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Nuclear science: The heart of the "Plateau Nord"

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The impact of technology - Embracing innovation

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Nuclear science: The heart of the "Plateau Nord"

EXECUTIVE SUMMARY

Energy needs worldwide are expected to increase for the foreseeable future, but fuel supplies are limited. Completed by others alternative sources, nuclear energy can be a solution to overcome this problem. France, like many other countries such as Japan, China, etc., has chosen to develop nuclear energy production. Even if this production is known and mastered from several years it can appear some radioactive health hazards. Besides weapons most of people considers nuclear science only as a way of energy production and dangerous for health.

The Science Park "Plateau Nord" in Caen (Normandy), has chosen to improve knowledge about nuclear sciences and applications specifically in health. By its nuclear potential Caen wanted to focus research on health. Nowadays nuclear sciences are important in the research and treatment of cancer, heart and nervous diseases.

INTRODUCTION

The discovery of radioactivity in the late 19th century marked the history of humanity and led to major changes in our understanding of matter. The first application targeted medicine and biology via the possibility of "seeing" through the body and of treating it. At the time, "miraculous" powers were attributed (sometimes to excess) to radioactivity. Relatively quickly, awareness grew on the fact that radioactivity could also kill living organisms and that drastic protective measures were required to guard against it.

Progress was never-ending; equipment safety was improved, as was the protection of individuals receiving medical treatment; a concern that remains to this day, hence the major challenges involved in control and radioprotection.

Other applications of nuclear science, such as electricity production, were developed during the 20th century. Yet nuclear science is not currently limited to the energy sector, even if it appears to predominate, given its dedicated resources and generated activity. In the field of medicine, nuclear science is also used to diagnose and to treat affections that could, otherwise, not be treated.

Several other sectors use the effects of radioactive rays, such as industrial radiation, for the production of electronic components, the control of materials and welds or the sterilisation of foodstuffs...
Nuclear science is also used in naval propulsion on certain military ships and, more rarely, civilian vessels.

In the field of culture, nuclear applications are also involved in dating procedures, based on the isotopes contained inside objects, and for heritage preservation.

The "Plateau Nord" Science Park:
The "Plateau Nord" Science Park reunites facilities, pluridisciplinary skills, higher education and research infrastructures in state-of-the-art fields such as:

- Matter, materials, energy
- Health: biomedical, nuclear science for health, oncology, the neurosciences, imaging
- Digital.

THE NUCLEAR INDUSTRY

France

France's nuclear industry was initiated in the 1950s. Whereas nuclear energy is France's leading source of electricity production, it is only the 3rd-ranking source in the world. With around 200,000 direct and indirect jobs, the nuclear sector currently occupies a major position in French industry.

Mapping of nuclear power plants

Normandy

Throughout its territory, Normandy concentrates a large number of nuclear activities divided between 2 major hubs: energy and research on nuclear science and biomedicine.

Normandy localisation

EPR nuclear reactor under construction
Source EDF – Morin Alexis

· **Energy production**

Nuclear energy has been an established activity in Normandy since several decades and includes:

· 3 EDF (French Electricity Board) nuclear power stations
· the AREVA reprocessing plant in La Hague
· the ANDRA (French National Agency for Radioactive Waste Management) storage centre
· the DCNS plant (nuclear-powered submarines).

The establishment of the new EPR nuclear reactor on the Flamanville site is further proof of the sector's significance locally.

Health

The field of medicine has gained a great deal from French expertise in the nuclear sciences. Indeed, ionising radiation is used to diagnose and to treat affections in oncology, neurology and cardiology.

Several major infrastructures have consequently been created in Caen over the past century:
· the François Baclesse Regional Cancer Centre in 1925
· the National Heavy Ion Accelerator (GANIL) in 1975
· the CYCERON medical imaging platform in 1985

The nuclear "energy and health" sector is estimated to represent at least 14,000 jobs in Lower Normandy. Furthermore, Lower Normandy is the only French region to boast the entire nuclear science skills chain, from fundamental research via renowned facilities (CYCERON and GANIL) to industry, via healthcare establishments with state-of-the-art technical platforms (Caen University Hospital, François Baclesse Cancer Centre).

All of the sector's stakeholders are reunited within the NUCLEOPOLIS cluster, which federates industrial, higher education and training and research skills in the fields of energy, health and risk management.

Nucleopolis
NUCLEAR CLUSTER FOR HEALTH & ENERGY

THE NUCLEAR SCIENCES

The power that is captured within the atomic nucleus can be used in a number of civil applications. The first and most obvious application is the production of consumable energy to satisfy the needs of populations and their associated activities, but it is not the only one.

Nuclear energy is also used to diagnose and to cure certain affections, contributing a great deal in cancer care.

Applied to health

For over a century, nuclear medicine has been relying on the use of radionuclides for diagnostic and therapeutic purposes. This discipline largely owes its development to research and to acquired knowledge in the fields of atomic and nuclear physics. In the beginning, France's nuclear medicine and functional imaging were born from the Atomic Energy Commission's will to promote and develop nuclear applications in the fields of biology and health.

In medicine, radionuclides are extensively used:

· to detect and identify potential patients diseases (diagnosis)

· to treat diseases (therapy)

Nuclear medicine uses radiopharmaceuticals that are based on radionuclides which provide radiation component combined to vectors (antibody, small molecule, peptide...) which help to target specifically diseased tissues or cells.

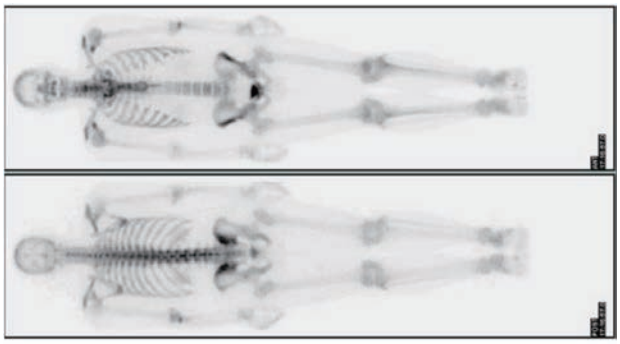
Diagnostic (functional imaging)

Concurrent to their therapeutic action, nuclear applications coupled with state-of-the-art imaging techniques also play a major role during the diagnostic phase and for screening, of cancer in particular. Nuclear imaging consists in the study of an organ or a tissue using radioactive tracers in order to monitor their function to detect potential anomalies.

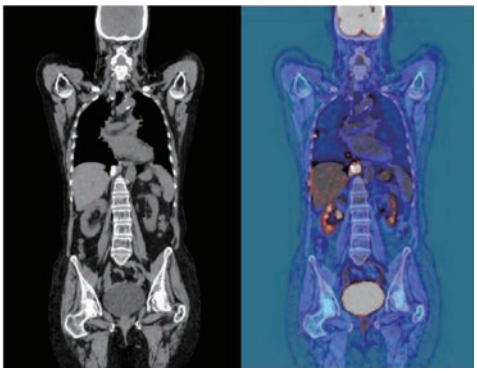
On the North Plateau, CYCERON and its partners are committed to developing this promising prospect.

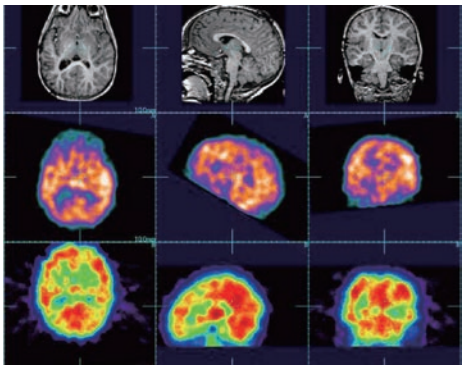
External detectors capture and form images from the radiation emitted by the radiopharmaceuticals taken internally by the patient (intravenously, orally).

· SPECT (Single photon emission computed tomography):



· PET (Positron emission tomography):
Positron Emission Tomography (PET) consists in intravenously administering molecules marked with a radioactive isotope in order to monitor, via external detection, an organ's normal or pathological function. The development of radiopharmaceutical molecules continuously offers nuclear medicine new potential for clinical investigation. The use of molecular markers enables tumoral cells to be monitored.





Economic and social issues
Develop more specifics tracers able to produce more effective images with: ·increased specificity ·sensitivity ·overall accuracy.

Therapy

The high-energy radiation used during radiotherapy permanently damages the DNA of cancer cells, causing them to die.
Radiation therapy can be external, when a device beams radiation at cancer cells from outside or internal, when radiation is introduced inside your body, in or near the cancer cells.

· **External beam radiation**
High-energy particles or waves, such as x-rays, gamma rays, electron beams, or protons, from a source external to the patient.
Radiotherapy, along with (and often in complement to) surgery and chemotherapy, is one of the principal techniques employed to treat cancerous tumours. Radiotherapy uses ionising beams which, by modifying the structure of atoms, alter the gene pool (DNA) of cells, hence leading to the destruction of tumours.
According the INCa (National Cancer Institute), among the 300,000 new cases of cancer diagnosed every year in France, over 180,000 patients benefit, at some point during their disease, from radiotherapy.

Radiation treatment is performed using accelerators that produce photon or electron beams. Thanks to the extreme precision of new techniques, treatment efficacy is increased, whilst reducing the side effects on surrounding healthy tissue.

The development of innovative radiotherapy techniques is a major challenge: latest generation accelerators,

tomotherapy, robotic radiosurgery (Cyberknife). Hadrontherapy is another new and even more efficient radiotherapy modality; however, it is also more complicated to implement. It does not use traditional X-ray beams but beams of particles referred to as hadrons (either protons or carbon-12 ions or other particles).

· Internal radiation or brachytherapy
Implanting (permanently or temporally) a small radiation source inside the body near the tumor.

· Nuclear medicine therapy
Injecting radiopharmaceutical into the patient in order to deliver low doses of radiation directly to the tumor without damaging nearby healthy cells.

Examples of radiotherapy applications:
· Treat and control cancers
· Used in combination with existing treatments to make them more effective
· Palliative treatment to relieve symptoms, such as pain or bleeding

Economic and social issues
· therapy more efficient · fewer side effects · define the best treatment · faster healing · economic impact (less treatments)

Other applications

Several industrial sectors use nuclear applications within their processes. Firstly, industrial radiation is used essentially for sterilising packaging, medical devices, pharmaceutical or cosmetic products and for preserving foodstuffs. Depending on the dose, radiation offers varying preservation durations of the products concerned.

Radioactive sources are also used in gammagraphy (non-destructive control), which offers an appreciation of potential lack of homogeneity in materials, metal in particular for which weld beads can be verified.
Radiation is also used to produce a number of new materials (composite ceramics for example).

In the field of plastics, radiation at the heart of polymeric materials can lead to significant changes in mechanical and physicochemical properties.

Furthermore, radioactive sources are used to control various parameters. For example, in air quality control, they enable atmospheric dust to be measured by controlling dust content in factory waste. They can help measure liquid, density and weight, soil density and humidity in agriculture and public works, and core logging which involves the measurement of geological soil properties using a probe.

The "Plateau Nord" SCIENCE PARK

History

Normandy boasts an exceptional scientific, technological, medical and industrial environment in the field of nuclear science applied to health (medical imaging and radiotherapy), covering the entire value chain from fundamental research to clinical development.

Caen, in Normandy, has chosen to improve knowledge about nuclear sciences and applications specifically in health. By its nuclear potential Caen wanted to focus research on health. Nowadays nuclear sciences are important in the research and treatment of cancer.

Key dates

· 1973: construction of Centre François Baclesse (Comprehensive Cancer Centre)
· 1974: construction of CHU (university teaching hospital)
· 1975: Created by the CEA (Nuclear Energy Commission) and the CNRS (National Centre for Scientific Research) in the GANIL (National Heavy Ion Accelerator) is a major facility serving
French and European research;
· 1983: First experiment was conducted in GANIL;
· 1985: creation of CYCERON (biomedical imaging platform);
· 2010: two new structures have been developed to ensure the continued development of the ARCHADE project: SAPHYN (a semi-public company the aim of which is to develop nuclear physics applications for health care and to transfer technologies towards industry);
· 2015: The project will be operational in and will open new horizons for research on nuclear properties.

Key figures

The "North Plateau" stretches over a surface area of 2,000 hectares and encompasses:
· 16,000 jobs
· 14,000 students
· 1,200 researchers

Over 30,000 people converge there every day. From the shopping precinct to the engineering schools, the University Hospital to training institutions, from the GANIL to the university campuses, the plateau concentrates a high density of activities.

Facilities and infrastructures

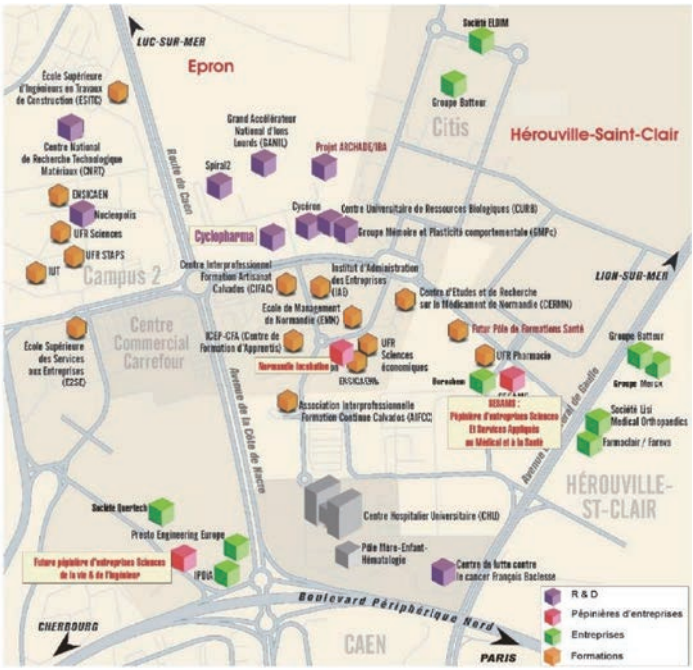
Several facilities and infrastructures are connected with nuclear science.

The "Plateau Nord" Science Park encompasses facilities and high excellence laboratories coordinated by major national (CEA, CNRS, INSERM) or regional (ENSICAEN, Caen University) organisations and institutions.

This research and innovation Science Park, located in the vicinity of the GANIL and the CYCERON imaging platform combines internationally renowned skills in the field of radiobiology, radiopharmacy, radiochemistry, hadrontherapy, dosimetry, instrumentation, beam control, medical imaging, image analysis and radioprotection.

The "North Plateau" Science Park reunites research, higher education and training and healthcare establishments which ensure the continuum between technological, preclinical and clinical research and

higher education and training.



The "Plateau Nord"
Source NUCLEOPOLIS

GANIL

The GANIL (National Heavy Ion Accelerator) is one of four of the world's leading laboratories in the field of ion beam research. Experimentations are in fields ranging from radiotherapy to atomic and nuclear physics, from condensed matter to astrophysics. GANIL researchers work with research teams and companies throughout the world.

In nuclear physics, the GANIL has contributed towards a number of discoveries on the structure of the atomic nucleus, on its thermal and mechanical properties and on nuclei referred to as exotic, for they do not exist in a natural state on Earth.

Every year, hundreds of researchers from across the globe conduct their experiments using beam's at the GANIL's host platform, CIRIL (Interdisciplinary Centre for Laser Ion Research).

The installation of SPIRAL2 (2nd generation Production System of On-Line Radioactive Ions), currently under construction at the GANIL, will offer France and Europe a genuine technological and scientific lead. The facility will use extremely high density and quite unique radioactive (exotic) beams. Before the 2015 year end, these original particle beams will enable, not only the exploration of new radioisotopes, but also the study of new radioactive element production modes for use in nuclear medicine.

Via the National Heavy Ion Accelerator (GANIL) and associated university laboratories, Lower Normandy is home to vast scientific potential in the fields of research into ion-matter interactions and materials. Furthermore, this specific research theme is a major federator for research and higher education throughout the region.

The GANIL is a facility shared by the CNRS and the CEA, each with an equal share and reunited within an EIG (Economic Interest group) since 1976, the year that followed the decision to install the facility in Caen. It has been operational since 1983 and acknowledged as a "Grande Installation Européenne" (Large European Facility) since 1995. It employs 250 physicists, engineers and technicians, and welcomes around 100 trainees and PhD students every year.

GANIL
Source Jean-Marc PIEL

CYCERON IMAGING PLATFORM

Created in 1985, CYCERON is a GIP (Public Interest Group) under the administrative supervision of major national institutions (CEA, CNRS and INSERM).

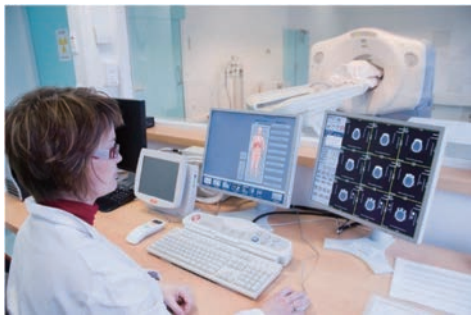
CYCERON is, first and foremost, an imaging platform, renowned for its biomedical research and innovation, the originality of which lies in the fact that it explores from the gene to human or animal behaviour.

This medical platform reunites radiopharmaceutical production tools and imaging machines: PETCT, MRI…

This nationally renowned platform's operation and development is coordinated by 40 engineers and technicians, pooled together in shared departments.

The platform concentrates on 4 key themes:
· Molecular and cellular biology: a theme reuniting activities such as neural cell culture, protein production. The unit is equipped with high-performance microscopic equipment in order to conduct fundamental research upstream of neuropathological disorders.

· Radiochemistry: which enables the development and synthesis of biological tracers marked with positron-emitting nuclei and for which CYCERON has its own cyclotron, robots, leaden hoods and clean room for producing and controlling radiopharmaceuticals prior to their injection.
· Preclinical imaging: essential phase in biomedical research, which uses an animal model. The unit's principal equipment comprises physiology and surgery rooms, a micro-PET machine and a 7 Tesla MRI, all specifically designed for small animals.
· Imaging in humans: a theme for which radiochemistry research is coupled with a hybrid positrons camera coupled with an X-ray scanner, a wide bore 3 Tesla MRI machine and an electroencephalography (EEG) recording room.



CYCERON
Source CYCREON

IMOGERE
Source IMOGERE

CURB
University Biological Resource Centre, animal production, hosting and experimentation platform for research purposes (for public and private laboratories)

· IMOGERE
Located within Caen University, the IMOGERE platform offers facilities and equipment adapted to suit the implementation of experimental protocols requiring the use of radioactive elements. This unit also offers services in the field of radioprotection, radioactive element storage and radioprotection training.

· La Maison des matériaux

A project to create a Maison des Matériaux (House of Materials) is underway with the aim of federating regional stakeholders in the field of materials. It will offer:
· meeting points via the hosting of research teams from a few laboratories
· business accommodation for start-ups
· international representation for associated structures

- The project: construction of 4 technological halls:
· Micro-electronics technology hall (thin films) with local SMEs and international groups located within the region
· Crystallogenesis technology hall: flash synthesis processes (SPS laboratory), HT microwave (CRISMAP laboratory),
· High-temperature Ceramic technology hall
Additive Production technology hall: additive production (3D printing).

Research laboratories

A number of laboratories on the "Plateau Nord" favour research excellence in the field of the nuclear sciences:

· LPC: Corpuscular Physics Laboratory, specializing in dosimetry and instrumentation

Within the laboratory, the "Industrial and medical applications" group is renowned in the fields of beam control, dosimetry and dose simulations and calculations for radiotherapy.

In partnership with the Belgian company IBA, the team has also developed an IC2/3 monitoring chamber for scanned proton beams (Pencil Beam Scanning), currently industrialised by IBA on its protontherapy machines.

· CIMAP: The Centre for Research on Ions, Materials and Photonics

The AMA (Atoms, Molecules, Aggregates) group focuses on understanding the physical phase of ionising radiation damaging.

· GREYC: Caen Research Group in Computer Science, Imaging, Control and Instrumentation

This laboratory boasts a number of skills in the health field: simulation, dosimetry, simplification algorithms, clinical trial data analysis, decision-making software for medical diagnosis, imaging analysis...

· LARIA and MILPAT:

The LARIA (Host Laboratory in Radiobiology with Accelerated Ions) and MILPAT (Cellular and Pathological Microenvironments) laboratories focus on the study of radiobiology during high-density electronic excitation on biological matter.

· ISTCT (Therapeutic Strategies and Imaging for Cerebral and Tumoral Pathologies):

The ISTCT unit is a pluridisciplinary team including the following 3 major skills:

1.Radiochemistry/radiopharmaceutical: chemistry, radiochemistry, automation, regulatory radiopharmaceutical procedures for clinical application

2.Preclinical: animal models and TEP and MRI imaging of rodents or non-human primates.

3.Clinical: PET and MRI imaging, clinical research centres, in particular early phase studies

Automated appartus
Source CEA LDM-TEP

The ISTCT laboratory works with a number of industrial partners and international academic laboratories. The ISTCT group is one of the partner teams of the IRON (Innovative Radiopharmaceuticals in Oncology and Neurology) Laboratory of excellence (Labex), created in 2012. The IRON project is a national network covering eight French towns including Caen and Nantes.

Lead-shielded hot-cell
Source CEA LDM-TEP

The IRON project aims at transferring innovative radiopharmaceuticals for use in PET imaging, for they are essential for developing personalised care programmes, a major challenge in the fields of neurology and oncology.

Cancer care centres

In Normandy, high-performance nuclear medicine is present in the form of the Caen University Hospital (CHU) and the François Baclesse Cancer Centre (CLCCFB), both establishments having missions in healthcare, research and teaching. They are both renowned as reference cancer care centres.

Imaging
Source CHU Caen

Cyberknife
Source CRLCC François Baclesse

They offer ultra high-performance nuclear medicine departments with state-of-the-art technical equipment (scintigraphy, PET-scan camera, CZT camera...).
Since 2008, the CLCCFB has made considerable investments to acquire a range of latest generation equipment which has rendered its radiotherapy department one of the most efficient in France:
brachytherapy, tomotherapy machine, Cyberknife…

The CHU and the CLCCFB also boast significant research team in the fields of clinical research and cancer research: the CLCC François Baclesse has also received Inca (National Cancer Institute) certification as a clinical research centre specialising in early phase trials on innovative molecules to treat cancer. Concurrently, the CHU has developed a Research hub comprising a clinical research
centre, a biological resource centre, a biostatistics unit, a clinical research unit in oncology and an epidemiology research and evaluation unit.

Higher education and training

The Lower-Normandy offers vast higher education and training potential which ranks Lower Normandy among France's 3 leading regions in the field.

Firstly, specific higher education establishments offer nuclear science courses and impressive learning platforms, such as:

- ENSICAEN (National Graduate School of Engineering)
- ESIX (Cherbourg Engineering School)
- INSTN (National Institute for Nuclear Science and Techniques).

These schools dispense over twenty top-level courses focusing on nuclear science applied to health, such as the International Master's Degree in "Sustainable Nuclear Engineering Applications and Management", including the NUTMA (NUclear Technologies for Medical Applications) option, which enables students to acquire scientific knowledge in the various nuclear technologies deployed in medicine (radioisotope production, diagnosis, therapy, radioprotection, waste management…).

The "Plateau Nord" Science Park concentrates a vast array of education and training options directly associated or related to the nuclear sciences.

Around 25,000 students prepare for tomorrow's associated professions within this Science Park:

- University of Caen
  - Faculty of medicine: 3,700 students
  - Faculty of pharmacy: 800 students
  - IAE (Business Administration Institute): 2,200 students

- ENSICAEN (National Graduate School of Engineering)
  - 750 engineering students,
  - a laboratory staff of 650 (lecturers, researchers, technicians, administrative employees) - 177 PhD students

- ESITC (Caen Higher School of Civil Engineering)
  - 260 engineering students

- EMN (Normandy Business School)
  - 2,900 students

Other block release courses are also on offer within the Science Park.

- Healthcare Training and Research Centre

This centre welcomes the 4,000 students from the faculty of medicine, the IFSI nursing school and the midwifery school. Researchers will be moving to their new premises at the start of the 2015 academic year.

The establishment comprises teaching classes, laboratories and work rooms. The construction is based on eco-responsible techniques including environmentally friendly materials such as wood. Renewable energies have also been integrated via photovoltaic panels, rain water recycling and a wood boiler room.

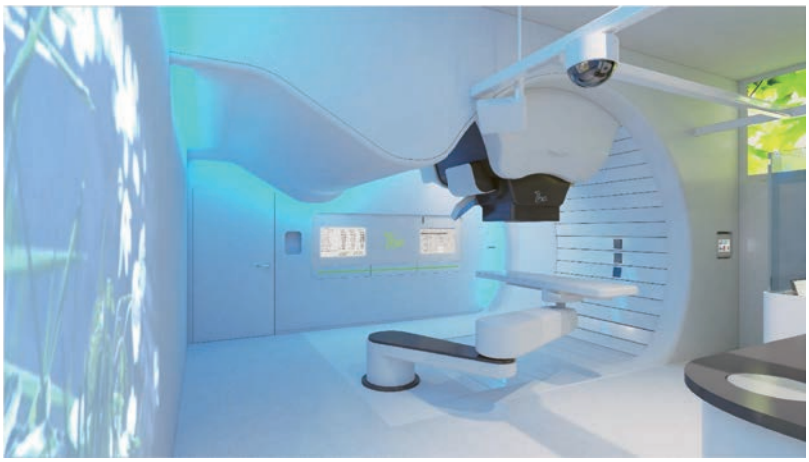
Healthcare Training and Research Centre
Source Caen University

MAJOR PROJECTS

ARCHADE

A great number of the structures in Lower Normandy involved in nuclear science applied to health have joined forces round a foundation project aimed at creating a European Hadrontherapy Resource Centre within the North Plateau: the project has been named ARCHADE (and will be entering its operational phase in 2018)

Funding was officially secured in December 2014. ARCHADE is a European research and development centre entirely dedicated to hadrontherapy, a new, more accurate and more efficient form of radiotherapy for certain types of cancer. Indeed, Hadrontherapy (protontherapy/proton or carbon ion beams) enables the maximum dose of radiation to be administered within the tumour, whilst offering improved protection of the patient's healthy tissue.



Proteus One
Source IBA

The 3 aims of the ARCHADE project:

· The Healthcare aim: One of the ARCHADE project's major aims, as early as 2018, is to provide cancer treatment thanks to an innovative protontherapy technology. In the wake of Nice and Orsay, Caen will become the third French town capable of treating cancer patients by protontherapy thanks to the "Proteus One" machine, supplied by the Belgian company IBA. The ARCHADE project will therefore satisfy increasing health needs in protontherapy.

· The Research aim: The ARCHADE project's second aim consists in developing, by 2020, a European Carbon Ion Research, Development and Training Centre in Caen. Today, carbon ions are already used in Japan, and more recently in Germany; however further research effort is needed to validate their therapeutic efficacy compared to other available treatment options.

· The Industrial aim: An industrial consortium, Normandy Hadrontherapy, comprised of the IBA group and highly committed French industrial partners, aims at developing, validating and manufacturing – in Caen -

a new latest generation particle accelerator (protons and carbon ions), the Cyclone®400 cyclotron. This R&D ambition made is possible in Lower Normandy thanks to the presence of a network of researchers and industrial stakeholders, reunited within the Nucleopolis cluster and offering the essential skills to ensure the programme's success.

Once tested and validated for therapeutic use by Normandy Hadrontherapy's teams, the C400 prototype will lead to the creation of a genuine and innovative industry sector: design, realisation, operation, maintenance and international marketing of the system. Production of other C400 cyclotrons, each at a cost of several tens of millions of Euros, will offer partner companies long-term activity to serve a high-growth international market. The project, coordinated by Normandy Hadrontherapy and supported by Nucleopolis, is no less than an emerging market that will generate a major and positive industrial, economic and social impact for Normandy.

The North Plateau will make Normandy the only French region to be currently equipped with carbon ion beams thanks to the GANIL facility and which, with the ARCHADE project, will offer a machine for protontherapy and a machine for hadrontherapy carbon for cancer care.

The presence of all these exceptional facilities, reunited on Caen's North Plateau, is unique in Europe and offers Normandy undeniable singularity.

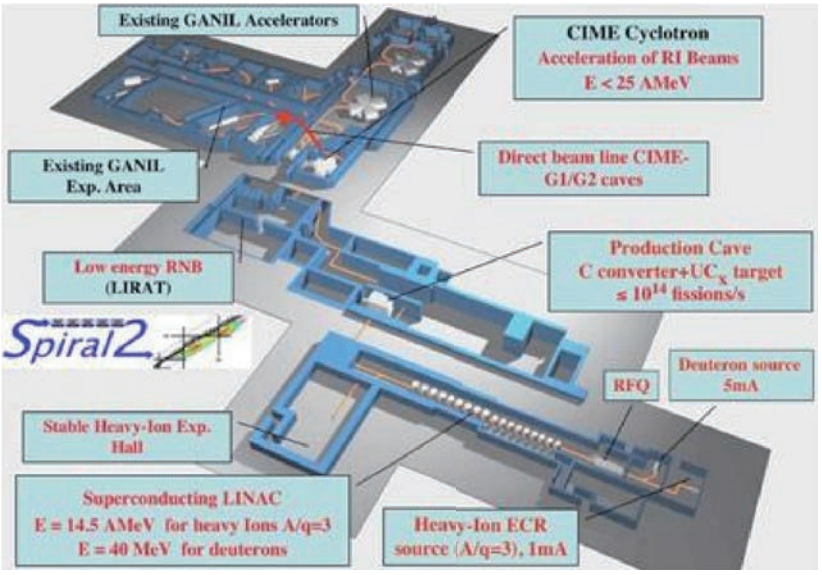
SPIRAL 2

SPIRAL2 (2nd generation Production System of On-Line Radioactive Ions) is a project to install a linear particle accelerator for fundamental nuclear physics study and interdisciplinary research at the GANIL.

The facility, which is as big as the present-day GANIL, will produce totally unique beams and will accelerate radioactive light and heavy (exotic) nuclei at extremely high intensities. Before the 2015 year end, these original particle beams will enable, not only the exploration of new radioisotopes, but also the study of new radioactive element production modes for use in nuclear medicine.

Within a context of demographic growth, population ageing and increased cancer incidence, the need for radiopharmaceuticals for nuclear medicine is quite considerable. One of the key obstacles in the development in radiopharmaceuticals is the supply of raw material in the form of medical radioisotopes. This is why the GANIL hopes to study new production methods for relevant radioisotopes in order to optimise their synthesis and ensure sufficient supply for clinical needs. Progress in the field at the GANIL could generate a considerable economic and social impact for the development of nuclear medicine.

With this prospect in mind, the GANIL is already working in partnership with teams in Normandy and laboratories in the Pays de Loire region, in order to study production methods for the following radioisotopes: $_{211}At$, $_{68}Ge$, $_{64}Cu$.



SPIRAL 2
Source Spiral 2

AREVA MED

AREVA Med is an AREVA subsidiary created in 2009 to develop innovative therapies to fight cancer.

Based on an R&D program started in 2005, AREVA Med develops new processes for producing highpurity lead-212 (212Pb), a rare radioactive isotope. 212Pb is currently at the heart of promising research projects in nuclear medicine to develop new treatments against cancer.

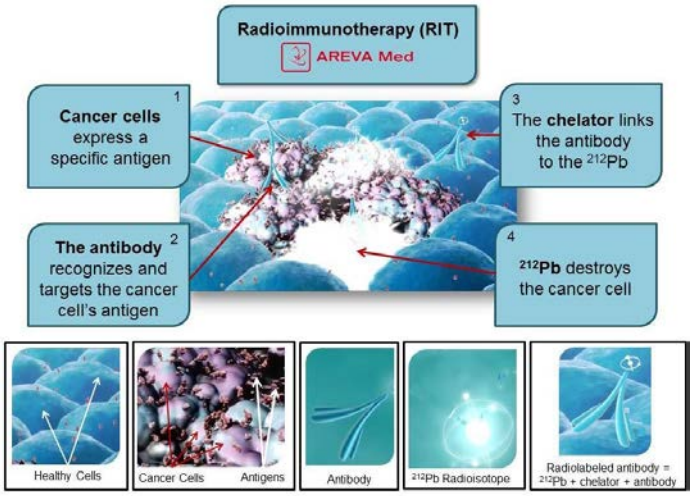
The innovative approach, known as targeted alpha therapy (TAT), recognizes and destroys cancer cells without damaging nearby healthy cells. Lead-212 is a rare metal used in the development of targeted and innovative treatments for certain cancers that do not respond to other conventional methods.

The scientific and technical environment of excellence, the reputation of Nuclear Medicine teams, the international influence and intensity of partnership relations with economic actors were decisive in the choice for the implementation in Caen for the production facility of AREVA Med
212Pb (alpha radioimmunotherapy).

The future production facility of AREVA Med, the subsidiary dedicated to the development of cancer treatments, will provide a large-scale production capacity. Based in the Basse-Normandie region, the construction of this facility will be confirmed following important scientific programs underway.

Lead-212 is being used currently in a Phase 1 clinical trial coordinated by AREVA Med at the University of Alabama at Birmingham in the United States. Several new scientific partnerships are currently being studied.

Today, the time has come to move on to the construction of a new production unit on Caen with the objective - if clinical trials are successful – to plan the first production for 2020.



AREVA Med
Source Areva Med

INNOVATION AND VALORISATION

The Caen conurbation is home to a number of different structures which, on a day-to-day basis, offer support to project initiators to help them valorise their innovations and create new innovative businesses: valorisation cells at Caen University, ENSICAEN, GANIL, Normandie Incubation and the Business Innovation Centre (SYNERGIA).

In complement, business incubators and enterprise zones offer these young companies a framework and support to satisfy their needs.

Technology transfer

4 Examples of research valorisation:

· Creation of Pantechnik: Pantechnik is a company created in 1991 in order to valorise GANIL patents.

· Technology transfer between the Caen University Hospital and the company APTIPLUS, to valorise a tool for cardiac imaging.

· Creation of Datexim: Datexim is a company created in 2011 by members of ENSICAEN's GREYC laboratory.

· Clinical development of a radiopharmaceutical: The ISTCT's LDM-TEP team (located within the CYCERON PIG) recently developed a new radiopharmaceutical drug ([18F]-Fludarabine) for use in PET imaging of lymphoproliferative diseases.

A preclinical study conducted in Caen has already established proof of the concept on animal models, demonstrating the superiority of this new radiopharmaceutical in terms of specificity, compared to the current reference molecule, [18F]-FDG. In 2014, following approval from the ANSM (National Drug Safety Agency), the LDM-TEP team was able to launch the first clinical study using its new drug on humans (ongoing phase 0 trial).

Support for start-ups

· The regional incubator

Normandie Incubation, the regional incubator for innovative technology businesses, was created in 2000 by the University of Caen Basse-Normandie (UNICAEN) the National Graduate School of Engineering (ENSICAEN) and the Large Heavy Ion Accelerator (GANIL).

The incubator's mission is to encourage business creation in the field of innovative technology, in association with public and private research throughout Lower Normandy. Technological innovation project initiators are from:

· public research
· the private sector in partnership with a public laboratory - industrial spin-off.

· Business incubators

· SESAMS (Sciences and Services Applied to Medicine and Health):

SESAMS is an incubator and enterprise zone for businesses from the healthcare and medical sector.

Within SESAMS, companies can find solutions to suit their needs, depending on their date of creation and their aims. The incubator can accommodate up to 7 businesses, over a surface area of 1,600m2. SESAMS is also a commercial lessor, offering businesses leased offices.

Ideally located on the "Plateau Nord" Sciences Park, at the heart of higher education & training, innovation and research, SESAMS adapts to suit the needs of the businesses it hosts via a range of packages.

Five young companies are already accommodated by the business incubator:

· BOROCHEM (production of chemical products)
· MEDGIC Group (technologies et services numériques pour la santé et l'automobile)
· NORMANDY BIOTECH (thérapie cellulaire)
· SC Partners (prestataire de communication scientifique)
· Laboratoire LCS (contact lens manufacturer)

LCS
Source Ouest-France

· PLUG N'Work (digital sciences):
Business accommodation and coaching solutions over a surface area of 1,000m2 are also available in the vicinity of the Science Park, in the "Plug N'Work" enterprise zone.

The nuclear cluster for health and energy

By creating synergies among its resources via the NUCLEOPOLIS cluster, Normandy has become an unquestionable reference in the field of "Nuclear science for health", serving oncology in particular. Over recent years, the Lower Normandy Regional Council, the Caen la Mer Urban Community and Caen University have decided to make nuclear science applied to health a priority in their specialisation strategy.

Source NUCLEOPOLIS

An innovative industrial fabric

The "North Plateau" Science Park enables the region to attract enterprise within a centre of excellence.

These companies combine to offer the essential skills required for the creation of a genuine industrial sector devoted to nuclear science for health:
· instrumentation and dosimetry
· development and manufacture of equipment for particle accelerators
· development and production of radiopharmaceuticals
· image analysis
· evaluation of clinical trials and radioprotection.

A few examples of companies established within the vicinity of the "North Plateau" Science Park and which work in direct association with the park's stakeholders:

· **PANTECHNIK :**

PANTECHNIK was created in 1991 in order to valorise GANIL patents. Today, the company is the world leader in the development and the production of ECR (Electron Cyclotron Resonance) ion sources.

PANTECHNIK
Source PANTECHNIK

· **CYCLOPHARMA :**

The CYCLOPHARMA laboratories specialise in the design, production and exploitation of radiopharmaceutical products. CYCLOPHARMA uses the technical equipment available on the CYCERON platform to produce Glucotep, an isotope used to diagnose and monitor cancerous pathologies. With a market share of around 40%, CYCLOPHARMA is the French leader in the sector.

CYCLOPHARMA
Source CYCLOPHARMA

· ADCIS:

ADCIS is a company which publishes software and develops 2D and 3D image processing and analysis applications, together with applications specifically designed for the medical field.

· CERAP:

CERAP is one of the region's healthcare establishments' key partners for it accompanies them, from design to facility control, whilst ensuring staff training and the necessary technical and regulatory support for the in-house use of ionising radiation sources.

· IBA:
IBA is the world leader in the development and manufacturing of medical devices and software for cancer diagnosis, cancer care by protontherapy and for dosimetry.

· OREKA Ingénierie:
Created in 2010, OREKA Ingénierie offers engineering services in mechanical design, boilermaking, ventilation and tubing. To position and distinguish itself and to promote its high added value, the company has chosen to specialise in the field of 3D video animation for technical applications, for training and for ergonomic adaptation of work rooms and stations.

· PIERCAN :
PIERCAN is the leading company in the field of glovebox and laboratory gloves and of technical parts in natural or synthetic rubber. Among other products, the company develops and markets gloves that protect against ionising radiation and radioactive contamination.

· ROBATEL :
Designs, fabrication, assembly and tests of Hot cells and glove boxes, Neutronical and thermal shielding, Shielded doors and hatches, Lead shielding, Treatment installations for radioactive wastes.

PARTNERSHIPS

In the field of nuclear science applied to health, Normandy's researchers work in collaboration with industrial and academic partners from across the globe.

Examples of international projects

· VP2HF (Plateform for understanding and treating heart failure)
Heart Failure (HF) is one of the major health issues in Europe affecting 6 million patients and growing substantially because of the ageing population and improving survival following myocardial infarction. The poor short to medium term prognosis of these patients means that treatments such as cardiac re-synchronisation therapy and mitral valve repair can have substantial impact. However, these therapies are ineffective in up to 50% of the treated patients and involve significant morbidity and substantial cost.

The primary aim of VP2HF is to bring together image and data processing tools with statistical and integrated biophysical models mainly developed in previous VPH projects, into a single clinical workflow to improve therapy selection and treatment optimisation in HF.

The tools will be tested and validated in 200 patients (including 50 historical datasets) across 3 clinical sites, including a prospective clinical study in 50 patients in the last year of the project. The key innovations in VP2HF that make it likely that the project results will be commercially exploited and have major clinical impact are:
1)all tools to process images and signals, and the obtained statistical and biophysical models, will be integrated into one clinical software platform that can be easily and intuitively used by clinicians and tried out in the prospective clinical study and

2)by utilising a decision tree stratification approach, only the appropriate parts of the tool chain, that will add maximum value to the predictions will be used in individual patients, so that the more resource intensive parts

will be used when they will add real value.

· ERIVAC (European Radiopharmaceutical Industry Value Chain)
NUCLEOPOLIS, Norman cluster of nuclear sciences, participates in an EU project “ERIVAC” within Horizon 2020 INNOSUP call-1-2015 “Cluster facilitated projects for new industrial value chains”.

The consortium consists of 5 clusters from France, Belgium, Italy and Germany with health, radiopharmaceutical innovation and 4P-medicine as part of their focused areas of expertise.

Others projects
Over and above INTERREG (European programs), several collaborative projects have been developed in nuclear science applied to health with, in particular:

· Research centres:
  · Karolinska Institutet à Stockholm (Sweden)
  · Southampton University (UK)
  · ANSTO à Sydney (Australia)
  · Hôpitaux Universitaires de Genève (Switzerland).

· Industrial partners:
  · CYCLOPHARMA (France)
  · GUERBET (France)
  · MDS NORDION (Canada)
  · ONCODESIGN (France) - ARIANA (France)
  · TRASIS (Belgium).

Examples of national projects
· IRON Labex

The scientific objective of the IRON « Innovative Radiopharmaceuticals in Oncology and Neurology » Labex is to develop innovative radiopharmaceuticals and transfer them to the clinic for molecular imaging diagnosis (PET: Positron Emission Tomography) in neurology and oncology and targeted radionuclide therapy of cancer.

These radiopharmaceuticals will participate in the development of personalized medicine, to guide patients to appropriate targeted therapies or treat tumor disease refractory to conventional treatment.

To achieve this objective, the IRON Labex is based on:
· an ambitious cooperative translational research program in nuclear medicine,
· research teams with complementary areas of expertise, from innovative radionuclide production to clinical research, located in Angers, Caen, Orléans, Nantes, Rennes, Strasbourg, Toulouse, et Tours,
· a network of cyclotrons producing fluor-18 (Caen, Tours, Toulouse), but also innovative radionuclides for diagnostic applications (cuivre-64, scandium-44/44m, gallium-68, zirconium-89) and therapy (cuivre-67, scandium-47, astate-211) (cyclotron ARRONAX in Nantes, cyclotron Cyrcérecently installed in Strasbourg).

GENESIS

Developing the experimental analysis of radiated materials on the nanoscale to improve safety studies, as well as of aging of new materials used, especially in nuclear facilities (including ceramics for Generation IV or materials for nuclear fusion and ITER, the International Thermonuclear Experimental Reactor).

· Impacts for communities and peoples' lives

SCIENCES
These studies are intended to lift some technological blocks in the analysis of degradation due to radiation by neutrons of materials. The results will make it possible to better understand phenomena on the atomic scale and improve the modelling and simulations, especially on the aging of components of nuclear systems. Observations on the nanoscale will make possible real progress in the understanding of phenomena causing the degradation of materials
COMMUNITIES
Maintain throughout the life of a nuclear reactor, a high level of safety and energy and economic performance capabilities meet major challenges. In this area, the control of materials aging plays a key role. The general problem of the energy mix, the questions about extending the life of existing power plants, the nuclear safety after the Fukushima accident are crucial.

EMC3

The EMC3 projet called « Energy Materials and Clean Combustion Center ». This research centre is the only one dedicated to Materials for Energy and Clean Combustion.

Involving 700 researchers including more than 200 PhD students, the EMC3 activities focus in particular on materials for energy recovery, safety of nuclear installations, development of new materials from eco-friendly methods and on the improvement of fuel, combustion, exhaust gas decontamination and thermal energy recovery.

· Impacts for communities and peoples' lives

SCIENCES
Continuum of research from basic research of the highest level on materials to applied research and partnership in the automotive field.
COMMUNITIES
Research for new eco-compatible materials for energy. Research to reduce energy consumption and recover it.

France HADRON

Radiotherapy is the medical use of ionizing radiations to treat cancer. Conventional radiotherapy uses X-rays (high-energy photons) administered to the patient in order to destroy tumorous cells. When these radiation beams consist of charged particles (protons and other

ions such as carbon), this radiation therapy is known as hadrontherapy. Hadrontherapy strength lies in the unique physical and radiobiological properties of these particles. Indeed they can penetrate tissues with little diffusion and can deposit a maximum of energy just before stopping. This allows a precise balistic of the specific region to be irradiated. Tumor can be efficiently irradiated while damages to healthy tissues are lower than those done with X-rays.

To enable the consolidation of all medical, scientific and technical teams involved in hadrontherapy in France, the actors, mainly federated by universities and national public research institutions (CNRS, CEA, INSERM, IRSN) have gathered themselves to present a project in response to the call for projects "National biology and Health Infrastructure" called France HADRON. In April 2012, the project gets the label Future Investment and was financed with 15M €.

France HADRON aims are to:
· coordinate and organize the national program of research and training in hadrontherapy. This program goes from the physics of particle to clinical research through dosimetry, radiation biology, imaging, control of positioning target, and quality control instruments
· organize, facilitate and finance the access of the researchers to the particle beams required for the experimental work;
· finance certain methodological research to increase the research-platforms efficiencies;
· finance part of the equipment and research buildings platforms;
· and finally ensure participation in international programs such as those already existing and highly invested by the French teams: ENLIGHT, Partner, ULICE, ENVISION, ENTERVISION.

· Production of an innovative radioisotope
Since 2014, researchers from Caen (GANIL, LPC) and from Nantes (ARRONAX) have initiated a collaborative project aimed at studying the production of an innovative radioisotope: astatine-211.

· Higher education and training
Master International «Sustainable Nuclear Engineering Applications and Management»
The MSc in Sustainable Nuclear Enigneering – Applications and Management (SNEAM) is a Joint Degree between ENSICAEN and Mines-Nantes.

It consists of a two year program with the first year dedicated to base teaching and training (physics of ionizing radiation, radioprotection, physic-chemistry of environment, introduction to nuclear technology….) and the second year is dedicated to 3 specializations.

The students have to choose one among:
· Advanced Nuclear Waste Management
· Nuclear Energy Production and Industrial Application
· Nuclear Technologies for Medical Applications

The 4th semester consists of the Master thesis project in industry or R&D laboratory.
The scientific and technical skills acquired are complemented with economy and management skills.

CONCLUSION

The "Plateau Nord": at the heart of territorial development

In Normandy, the field of nuclear science applied to health represents an exceptional environment. This ecosystem generates valorisation in a number of forms (industrial contracts, publications, patents, creation of start-ups) and encourages the emergence of foundation projects such as the creation of the ARCHADE hadrontherapy centre.

The "Plateau Nord" represents:

· 15 laboratories that are certified by major organisations (CEA, CNRS, INSERM)
· 4 "Investissements d'Avenir" (Investments for the Future) programmes
· 1 "Equipex" facility of excellence (project funded by the French gouvernement)
· renowned healthcare centres: Caen University Hospital (largest in Normandy) / Baclesse Centre (Cancer care)
· internationally renowned research platforms (GANIL, CYCERON, CURB, IMOGERE)
· top-level higher education and training

The NUCLEOPOLIS cluster federates stakeholders and innovative businesses via close links with the "Plateau Nord".

The "Plateau Nord": a tool to serve attractiveness

The "North Plateau" Science Park concentrates facilities and high excellence laboratories coordinated by major regional and national organisations.

Every year, health-related skills that are internationally acknowledged draw hundreds of experimenters from across the globe.

The Science Park's great scientific wealth, complemented by territorial development institutions, leads to the emergence of sustainable economic activities. It enables significant societal, environmental and economic repercussions: it confers the "Plateau Nord" with the role of a "promise for the future"...