of a ring to the facility that would be used for particle therapy (and led to the name of the project being changed to MedAustron). Amaldi, Regler and Bryant then decided to work on a common project, and the “Proton-Ion Medical Machine Study” (PIMMS) was created. Developed at CERN between 1996 and 2000 under the leadership of Bryant and with the collaboration of several CERN physicists and engineers, PIMMS aimed to be a toolkit for any European country interested in building a proton–ion facility for hadron therapy. Rather than being a blueprint for a final facility on a specific site, it was an open study from which different parts could be included in any hadron-therapy centre according to its specific needs.

The design of CNAO itself is based on the PIMMS project, with some modifications introduced by TERA to reduce the footprint of the structure. The MedAustron centre, designed in the early 2000s, also drew upon the PIMMS report. Built between 2011 and 2013, with the first beam extracted by the synchrotron in autumn 2014, MedAustron received official certification as a centre for cancer therapy in December 2016 and, a few days after, treated its first patient. “In the past few years we have worked hard to provide the MedAustron trainees with a unique opportunity to acquire CERN’s know-how in the diverse fields of accelerator design, construction and operation,” says Michael Benedikt of CERN, who led the MedAustron accelerator project. Synergies with other CERN projects were also created, he explains. “The vacuum control system built for MedAustron was successfully used in the Linac4 test set-up, while in the synchrotron a novel radiofrequency system that was jointly developed for the CERN PS Booster and MedAustron is used. The synchrotron’s power converter control uses the same top-notch technology as CERN’s accelerators, while its control system and several of its core components are derived from technologies developed for the CMS experiment.”

All the existing facilities using hadrons for cancer therapy are based on circular cyclotrons and synchrotrons. For some years, however, the TERA Foundation has been working on the design of a linear accelerator for hadron therapy. As early as 1993, Amaldi set up a study group, in collaboration with the Italian institutions ENEA and INFN, dedicated to the design of a linac for protons that would run at the same frequency (3 GHz) as the electron linacs used for conventional radiotherapy. The linac could use a cyclotron as an injector, making it a hybrid solution called a cyclinac, which reduces the sizes of both accelerators while allowing the beam energy to be rapidly changed from pulse to pulse by acting on the radiofrequency system of the linac. In 1998 a 3 GHz 1.2 metre-long linac booster (LIBO) was built by a TERA–CERN–ENEA/INFN collaboration led by retired CERN engineer Mario Weiss, and in 2001 it was connected to the cyclotron of the INFN South Laboratories in Catania where it accelerated protons from 62 MeV to 74 MeV. This was meant to be the first of 10 modules that would kick protons to 230 MeV.

Linear ambition

In 2007 a CERN spin-off company called ADAM (Applications of Detectors and Accelerators to Medicine) was founded by businessman Alberto Colussi to build a commercial high-frequency linac based on the TERA design. Under the leadership of Stephen Myers, a former CERN director for accelerators and technology and initiator of the CERN medical applications office, ADAM is now completing the first prototype. It is called Linac for Image Guided Hadron Therapy (LIGHT), and the full accelerator comprises: a proton source; a novel 750 MHz RF quadrupole (RFQ) — designed by CERN — which takes the particles up to 5 MeV; four side-coupled drift-tube linacs (SCDTL) — designed by ENEA — to accelerate the beam from 5–37.5 MeV; and a different type of accelerating module, called coupled-cavity linac (CCL) — the LIBO designed by TERA — which gives the final kick to the beam from 37.5 to
The 25 m-diameter synchrotron of CNAO in Italy.

The ion-beam injectors of the MedAustron facility in Austria.

230 MeV. The complex will be 24 m long, similar to the circumference of a proton synchrotron.

Compared to cyclotrons and synchrotrons, linear accelerators are lighter and potentially less costly because they are modular. Most importantly, they produce a beam much more suited to treat patients, in particular when the tumour is moving, as in the lungs. The machine developed by ADAM is modular in structure to make it easier to maintain and more flexible when it comes to upgrading or customising the system. In addition, thanks to an active longitudinal modulation system, the beam energy can be varied during therapy and thus the treatment depth changed. LIGHT also has a dynamic transversal modulation system, allowing the beam to be rapidly and precisely modulated to “paint the tumour” many times in a short time – in other words, delivering a homogeneous dose to the whole cancerous tissue while minimising the irradiation of healthy organs. The energy variation of cyclotrons and synchrotrons is 20–100 times slower.

“The beauty of the linac is that you can electronically modulate its output energy,” Myers explains. “Since our accelerator is modular, the energy can be changed either by switching off some of the units or by reducing the power in all of them, or by re-phasing the units. Another big advantage of the linac is that it has a small emittance, i.e. beam size, which translates into smaller, lighter and cheaper magnets and allows to have a simpler and lighter gantry as well.” In the last decade, LIBO has inspired other

TERA projects. Its scientists have designed a linac booster for carbon ions (while LIBO was only for protons) and a compact single-room facility called TULIP, in which a 7 m-long proton linac is mounted on a rotating gantry.

The new frontier of hadron therapy, however, could be helium ion treatment. Some tests with these ions were done in the past, but the technique still has to be proven. TERA scientists are currently working on a new accelerator for helium ions, says Amaldi. “Helium can bring great benefit to medical treatments: it is lighter than carbon, thus requiring a smaller accelerator, and it has much less lateral scattering than protons, resulting in sharper lateral fall-offs next to organs at risk.” In order to accelerate helium ions with a linac, we need either a longer linac compared to the one used for protons or higher gradients, as demonstrated by high-energy physics research at CERN and elsewhere in Europe. The need for future, compact and cost-effective ion-therapy accelerators is being addressed by a new collaborative design study coordinated by Maurizio Vretenar and Alessandra Lombardi of CERN, dubbed “PIMMS2”. A proposal, which includes a carbon linac, is being prepared for submission to the CERN Medical Application group, potentially opening the next phase of TERA’s impressive journey.

Résumé

Particules thérapeutiques

Les technologies d’accélérateur qui se sont concrétisées par les premières installations de thérapies par particules en Europe ont été en grande partie le résultat du travail de la Fondation TERA. Celle-ci, au cours des 25 dernières années, a rassemblé et formé des centaines de scientifiques, lesquels ont ensuite mené des recherches sur la physique des accélérateurs. Tout cela a abouti au premier centre d’hadronthérapie à ions carbone d’Italie (le CNAO), ou encore à la mise en place de MedAustron en Autriche. Les efforts se concentrent à présent sur la création de centres de traitement plus petits utilisant des accélérateurs linéaires.

Virginia Greco, CERN.
The use of radioisotopes to treat cancer goes back to the late 19th century, with the first clinical trials taking place in France and the US at the beginning of the 20th century. Great strides have been made, and today radioisotopes are widely used by the medical community. Produced mostly in dedicated reactors, radioisotopes are used in precision medicine, both to diagnose cancers and other diseases, such as heart irregularities, as well as to deliver very small radiation doses exactly where they are needed to avoid destroying the surrounding healthy tissue.

However, many currently available isotopes do not combine the most appropriate physical and chemical properties and, in the case of certain tumours, a different type of radiation could be better suited. This is particularly true of the aggressive brain cancer glioblastoma multiforme and of pancreatic adenocarcinoma. Although external beam gamma radiation and chemotherapy can improve patient survival rates, there is a clear need for novel treatment modalities for these and other cancers.

On 12 December, a new facility at CERN called MEDICIS produced its first radioisotopes: a batch of terbium (\(^{155}\text{Tb}\)), which is part of the \(^{149/152/155/161}\text{Tb}\) family considered a promising quadruplet suited for both diagnosis and treatment. MEDICIS is designed to produce unconventional radioisotopes with the right properties to enhance the precision of both patient imaging and treatment. It will expand the range of radioisotopes available — some of which can be produced only at CERN — and send them to hospitals and research centres in Switzerland and across Europe for further study.

Initiated in 2010 by CERN with contributions from the Knowledge Transfer Fund, private foundations and partner institutes, and also benefitting from a European Commission Marie Sklodowska-Curie training grant titled MEDICIS-Promed, MEDICIS is driven by CERN’s Isotope Mass Separator Online (ISOLDE) facility. ISOLDE has been running for 50 years, producing 1300 different isotopes from 73 chemicals for research in many areas including fundamental nuclear research, astrophysics and life sciences.

Although ISOLDE already produces isotopes for medical research, MEDICIS will more regularly produce isotopes with specific types of emission, tissue penetration and half-life — all purified based on expertise acquired at ISOLDE. This will allow CERN to provide radioisotopes meeting the requirements of the medical research community as a matter of course.

ISOLDE directs a high-intensity proton beam from the Proton Synchrotron Booster onto specially developed thick targets, yielding a large variety of atomic fragments. Different devices are used to ionise, extract and separate nuclei according to their masses, forming a low-energy beam that is delivered to various experimental stations. MEDICIS works by placing a second target behind

MEDICIS will expand the range of novel radioisotopes available, which will be sent to hospitals and research centres.

The robot sample handler at MEDICIS, a unique facility for the production of unconventional isotopes.
CERN-MEDICIS

ISOLDE’s: once the isotopes have been produced on the MEDICIS target, an automated conveyor belt carries them to a facility where the radioisotopes of interest are extracted via mass separation and implanted in a metallic foil. The final product is then delivered to local research facilities including the Paul Scherrer Institute, the University Hospital of Vaud and Geneva University Hospitals.

Clinical setting
Once in a medical-research environment, researchers dissolve the isotope and attach it to a molecule, such as a protein or sugar, which is chosen to target the tumour precisely. This makes the isotope injectable, and the molecule can then adhere to the tumour or organ that needs imaging or treating. Selected isotopes will first be tested in vitro, and in vivo by using mouse models of cancer. Researchers will test the isotopes for their direct effect on tumours and when they are coupled to peptides with tumour-homing capacities, and establish new delivery methods for brachytherapy using stereotactic or robotic-assisted surgery in large-animal models for their capacity to target glioblastoma or pancreatic adenocarcinoma or neuroendocrine tumour cells.

MEDICIS is not just a world-class facility for novel radioisotopes. It also marks the entrance of CERN into the growing field of theranostics, whereby physicians verify and quantify the presence of cellular and molecular targets in a given patient with a diagnostic radioisotope, before treating the disease with the therapeutic radioisotope. The prospect of a dedicated facility at CERN for the production of innovative isotopes, together with local leading institutes in life and medical sciences and a large network of laboratories, gives MEDICIS an exciting scientific programme in the years to come. It is also a prime example of the crossover between fundamental physics research and health applications, with accelerators set to play an increasing role in the production of life-changing medical isotopes.

Résumé
Des isotopes pour une médecine de précision

Le 12 décembre, une nouvelle installation au CERN, appelée MEDICIS, a produit son premier radio-isotope : le terbium-155. Lancée en 2010, l’installation MEDICIS est conçue pour produire des radio-isotopes spécifiques capables d’améliorer la précision de l’imagerie et du traitement, ciblant des agents de diagnostic et des traitements innovants pour, notamment, le cancer du cerveau ou du pancréas. MEDICIS développera la gamme de radio-isotopes innovants disponibles, dont certains ne peuvent être produits qu’au CERN ; ces nucléides seront envoyés à des hôpitaux et des centres de recherche en Suisse et dans toute l’Europe pour de nouvelles études.

Thierry Stora, CERN.
A major effort is under way to develop innovative, robust and affordable medical linear accelerators for use in low- to middle-income countries.

If you live in a low- or middle-income country (LMIC), your chances of surviving cancer are significantly lower than if you live in a wealthier economy. That’s largely due to the availability of radiation therapy (see p32). Between 2015 and 2035, the number of cancer diagnoses worldwide is expected to increase by 10 million, with around 65% of those cases in poorer economies. Approximately 12,600 new radiotherapy treatment machines and up to 130,000 trained oncologists, medical physicists and technicians will be needed to treat those patients.

Experts in accelerator design, medical physics and oncology met at CERN on 26–27 October 2017 to address the technical challenge of designing a robust linear accelerator (linac) for use in more challenging environments. Jointly organised by CERN, the International Cancer Expert Corps (ICEC) and the UK Science and Technology Facilities Council (STFC), the workshop was funded through the UK Global Challenges Research Fund, enabling participants from Botswana, Ghana, Jordan, Nigeria and Tanzania to share their local knowledge and perspectives. The event followed a successful inaugural workshop in November 2016, also held at CERN (CERN Courier March 2017 p31).

The goal is to develop a medical linear accelerator that provides state-of-the-art radiation therapy in situations where the power supply is unreliable, the climate harsh and/or communications poor. The immediate objective is to develop work plans involving Official Development Assistance (ODA) countries that link to the following technical areas (which correspond to technical sessions in the October workshop): RF power systems; durable and sustainable power supplies; beam production and control; safety and operability; and computing.

Participants agreed that improving the operation and reliability of selected components of medical linear accelerators is essential to deliver better linear accelerator and associated instrumentation in the next three to seven years. A frequent impediment to reliable delivery of radiotherapy in LMICs, and other underserved regions of the world, is the environment within which the sophisticated linear accelerator must function. Excessive ambient temperatures, inadequate cooling of machines and buildings, extensive dust in the dry season and the high humidity in some ODA countries are only a few of the environmental factors that can challenge both the robustness of treatment machines and the general infrastructure.

Simplicity of operation is another significant factor in using linear accelerators in clinics. Limiting factors to the development of radiotherapy in lower-resourced nations don’t just include the cost of equipment and infrastructure, but also a shortage of trained personnel to properly calibrate and maintain the equipment and to deliver high-quality treatment. On one hand, the radiation technologist should be able to set treatments up under the direction of the radiation oncologist and in accordance with the treatment plan. On the other hand, maintenance of the linear accelerators should also be as easy as possible – from remote upgrades and monitoring to anticipate failure of components. These centres, and their
Linacs in challenging regions

Radiotherapy treatment setups in Tanzania (left and right, the latter based on a cobalt-60 source). Middle: imaging equipment in Nigeria lies dormant.

machines, should be able to provide treatment on a 24/7 basis if needed, and, at the same time, deliver exclusive first-class treatment consistent with that offered in richer countries. STFC will help to transform ideas and projects presented in the next workshop, scheduled for March 2018, into a comprehensive technology proposal for a novel linear accelerator. This will then be submitted to the Global Challenges Research Fund Foundation Awards 2018 call for further funding. This ambitious project aims to have facilities and staff available to treat patients in low- and middle-income countries within 10 years.

Résumé
Réduire la fracture thérapeutique

Une réunion d’experts, tenue au CERN les 26 et 27 octobre, était consacrée au développement d’un accélérateur linéaire pour applications médicales pouvant être utilisé dans des situation difficiles, telles qu’alimentation électrique peu fiable, climats extrêmes ou communications défectueuses.

Charlotte Jamieson, STFC, Norman Coleman, ICEC, Paul Collier, CERN.
Networking against cancer

Established in 2002, the European network for light-ion hadron therapy (ENLIGHT) is focusing on education and training to promote hadron therapy in Europe.

The inaugural meeting of the European Network for Light Ion Hadron Therapy (ENLIGHT) took place at CERN in February 2002, with the aim of co-ordinating European efforts in innovative cancer treatment strategies using radiation. Specialists from different disciplines, including radiation biology, oncology, physics and engineering, with experience and interest in particle therapy have nurtured the network ever since.

Today, ENLIGHT can count on the contribution of more than 700 members from all continents. Together, they identify and tackle the technical challenges related to the use of highly sophisticated machines, train young and specialist researchers, and seek funding to ensure the sustainability and effectiveness of the organisation.

Started with the support of the European Commission (EC), ENLIGHT has coordinated four other EC projects in particle therapy: U-LICE, PARTNER, ENVISION and ENTERVISION. In the past 15 years, the network has evolved into an open, collaborative and multidisciplinary platform to establish priorities and assess the effectiveness of various treatment modalities. Initially based on the three technologies and innovation pillars – accelerators, detectors and computing – of high-energy physics, the ENLIGHT initiative has evolved into a global effort.

Training essential
ENLIGHT has witnessed a large increase in dedicated particle therapy centres, and innovative medical imaging techniques are starting to make their way into hospitals. Skilled experts for high-tech cancer treatment are, therefore, in high demand. Thanks to the large number of scientists involved and its wide reach, ENLIGHT has enormous potential to offer education and training and, since 2015, has included training sessions in its annual meetings.

Education and training, in addition to pitching for research funding, are the main thrusts of ENLIGHT’s activities today. A project within the CERN & Society Foundation has just been approved, opening a new chapter for ENLIGHT and its community. The benefits lie, not only in reinforcing the hadron therapy field with qualified multidisciplinary groups of experts, but especially in helping young scientists flourish in the future.

More information is available on the ENLIGHT website, www.cern.ch/ENLIGHT.

Résumé
Un réseau contre le cancer

Mis en place en 2002, le réseau européen consacré à l’hadronthérapie par ions légers centre ses efforts sur l’éducation et la formation en vue de promouvoir l’hadronthérapie en Europe.

Manjit Dosanjh, CERN.
CERN and Member States talk med-tech

The first annual knowledge-transfer thematic forum on medical applications took place at CERN on 30 November, bringing CERN and its Member State and associate Member State representatives together to discuss the application of CERN’s technologies and know-how to the medical field.

The knowledge transfer (KT) forum, known as ENET until the end of 2015 comprises one or more representatives for each country, allowing CERN to develop common approaches with its Member States and to identify potential industry and academic partners while minimising duplication of effort. Medical applications are one of CERN’s most significant KT activities, and this year CERN gave each country the chance to nominate an expert in the field to attend special sessions of the KT forum dedicated to medical applications.

Some 20 invited speakers from the physics and medical communities took part in the inaugural event in November. The scope of the discussions demonstrated CERN’s deep and longstanding involvement in areas such as medical imaging, hadron therapy and computing, and highlighted the enormous potential for future applications of high-energy physics technologies to the medical arena.

After an introduction regarding CERN’s strategy for medical applications and the governance put in place for these activities (see p5), much of the event was devoted to updates from individual Member States and associate Member States, where much activity is taking place. Some of them clearly indicated that medical applications are an important activity in their countries, and that engaging with CERN more closely is of great added value to such efforts.

In the second half of the meeting, presentations from CERN experts introduced the various technology fields in which CERN is already actively pursuing the application of its technologies to the medical fields, such as high-field superconducting magnets, computing and simulations, and high-performance particle detectors.

The event was an all-round success, and more will follow this year to continue identifying ways in which CERN can contribute to the medical applications strategy of its Member States.
CERN presents high readiness-level technologies in Atlanta

During the IEEE Nuclear Science Symposium and Medical Imaging Conference (NSS/MIC), held on 21–28 October in Atlanta in the US, a technology-transfer programme organised by HEPTech, CERN and Siemens presented CERN technologies with a high technology-readiness level. To be selected for the programme, the technologies had to prove the availability of solid academic substance in addition to clear IP access conditions, applications and dissemination/commercialisation plans. Ten posters were exhibited, representing mature technologies originating from the US, Canada and Europe. Seven of them visualised CERN’s radiation detection, pixel detector and electronic technologies, as well as software developments.

Among the CERN technologies presented were: Timepix3, a general-purpose integrated circuit for read-out of semiconductor and gas-filled detectors that can be applied in X-ray imaging, particle track reconstruction or radiation detection and monitoring; GEMPix, a novel generation of radiation detectors for dose measurements in hadron therapy; NINO ASIC, an ultrafast and low-power front-end amplifier discriminator ASIC chip for use in medical imaging, life science or materials research; FLUKA, a particle-transport simulation code with many applications in high-energy particle physics and engineering; and RaDoM, a very compact radon detector measuring indoor radiation concentrations rapidly and accurately. The annual IEEE NSS/MIC forum is the main event for the detector and electronic community and attracts more than 1500 participants.