CHAPTER 10

HOW PARTICLE PHYSICS RESEARCH AT CERN CONTRIBUTES TO MEDICAL INNOVATION

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Since the discovery of X-rays at the end of the 19th century, physics has been having a tremendous impact on modern medicine. Physics phenomena underpin many advanced techniques and technologies that are routinely used in hospitals for both diagnosis and treatment of diseases. Radiotherapy for cancer treatment, radiopharmaceuticals, magnetic resonance imaging (MRI), and positron emission tomography (PET) imaging are just some examples. In addition, many of the state-of-the-art technologies behind these healthcare innovations were initially developed for particle physics research. Some have been pushed well beyond the industrial know-how by the stringent requirements of frontier instruments, like the particle accelerator Tevatron at Fermilab,[1] or the Large Hadron Collider (LHC) at CERN,[2] as well as the detectors used in these machines. Particle detectors and particle accelerators are not only found at CERN and other particle physics laboratories but are ubiquitous in hospitals. Accelerators are the core of radiotherapy devices, while PET scanners contain photon detectors. Computer simulations of how particles interact with matter are also widely used to model the effects of radiation on biological tissues. More recently, the healthcare sector has become interested in artificial intelligence techniques. Personalized medicine, an increasingly data-hungry discipline, is a major driver of this trend, which in turn is triggering an interest in the data analytics techniques being developed by particle physicists to deal with their large data sets.

There is a giant leap between a bespoke 27-kilometer long accelerator like the LHC and an off-the-shelf room-sized medical accelerator. Understanding how the transfer of technologies and know-how from particle physics to the medtech industry and medical research happens is a challenge. This knowledge can offer keys to improve the process and to maximize the impact of basic science on societally relevant topics, such as healthcare.

This article mainly focuses on the example of knowledge transfer from CERN, the world's largest particle physics laboratory. Some of the strategic issues described are relevant for the broad community of particle physics research and for "big science" in general. However, CERN also faces some specific challenges due to it being a publicly funded international organization with a core mission of fundamental research.

The impact of basic research

Beyond scientific achievements, the search for answers to fundamental questions often leads to major technological breakthroughs. However, measuring the worth of basic research is not a simple cost-benefit analysis. Often, the impact of basic research on the medtech market is indirect and difficult to track. One such case is particle physics' contribution to modern medical imaging technology. Today, MRI scanners deliver amazingly detailed images of the human body thanks to powerful magnets engineered with coils of a superconducting material called niobium-titanium. In the early seventies when the MRI technique was in its infancy, this material was industrially available only in small quantities, so the first scanners were built using conventional magnets. At the same time, particle physics was in dire need of niobium-titanium to build the strong magnets necessary for the Tevatron particle accelerator at Fermilab.[3] This is where the role of big science in pushing technologies beyond state-of-the-art becomes manifest: Fermilab bought the raw material in quantities that were orders of magnitude larger than standard orders for niobium-titanium and worked alongside manufacturers to achieve the perfect coils for the Tevatron. This paved the way for commercial use of niobium-titanium in MRI machines and, later, in medical accelerators.

A similar pattern can be found in the history of technology for PET scanners, often quoted as the epitome of the cross-fertilization between particle physics detectors and imaging tools. Experiments at the Stanford Linear Accelerator Center and CERN pioneered the large-scale use of detectors that are now ubiquitous in PET scanners. The mammoth scale of these next-generation experiments fueled the development of state-of-the-art photon-sensitive devices—which are used in the latest commercial PET scanners.

In some cases, there can be a direct transfer of a technology developed for particle physics research to medical applications. A recent successful example is a breakthrough application of a chip developed at CERN by the Medipix3 Collaboration for LHC experiments. Members of the Medipix3 collaboration founded a company, MARS Bioimaging Ltd., which has been granted a license to exploit the chip for spectral computed tomography imaging—X-Ray imaging in color. In 2018, the company developed a scanner based on the Medipix3 technology and managed to take the first 3D color X-ray images of human body parts.[4] However, such a direct transfer is not common—particularly in laboratories or institutions like CERN, which have a mandate of pure basic research. In such places, technologies are developed to satisfy the needs of upcoming or on-going projects and are often tailored to the end use in a particle physics environment.

International collaborations play a vital role also in providing fertile ground for the application of technologies developed for basic research to other fields. For example, the Geant4 computing simulation toolkit is developed and maintained by a world-wide collaboration of scientists and software engineers.[5] Today it is adopted by thousands of users worldwide for application in a variety of domains, including the study of the radiation environment on the International Space Station as well as radiation effects on possible future manned space missions to the Moon or Mars.

Success stories of medtech applications of CERN technology

CERN is the world's largest particle physics laboratory, located at the border between France and Switzerland. Its core mission is fundamental research in particle physics. As a publicly funded laboratory, it also has a remit to ensure that its technology and expertise deliver immediate and tangible benefits to society wherever possible. Other physics research laboratories and institutes were early adopters of CERN technologies, thanks to the highly collaborative nature of particle physics. Since its creation in 1954, CERN has also been active in transferring its technology and expertise outside particle physics. The most known example is the invention of the World Wide Web by CERN scientist Tim Berners-Lee in 1989, but the laboratory has contributed to applications in many other fields, from medical and biomedical technologies to aerospace applications, safety, "Industry 4.0", cultural heritage, and emerging technologies (Figure 10.1).

Applications of CERN technologies and know-how to the health domain represent one of the most relevant knowledge transfer opportunities in terms of potential impact on society.

At CERN, early activities with pertinence to medical applications date back to the 1970s. At that time, knowledge transfer happened—mostly serendipitously—through specific initiatives of individual researchers. CERN physicist Georges Charpak not only opened a new era for particle physics with the detector he conceived in 1968, for which he earned the 1992 Nobel Prize in Physics, but also strived to ensure that his invention could be applied in medicine. Charpak's detector has found important applications in biology, radiology, and nuclear medicine. He was a firm believer in entrepreneurship as a tool to transfer technologies from basic research to society—the company he founded in 1989 is still active in the field of medical imaging, with a system based on his original detector.[6]

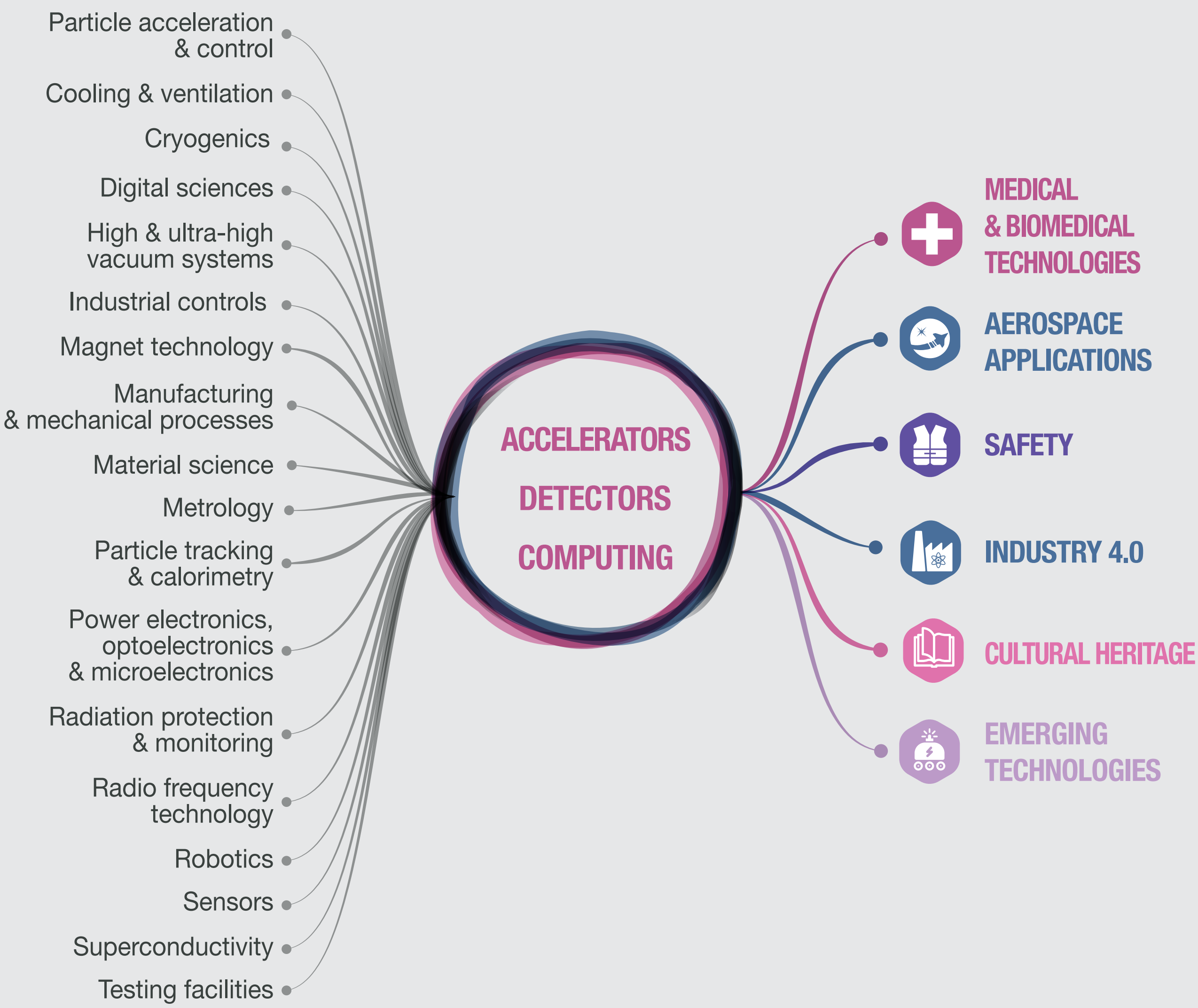
In 1975, CERN physicists David Townsend and Alan Jeavons had the idea of using a version of Charpak's detector for PET imaging, by looking at the work of a group in Berkeley and University of California, San Francisco (UCSF). Townsend developed software to reconstruct the data from Jeavons' detectors and, in 1977, they took the first mouse image, with the participation of radiobiologist Marilena Streit-Bianchi. PET was not invented at CERN, but the work carried out by Jeavons and Townsend made a major contribution to its early development.[7]

After these individual efforts, CERN acted in the 1990s as a catalyst for collaborative endeavors spanning beyond particle physics: the Crystal Clear and Medipix international collaborations aimed at developing particle physics detectors and exploring their applications to other fields, including healthcare.[8] Such collaborative efforts often provide the much-needed support to bridge the gap between CERN R&D and the end-user application. Given CERN's focus on fundamental research, it is not surprising that there are a limited number of cases of direct transfer to the healthcare sector, where a technology developed for particle physics is used "as-is" in a medical device. One example is the color X-ray scanner mentioned above. Another recent case is a compact, modular, low-cost linear accelerator manufactured by CERN, which capitalizes on the skills and expertise developed while designing the laboratory's latest linear accelerator.[9] The compact accelerator is suitable for medical applications and has been licensed to a company, ADAM, that is building a next-generation machine for hadron therapy, an advanced form of cancer radiation therapy that uses protons or other ions to treat cancer. Simulation codes initially developed for particle physics have also become crucial to modeling the effects of radiation on biological tissues for a variety of applications in the medical field. The FLUKA simulation package, jointly developed by CERN and the Istituto Nazionale di Fisica Nucleare (INFN), is licensed to various medtech companies.

A major asset to institutions like CERN is their human capital—scientists, engineers, and technicians who have the expertise to develop and maintain innovative technologies and complex technical systems. For example, in the 1990s, CERN leveraged this expertise by contributing to a collaborative design study for a next-generation cancer treatment center that would use

FIGURE 10.1

From CERN knowledge to society



Source: CERN/Geoffrey Dorne.
Notes: Through the laboratory's main technology pillars—Accelerators, Detectors, and Computing—CERN has developed expertise (left) that have found applications in many fields outside particle physics (right). These represent fields where a meaningful knowledge transfer has happened.

both protons and carbon ions.[10] This study provided the technical background for building two of the four European centers providing cancer therapy with protons and carbon ions—the National Centre of Oncological Hadrontherapy (CNAO), Italy,[11] and MedAustron, Austria.[12] CNAO's design was based on the original study, improved by the Foundation for Oncological Hadrontherapy (TERA foundation) and realized with seminal contributions from the INFN—all based in Italy. MedAustron was later constructed using the CNAO design. Beyond the initial design study, CERN had an ongoing agreement with both treatment centers to provide expertise in accelerators, magnets, and training of personnel.

CERN also has unique infrastructures that attract the interest of medtech companies and medical researchers. One example is the CERN-MEDICIS facility that, since 2018, has been producing innovative isotopes for medical and biomedical research by hospitals and other institutes.[13]

Challenges of knowledge transfer from fundamental research

Particle physics has an important role to play in contributing to medical innovation and healthcare technologies. Maximizing the societal impact of basic research requires setting up a number of knowledge transfer strategies and being aware of the challenges ahead. Many of the hurdles faced when trying to apply CERN technologies to the medical and biomedical fields provide important clues for how to optimize these strategies in other application domains, as well as in other fundamental research environments.

As discussed earlier, basic research centers develop technologies primarily for their internal needs. Such technologies are honed and fine-tuned to meet demanding specifications and adapting them to a different application is often not straightforward—and might even require rolling back to an earlier, less customized version. These adaptions may require collaboration with visionary companies who are willing to engage in medium- to long-term partnerships. Even companies with the right mindset and spirit might have difficulty funding such endeavors—when the technology is so disruptive that the market application won't be realized for years and hence does not fit the current market strategy. Funding schemes to bridge the gap between in-house development and market application would catalyze public-private collaborations. Most of the available schemes either fund the initial R&D (proof-of-concept and first prototyping) or the development of a market-ready medical device. However, between prototype and final product, several years of technical developments in close collaboration with clinicians and industry are often needed, and more funding should be made available for this stage. One pioneering initiative is the ATTRACT funding scheme, which is supported by the European Commission's Horizon 2020 Programme and aimed at creating a co-innovation ecosystem for fundamental research and industrial communities to develop breakthrough detection and imaging technologies for scientific and commercial uses.[14]

There is also a need to bridge the cultural gap between companies and the particle physics community. For example, companies do not always know what to expect from a collaboration with scientists and engineers working in big-science endeavors like the Large Hadron Collider. Scientists and engineers not only develop innovative technologies but also have an in-depth understanding of how these technologies work and can be adapted to harsh and challenging environments—ultra-high vacuum, high radiation exposure, superconductivity, superfluidity, and other extreme phenomena. In addition, they are familiar with facing complex problems related to integrating technologies and systems. This unique blend of technical competences and experience in a highly collaborative and interactive environment would be ideal for assisting companies in overcoming their technical challenges.

At the same time, the particle physics community needs to sharpen its efforts: when a potential application for a technology is identified, it is essential to evaluate whether this development would fill an existing need in the medical market or whether the application is trying to solve a problem that is not perceived as such by healthcare professionals. While blue-sky R&D is what drives basic research forward and allows building the experiments of the future, it is important to understand market needs when trying to adapt a given technology to a medical application. A dialogue with all the relevant players on the healthcare side—doctors, medical physicists, and medtech companies—is key to properly assess the potential of a given technology for a specific application, and hence to be able to focus the efforts on the most promising cases. A particularly relevant example is CERN's competences in the data analytics and machine learning domains; as discussed earlier, these competences are essential to harness the full potential of large data sets for personalized medicine. While the LHC experiments generate a vast amount of data, the technical challenges are not the same as those of the healthcare communities. In addition, the computing tools developed at CERN are often highly specialized and only usable by highly skilled scientists. The expectations of end users, such as medical researchers and companies operating in medical and biomedical technologies, may be far from the reality of the computing tools developed at CERN. It would be unrealistic to expect turnkey solutions without further technical developments due to the very different nature of the data sets available in high-energy physics and the medtech field. This makes it crucial to ensure an early dialogue between CERN and potential external partners, as realistic expectations are more likely to result in effective collaborations.

Knowledge transfer at CERN

While a lot of the above can be applied, with some variations, to most laboratories dedicated to fundamental research, a set of challenges is explicitly connected to the CERN environment. For example, the industrial culture at CERN is not as strong as in other research institutions, and therefore it is not always easy to motivate busy scientists to work with a company on the development of a medical device. The nature of CERN as an international organization that is funded by 23 Member States also has implications for the knowledge-transfer process. CERN is bound by its mandate of basic research and cannot become an applied laboratory, meaning that its technologies must be brought to the market by industrial partners. At the same time, CERN being publicly funded implies that companies from all Member States should be given equal opportunities to exploit CERN's technologies. A strategy document outlining knowledge transfer from CERN for the benefit of medical applications sets clear boundaries for these activities.

The knowledge created by CERN's community has the potential to lead to innovation in fields beyond particle physics. This innovation can happen organically, as proved by the early examples of transfer from CERN to medical technologies, but actively investing in the process can also boost its impact and reach. The CERN Knowledge Transfer (KT) group provides advice, support, training, networks and infrastructure to ease the transfer of CERN's know-how to industry and society.[15]

Intellectual property (IP) lies at the core of successful knowledge transfer at CERN. It enables CERN to claim being at the origin of a novel technology, making it possible to share its knowledge and create societal impact. CERN's policy is to disseminate its technologies as widely as possible to industrial and institutional partners within its Member States, however, patenting represents only a tiny part of CERN's approach to IP. CERN will only consider patenting where it might help mitigate the financial risks of investing further in the development of a technology. CERN's patent portfolio currently comprises 34 patent families, a number significantly lower than organizations of a similar size. In addition to its technology portfolio, CERN also has a wealth of scientific and technical competence across areas of expertise, which is accessible through collaboration and consultancy agreements.

Open innovation has been part of CERN's DNA since its inception. Several CERN software technologies are developed with open collaboration in mind. The CERN laboratory is also contributing to many open source projects, small and large, that promote collaboration within the larger community, not only the scientific world. The CERN Open Hardware License, drafted and published by the CERN KT group, was born out of the wish to openly disseminate CERN's hardware designs. The license fosters the dissemination of schematics, hardware documentation, and improvements made to the hardware. The license itself can be used by anyone and is a good example of how CERN's work can have surprising benefits for society—even the availability of open hardware worldwide.

One of the main challenges in the knowledge-transfer sphere is to make it as easy as possible for scientists and other specialists to turn their research into innovations, and CERN invests much effort in such activities. Launched in 2011, the CERN KT Fund bridges the gap between research and industry by awarding grants to projects proposed by CERN personnel where there is a high potential for positive impact on society. Since its creation, 40 projects have been funded, each receiving grants with a value between 15,000 and 240,000 Swiss francs (CHF) over one or several years. In 2016, two European Commission funded projects, AIDA-2020 and ARIES, incorporated a proof-of-concept fund modeled on CERN's KT Fund. CERN also provides a limited amount of seed funding for projects aimed at transferring its technologies and know-how to the medical field. Between 2014 and 2017, 25 projects have been funded with an average grant of about CHF 64,000 per project.

Since the early days of technology transfer at CERN, one main focus has been on knowledge transfer through people—especially early career scientists who work in industry following their contracts at CERN or who start their own company. Over the last 20 years, CERN has continued to build a general culture of entrepreneurship within the organization through many avenues. There are currently over 20 start-ups and spin-offs that use CERN technologies in their business. To assist entrepreneurs and small technology businesses in taking CERN technologies and expertise to the market, the CERN laboratory has also established a network of ten Business Incubation Centres (BICs) throughout its Member States where companies can directly express their interest in adopting a CERN technology. The BIC managers provide office space, expertise, business support, access to local and national networks, and support in accessing funding. Every year since 2008, students from the School of Entrepreneurship (NSE) at the Norwegian University of Science and Technology (NTNU) spend a week at CERN to evaluate the business potential of CERN technologies. Three of the students attending the CERN-NTNU screening week in 2012 started TIND, a spin-off based on CERN's open-source software, Invenio.

Getting the next generation of scientists into the habit of thinking about their research in terms of impact is vital for knowledge transfer to thrive. In 2015, the CERN KT group launched a series of Entrepreneurship Meet-Ups (EM-Us) to foster entrepreneurship within the CERN community. The CERN KT group, with the support of the CERN & Society foundation, also launched the CERN Entrepreneurship Student Programme (CESP), bringing together graduate students from all around the world for 5-weeks of practical and theoretical training at CERN. In 2018, CERN organized the CERN Medical Technology Hackathon (CERN MedTech:Hack) to explore new ways of developing viable applications of CERN technologies in the medical field. The CERN MedTech:Hack took place over three days, during which international teams of students competed to solve topical problems pitched by healthcare organizations and industry partners in the medical field.

Conclusions

Basic research in particle physics is an effective driving force for major technological advances. Bringing such disruptive technologies on the medtech scene is a non-trivial exercise, often because the actual market needs are too far away in time and it is difficult for companies to invest resources in developments outside of their current business plan. CERN and other basic research laboratories should hone their tools and strategies to maximize the impact of their technologies and expertise on societally relevant topics such as healthcare. Understanding what challenges are involved in transferring knowledge from particle physics to the medical field and what lies behind successful cases can offer keys to improving and streamlining the process.

Projects like the LHC can only happen through large-scale international cooperation based on mutual trust. This successful model should be of inspiration when it comes to knowledge transfer, where it is essential for different communities of experts—from academia, industry, and other disciplines—to be in contact and to know and trust each other. When a possible application of a technology is identified, it is essential to evaluate whether this development would fill an existing need in the medical market or whether one is trying to solve a problem that is not perceived as such by healthcare professionals. The scale, complexity, and unprecedented technology needs of such basic science projects require human capital with unique competences. Scientists and engineers from CERN and other research institutes are at the heart of knowledge transfer, as they collaborate with industry while remaining involved in fundamental research, move to the private sector, or start their own business. Getting the next generation of scientists into the habit of thinking about their research in terms of impact is vital for knowledge transfer to thrive.

Fundamental research has a priceless goal: knowledge for the sake of knowledge. Even though the lead times from basic scientific discoveries to practical applications are often long, it is thanks to knowledge that humankind has got to where it stands today. The theories of relativity and quantum mechanics were considered abstract and almost esoteric when they were developed; a century later, we owe them, respectively, the remarkable precision of GPS systems and the transistors that are the foundation of the electronics-based world we live in. Beyond this, particle physics research acts as a trailblazer for disrupting technologies in the fields of particle accelerators, detectors, and computing; these technologies have already greatly contributed to the advances of modern medicine, although their impact is often difficult to track as it is indirect and diffused over time. Supporting the knowledge-transfer process from particle physics to medical research and the medtech industry is a promising avenue to boost healthcare innovation and provide solutions to present and future health challenges. CERN will certainly continue its efforts to maximize the impact of our laboratory's know-how and technologies on society, including—but not limited to—the medical sector.

Notes:

1 Further information about Fermilab is available at www.fnal.gov/

2 Further information about CERN is available at https://home.cern

3 Cofield, 2008.

4 Muller, 2018.

5 Further information about Geant4 is available at http://cern.ch/geant4

6 Illés et al., 2012.

7 Raynova, 2017; Bressan, 2005.

8 Further information is available about the Crystal Clear Collaboration at http://cern.ch/crystalclear and about Medipix at http://cern.ch/medipix

9 Del Rosso, 2015.

10 Bryant, 2000.

11 Further information about CNAO is available at http://fondazionecnao.it

12 Further information about MedAustron is available at https://www.medaustron.at/en

13 CERN, 2017.

14 Further information about ATTRACT is available at https://attract-eu.com

15 Further information about the CERN Knowledge Transfer group is available at http://kt.cern

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