



## PRESS RELEASE

January 28, 2025

With the support of



World Cancer Day February 4, 2025



Flash RAdiation THerapy Electron Acceleration

## Institut Curie enters a new era of FLASH radiotherapy

On the eve of World Cancer Day, February 4, 2025, Institut Curie announces the operational launch of a project of unparalleled scope: FRATHEA (*Flash Radiation THerapy Electron Acceleration*) on its Orsay site, located in the heart of the Saclay plateau. Led by Institut Curie, in collaboration with CEA, the FRATHEA project is funded by France 2030 and the Île-de-France Region, with a total investment of 37 million euros. The goal is to install a very high-energy electron beam irradiator (VHEE) at the heart of Institut Curie hospital in Orsay and to demonstrate the effectiveness and safety of FLASH-VHEE radiotherapy. By 2028, the aim is to have a one-of-a-kind platform in the world to begin the first clinical trials involving patients with cancers of poor prognosis. This groundbreaking technology aims to treat incurable cancers for which current treatments have been largely ineffective and where little to no therapeutic progress has been made in recent years. It also seeks to minimize the side effects of anti-cancer therapies while shortening and lessening the burden of treatments.

**Prof. Alain Puisieux, Chairman of Institut Curie's Executive board :** " *A historic cradle of radiotherapy, Institut Curie, thanks to its multidisciplinary teams, has acquired unrivalled international expertise in FLASH technology. Today, the FRATHEA project is the culmination of Dr. Vincent Favaudon's research work, and the turning point initiated some ten years ago at Institut Curie. Our ambition is to create a groundbreaking industrial dynamic at the heart of a scientific and medical cluster in the Paris region that is unique in Europe, and to transform our commitment into a clinical reality for patients.*"

By 2050, the number of new cancer cases worldwide is projected to exceed 35 million—a 77% increase from the 20 million estimated in 2022 ([OMS](#), 2024). This sharp rise makes cancer a major global public health concern, highlighting the urgent need for new therapeutic options in oncology.

**For François Jacq, General Administrator of the CEA:** " *This innovative feat could change the daily lives of millions of patients. Our collaboration with Institut Curie illustrates our respective historical expertise in digital instrumentation, metrology and radiobiology. FRATHEA reflects our determination to develop groundbreaking technologies to meet one of the greatest healthcare challenges of our century.*"

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<sup>1</sup> Radiobiologist at Institut Curie

## FLASH radiotherapy, a discovery made in Curie

The development of **innovative radiotherapy technologies** is one of the most promising **avenues** in cancer treatment, and FLASH radiotherapy is emerging as a revolutionary breakthrough. **The FLASH effect was first discovered in the laboratories of Institut Curie<sup>2</sup>. This technique delivers extremely intense radiation—around 10 Gray compared to the 2 Gray used in conventional radiotherapy—in less than a second (under 100 milliseconds). It effectively destroys tumor cells while sparing healthy tissue, representing a significant advancement in cancer therapy.** For over a decade, scientists at Institut Curie have been researching and accumulating scientific data <sup>3</sup> on this new radiotherapy approach using low-energy electron or proton beams. However, a significant challenge remains: low-energy electron beams lack the ability to penetrate deeply enough to reach tumors effectively.

**To overcome this technological challenge, Institut Curie is focusing on combining FLASH with radiotherapy using Very High Energy Electrons (VHEE).** These VHEE beams, with an energy range of 100 to 250 mega-electronvolts (MeV) compared to just 10 MeV in conventional radiotherapy, offer significant physical and biological advantages for treating deep-seated tumors. This highly precise technology is designed to shorten treatment times and specifically target cancers with poor prognoses located near vital organs—previously considered inaccessible—offering new hope for patients.

The preclinical implementation of these extremely intense, high-speed beams presents Institut Curie with major technological challenges in largely unexplored fields. To tackle these challenges, Institut Curie is collaborating closely with the CEA. This partnership focuses on three key objectives: developing innovative dosimetry methods to precisely control the dose delivered by the new irradiator and demonstrating its safety and efficacy to regulatory authorities (ASNR). Additionally, the collaboration aims to design advanced measurement instruments and conduct joint radiobiological studies. **Delphine Lazaro, research director and FRATHEA project coordinator at CEA—an expert in nuclear instrumentation and modeling—describes FRATHEA as “an extraordinary opportunity to take a major step forward in the treatment of poor-prognosis cancers.” “To achieve this, we must harness all our expertise in healthcare, working alongside Institut Curie to accomplish a technological feat. This means redefining standards, inventing cutting-edge instrumentation, understanding the physical and biological mechanisms behind the FLASH effect, and optimizing them to benefit patients.”**

## FRATHEA: A Unique Île-de-France Platform at the Heart of a Leading European Medical and Scientific Hub

To drive its strategic vision forward, Institut Curie is launching the operational phase of the FRATHEA (Flash RAdiation Therapy Electron Acceleration) project in collaboration with the CEA. **The project is backed by a €37 million investment over four years: €35 million from the Innovation Healthcare 2030 plan, part of the France 2030 initiative and €2 million from the Île-de-France Region’s “Grands lieux d’innovation” (GLI) scheme in 2023.** The GLI scheme fosters the development of cutting-edge R&D and experimental platforms, incubators, and industrial infrastructures essential for advancing technology transfer and collaborative innovation in the Paris Region.

> The first step is identifying a **partner to construct and install the FLASH-VHEE medical irradiator at the heart of Institut Curie’s Orsay hospital site.** The tender process is currently underway, with the partner set to be chosen by summer 2025.

> The second phase of the project involves **the construction, assembly and installation of the FLASH-VHEE irradiator on the Orsay site,** a historic site where Frédéric Joliot had the first proton accelerator in the 1950s. The biggest advantage is that FRATHEA's extraordinary equipment will be installed in a large area of Institut Curie's proton therapy center, which is already well identified and in the process of being fitted out. These premises meet all the conditions and infrastructures required for the installation of the FLASH VHEE irradiator, particularly in terms of safety and security. **At the same time, researchers and clinicians from**

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<sup>2</sup> See Fact Sheet 1 - History of a revolutionary discovery at Institut Curie

<sup>3</sup> See Fact Sheet 3 - List of publications

**Institut Curie, in collaboration with CEA teams, will conduct studies in dosimetry, physics, and radiobiology to lay the groundwork for future treatment protocols and the deployment of FLASH-VHEE radiotherapy.**

Finally, the project's last phase will focus on preclinical studies to demonstrate **the safety and effectiveness of FLASH-VHEE radiotherapy, a technology that is not yet available in France.** The FRATHEA project teams will be working together to prove that the new experimental platform in place is safe, effective and, above all, will enable a rapid response to therapeutic needs that have not yet been adequately addressed.

*" Today, Institut Curie boasts the most comprehensive radiotherapy technical platform in Europe. As the leading proton therapy center in France, Institut Curie is equipped with state-of-the-art facilities and is a leader in FLASH radiotherapy research", says Prof. Gilles Créhange, head of the Oncological Radiotherapy Department at Institut Curie and coordinator of the FRATHEA project. Tomorrow, with the support of the French government through France 2030, which is making the FRATHEA project possible, we are reaching a major milestone: demonstrating the clinical benefits of FLASH-VHEE radiotherapy and, within a few years, establishing a platform to treat patients with the most high-risk and hard-to-reach cancers. Cure better, suffer less, and age better—this is the essence of the clinical promise surrounding FLASH therapy. "*

### **The hope of opening clinical trials by 2028**

Once the FRATHEA project is completed, Institut Curie will have **an experimental platform open to a range of academic and private partners, in line with other major innovation facilities in the Paris region.** It will bring together state-of-the-art equipment, biological models and technological tools to accelerate development phases and clinical trials for all types of treatment, particularly in oncology. **Lung cancer, pancreatic cancer, brain tumors, pediatric tumors, re-irradiation: the first therapeutic targets for FLASH-VHEE will be cancers for which treatments are not sufficiently effective or are still too toxic, and for which little or no therapeutic progress has been observed for several years.**

*"The operational launch of the FRATHEA project illustrates Institut Curie's tremendous innovation drive, particularly in radiotherapy, a field in which we are deploying a €56 million investment strategy over 6 years. While the strength of this groundbreaking project lies in the historical, multidisciplinary and recognized expertise of Institut Curie teams, the installation of our FLASH-VHEE platform as close as possible to patients, at the very heart of a hospital site, makes this project unique worldwide", says Prof. Steven Le Gouill, Director of Institut Curie Hospital Group.*

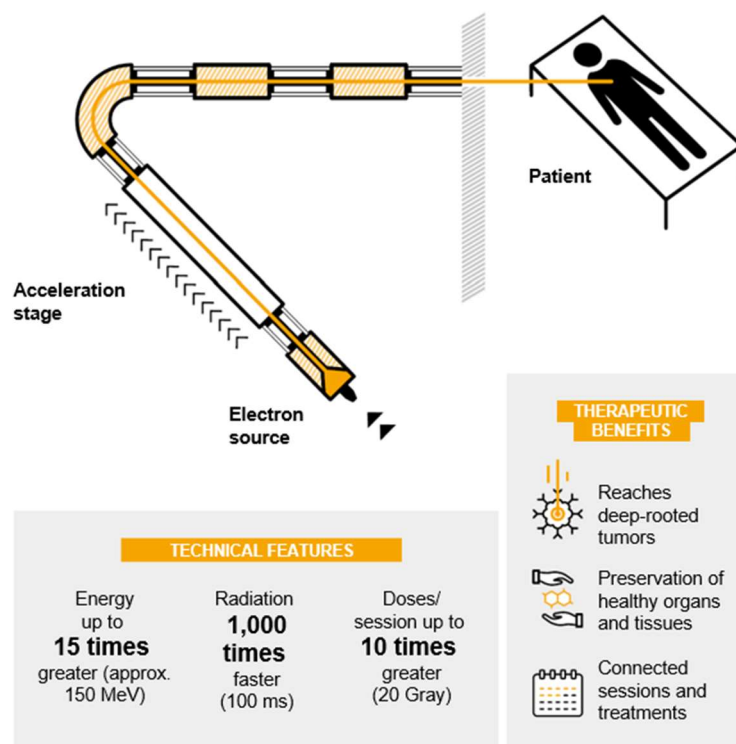
### **Crucial financial support from France 2030 and the Île-de-France Region**

**According to Bruno Bonnell, Secretary General for Investment,** *" the France 2030 government investment plan was designed to enable innovative technologies to be developed in France, making the country a leader in a number of strategic fields, including healthcare. With the FRATHEA project, we are investing to break down technological barriers in the field of radiotherapy and thus bring about a major improvement in patient care and a reduction in treatment costs. In addition to our investment, the support provided by the French Agency for Healthcare Innovation should enable us to demonstrate the proof of concept of this technology, make it available to the research community, and facilitate its adoption by as many people as possible."*

**For Valérie Péresse, President of the Île-de-France Region:** *"The FRATHEA project is fully in line with the strategic priorities of the Île-de-France Region, which aims to make our region a hub of innovation on a European scale, particularly in healthcare and especially in oncology. This "flash therapy" technology, developed by Institut Curie researchers, holds great promise and opens up new prospects for curing certain types of cancer which, until now, have remained without an effective therapeutic solution. By supporting this Institut Curie project, the Île-de-France Region is proud to contribute to the fight against cancer and to improve patients' healthcare " .*



## FLASH RADIOTHERAPY - VHEE



## Discover the FRATHEA project in pictures:

[FRATHEA: the new era of Flash radiotherapy opens at Institut Curie - YouTube](#)

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### About Institut Curie

Institut Curie, France's leading cancer center, combines an internationally renowned research center with a state-of-the-art Hospital Group that treats all cancers, including the rarest. Founded in 1909 by Marie Curie, Institut Curie has 3 sites (Paris, Saint-Cloud and Orsay) and employs more than 3,800 researchers, doctors and caregivers in its 3 missions: care, research and teaching. Institut Curie is a charitable foundation

authorized to receive donations and bequests. Thanks to the support of its donors, Institut Curie is able to speed up discoveries, thereby improving treatments and the quality of life of patients.

For more information: [curie.fr](https://curie.fr), [Facebook](#), [LinkedIn](#), [Instagram](#), [BlueSky](#)

## About the CEA

With its unique model, the CEA is a public research organization whose mission is to enlighten public decision-making and provide French and European companies, as well as local authorities, with the scientific and technological resources they need to better master major societal transformations around energy and digital transitions, healthcare of the future, and global defense and security. This mission is underpinned by three core values that guide the actions of the CEA and its teams: curiosity, cooperation and a sense of responsibility.

For more information: [cea.fr](https://cea.fr), [Facebook](#), [LinkedIn](#)

## About France 2030

- **France has a twofold ambition:** to drive long-term transformation in key economic sectors—healthcare, energy, automotive, aeronautics, and space—through technological innovation, and to establish itself not just as a participant, but as a global leader in the future economy. From basic research, to developing an idea, to producing a new product or service, France 2030 supports the entire innovation life cycle, right through to industrialization.
- **Is unprecedented in its scope:** 54 Bn€ will be invested so that our companies, universities and research organizations can successfully make the transition to these strategic sectors. The aim is to enable them to respond competitively to the ecological and attractiveness challenges of the world to come, and to nurture future leaders in key sectors. France 2030 is defined by two cross-functional objectives: to devote 50% of its spending to decarbonizing the economy, and 50% to emerging, innovative players, without spending money that is detrimental to the environment (in line with the Do No Significant Harm principle).
- **Is implemented collectively:** designed and deployed in consultation with economic, academic, local and European players to determine its strategic orientations and flagship actions. Project leaders are invited to submit their applications via open, demanding and selective procedures, in order to benefit from government support.
- **It is managed by the Secrétariat Général pour l'Investissement** on behalf of the Prime Minister, and implemented by the Agence de la Transition Ecologique (ADEME), the Agence Nationale de la Recherche (ANR), Bpifrance and the Banque des Territoires.

For more information: <https://www.gouvernement.fr/france-2030> | @SGPI\_avenir

## About the Île-de-France Region :

**The Île-de-France region is a leader in France and the European Union when it comes to innovation**, thanks to one of the world's most effective ecosystems: 1st economic region in Europe, leading hub for startups in the European Union with 8,000 startups representing 40% of French startups, 80% of funds raised and almost all unicorns valued at over 1 billion euros. These outstanding results stem from a regional policy that promotes the widespread adoption of educational digital technology, funds projects and innovation centers across the Paris region, and fosters collaboration and networking among key innovation stakeholders.



## Fact Sheet 1

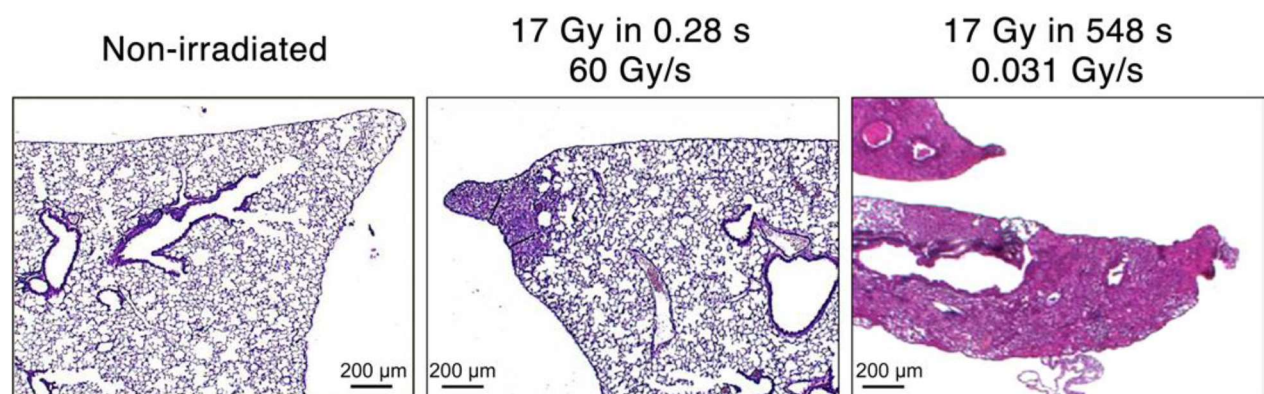
### The story of a revolutionary discovery at Institut Curie

Radiotherapy is, along with surgery, the most effective curative treatment for solid tumors, and more than half of all cancer patients require it. While considerable progress has been made in this field in terms of imaging, ballistics and dosimetry over the last few decades, dose delivery methods have not evolved much. **However, the discovery of the “Flash” effect in Institut Curie laboratories has led to a paradigm shift in radiotherapy.** Here's a look back at this discovery.

#### The breakthrough: delivering a swift and powerful attack on the tumor.

It all began in 1995: Dr. Vincent Favaudon, an Inserm radiobiology researcher at Institut Curie. He observed an unexpected effect of dose fractionation on cells *in vitro*, which he called the “W” effect. **After several years' work and the first communications in 2009, he published major results in 2014 in *Science Translational Medicine* demonstrating the “Flash effect” in a preclinical model<sup>4</sup>.** He demonstrated that very intense rays, delivered in a very short time, have the same anti-tumor effect as conventional radiotherapy, with two crucial advantages: sparing healthy tissue and considerably reducing treatment times. In conventional radiotherapy, the dose rate is around one Gray per second, with daily fractions of 2 Grays accumulated, whereas FLASH (ultra-high dose rate) delivers an irradiation dose of 10 Gy or more in a very short time of less than 100 ms (1,000 to 10,000 times faster than conventional radiotherapy).

In 2014, Dr. Favaudon's research on preclinical models demonstrated that a conventional 15 Gy dose used to treat lung tumors invariably resulted in pulmonary fibrosis—a significant late complication of radiotherapy—emerging between 8 weeks and 6 months post-irradiation. With FLASH irradiation, no fibrosis occurred below 20 Gy. This protective effect was also observed on apoptosis (programmed cell death produced by unrepaired DNA damage), blood capillaries and skin lesions. However, anti-tumor efficacy remained the same in all preclinical models. **FLASH irradiation therefore protects healthy tissue from side effects in a highly selective manner.**

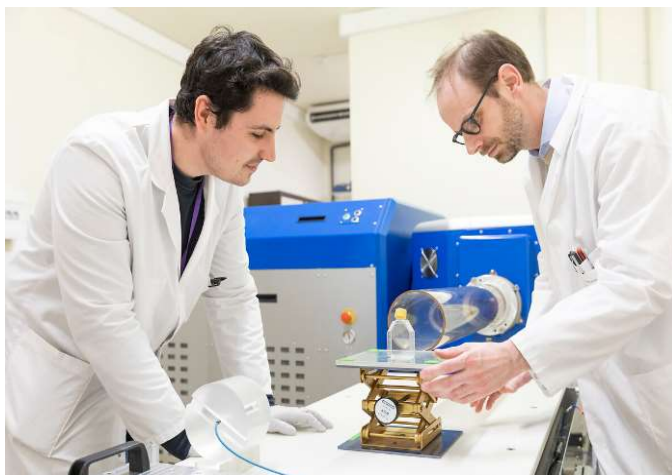


*Effect on healthy lung tissue of a 17 Gy irradiation delivered in 0.28 s, i.e. a dose rate of 60 Gy/s (center image) and in 548 s, i.e. a dose rate of 0.031 Gy/s (right image). Tissue irradiated at a very high dose rate has the same appearance as unirradiated tissue, whereas tissue irradiated at a low dose rate is totally altered.*

It took Vincent Favaudon and his team several years of basic research to accumulate sufficient data to unequivocally demonstrate this FLASH effect. Since then, numerous teams around the world have reproduced these results in different models, each time demonstrating **unchanged anti-tumor efficacy and protection against pulmonary fibrosis, memory loss, intestinal protection, etc.**

<sup>4</sup> See Fact Sheet 3 - List of publications

## A novel experimental device to validate clinical applications



**ElectronFlash 4000 installed at Orsay.** Maxime Dubail, PhD student, on the left, and Charles Fouillade on the right, radiobiologist in Institut Curie's Repair, Radiation and Innovative Anticancer Therapies team (Signaling, Radiobiology and Cancer Unit (UMR3347 / U1021)). Institut Curie / VOISIN Thibaut

The discovery of the FLASH effect in 2009 was made on a low-energy electron **accelerator installed in the laboratories of Institut Curie Research Centre in Orsay**: the kinetron (linear electron accelerator). In 2021, a new prototype device, the ElectronFlash4000, manufactured in Italy by SIT (pictured opposite), replaced the kinetron to conduct physical, physico-chemical, and radiobiological studies. These studies aim to better understand the mechanisms of FLASH irradiation compared to conventional irradiation. Such research is essential for advancing the next generation of electron accelerators, ultimately paving the way for clinical applications.

## Multidisciplinary research in radiobiology and radiophysics.

Teams at Orsay's Institut Curie focus their efforts on studying the physical, physico-chemical and biological mechanisms underlying the FLASH effect (optimal dose, dose rate, oxygenation, etc.). They analyze physiological compartments along with various molecular, cellular, and genetic pathways to unravel the mechanisms triggered by ultra-high dose-rate radiation. Their goal is to understand the key differences in how tumors and healthy tissue respond to radiation. Why do healthy tissues regenerate under the effect of FLASH radiotherapy whereas they do not under conventional treatment? There are many possible explanations, one of which lies in the role of oxygen, which is known to be a powerful radiosensitizer.

Teams at Institut Curie are involved in a number of research projects aimed at bringing the technique to the clinical trial stage (*see list of publications, FACT SHEET 3*).



## The Orsay site: ever more modern and efficient particle accelerators

Over the past 75 years, the Orsay campus has become one of the world's leading centers of scientific innovation, particularly in the field of nuclear physics. It is home to numerous research institutes, including the *Centre de Protonthérapie d'Orsay* (CPO) and Institut Curie laboratories.

### Particle accelerators

Particle accelerators use electric fields to speed up charged particles, such as electrons and protons—key components of atoms—while magnetic fields guide their trajectory. There are two types of particle accelerators: linear, where particles are accelerated in a straight line towards a target, and circular, where they follow a circular trajectory and collide. These collisions release large amounts of energy, enabling the creation of new particles or the modification of atomic nuclei.

### An annex of the Radium Institute at Orsay

**In the 1950s, the proton synchrocyclotron project initiated by Irène Joliot-Curie, then director of Institut Curie laboratory at Institut du radium, was born in Orsay.** Installation was completed in 1958. Frédéric Joliot-Curie also had a second circular accelerator moved to Orsay from the Collège de France: the historic cyclotron he had acquired in 1937, which was also used at Orsay until 1966.

### Accelerators to treat cancer

From 1991 to May 2010, Institut Curie's Centre de Protonthérapie d'Orsay (CPO) treated some 5,000 patients. In 2010, the CPO was equipped with a new, much more powerful particle accelerator to boost its clinical activity dedicated to treating patients with proton therapy (mainly ocular and pediatric tumors).

Today, the new FLASH-VHEE irradiator will be installed at the heart of the Orsay and CPO facilities, right where Frédéric Joliot Curie installed a cyclotron several decades ago...

For more information: <https://musee.curie.fr/blog/les-joliot-curie-et-la-naissance-du-campus-d-orsay>





## Fact Sheet 2

With the support of



### The FRATHEA project in detail :

#### **Flash RAdiation Therapy Electron Acceleration**

**Increasing recovery rates and reducing radiation-induced side-effects by combining FLASH radiotherapy with very high energy electrons (VHEE): this is the aim of the FRATHEA project led by Institut Curie, in collaboration with the CEA.**

This major project, launched in 2024, is being financed over a four-year period by a €37 million grant (€35 million as part of the Innovation Santé 2030 plan, the healthcare component of France 2030, which will be funded by the ANR on behalf of the French government, and €2 million by the Île-de-France Region as part of its major innovation projects). FRATHEA brings together multidisciplinary teams from Institut Curie and the CEA at Institut Curie site in Orsay. With the support of an industrial partner selected for the project, their goal is to position **France as a leader in the design and deployment of cutting-edge radiotherapy equipment.**

**The new and unexplored technological challenges of moving FLASH-VHEE radiotherapy into the clinic require both a radical change in medical irradiator design and new dosimetry methods.** The FRATHEA project aims to develop a unique, safe and effective experimental platform for FLASH-VHEE treatment in oncology by 2028.

Institut Curie and CEA teams involved in this groundbreaking project will have to provide innovative tools, instruments and tests to develop optimal treatment protocols and monitoring to ensure controlled clinical use. **Ultimately, this technology will not only cut costs, but above all reduce the duration and number of sessions, an invaluable advantage for patients' quality of life.**

Scientists will also be studying how this new generation of medical devices can be combined with other cancer treatment techniques. Finally, the complex nature of the project will require bringing together the best experts in the field, as well as providing training for the various personnel involved.

#### **Expert multidisciplinary teams**

**To adapt to this new FLASH-VHEE modality using a dose rate 10,000 times higher than that used in conventional radiotherapy, new methods must be implemented.** The FRATHEA project therefore calls on the multidisciplinary expertise of Institut Curie and CEA: physicists developing accelerator components and imaging or dosimetry equipment<sup>5</sup>, medical physicists for treatment planning and simulation, radiobiologists testing systems on tumors and animal models, and clinicians developing new treatment protocols.

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<sup>5</sup> Determining the dose of X-rays or other radiation to be administered in radiotherapy, and its distribution across the tumor zone.

## Nine working groups united and connected

### Nine groups are working on the FRATHEA project:

- ✓ Selecting a manufacturer, then building and installing the FLASH-VHEE irradiator at the heart of Institut Curie hospital site in Orsay.

In addition to overseeing the innovative procurement process for selecting a manufacturer—set to be announced in summer 2025—one of the working groups is focused on **developing the FLASH-VHEE demonstrator based on the technical specifications outlined in the tender**. The new instrument will have to provide different experimental configurations for beam delivery (FLASH, conventional, mini-beams, etc.), in order to explore different modalities for different therapeutic indications.

Meanwhile, another group is in charge of carrying out all the operations required at the hospital to **adapt the shielded room where the demonstrator will be installed**.

- ✓ Two other groups led by CEA teams are responsible for **the radiation protection and dosimetry studies** that are crucial to meeting current safety requirements. The teams involved here will ensure that the shielding required for radiation protection is in place at the demonstrator. Further **radiation protection** studies will be carried out to ensure that the FLASH-VHEE system and its environment meet radiation criteria for clinical use. In addition, another working group will develop **a complete set of dosimetry instrumentation, essential for controlling the doses delivered during FLASH-VHEE treatments**.

- ✓ Radiobiology and radiophysics studies

The final stage of the FRATHEA project involves validating the FLASH effect - i.e., the anti-tumor efficacy and absence of toxicity for healthy tissue - of the demonstrator through **experiments on different types of *in vitro* and preclinical models**. To prepare for clinical trials, a working group is also carrying out medical physics studies to **provide computational tools for simulating preclinical treatments on the demonstrator**. The scientists involved will identify challenges and opportunities in the initial stages of device development in terms of medical physics and technical specifications for preclinical and clinical applications.

- ✓ The final step involves preparing for clinical trials.

Preliminary clinical trials will be carried out by **simulating different configurations of the demonstrator (layout and number of beams, angles and sizes, type of delivery, etc.) on the basis of clinical cases and a reference system of possible indications** (in particular pancreatic, lung, brain and pediatric cancers, etc.). The aim is to illustrate the potential of FLASH-VHEE treatments in the clinic, before setting up the first patient trials.

## Fact Sheet 3

### List of Institut Curie's leading publications on FLASH radiotherapy

Teams at Institut Curie are engaged in a wide range of multidisciplinary projects to validate and explore the FLASH effect across all its dimensions, and above all to enable its transition to the clinic in the years to come.

#### 2024

1. **Differential Remodeling of the Oxylipin Pool After FLASH Versus Conventional Dose-Rate Irradiation In Vitro and In Vivo.** Portier L, Daira P, Fourmaux B, Heinrich S, Becerra M, Fouillade C, Berthault N, Dutreix M, Londoño-Vallejo A, Verrelle P, Bernoud-Hubac N<sup>2</sup>, Favaudon V. *Int J Radiat Oncol Biol Phys*. 2024 Aug 1;119(5): 1481-1492. doi: 10.1016/j.ijrobp.2024.01.210.
2. **Maria Grazia Ronga : Etude et modélisation de la radiothérapie par électrons de très haute énergie (VHEE).** Thèse CIFRE (IC/Thales) soutenue le 11/04/2024. <https://theses.fr/2024UPAST036>
3. **Conformation techniques for ultra-high dose rate very high energy electrons (VHEE) radiation therapy.** M. G. Ronga, U. Deut, F Gesualdi, A. Bonfrate, A. Patriarca, E. Jouglar, R. Ferrand, G. Créhange, I. Buvat, P. Girault, L. De Marzi. *Soumis dans Phys Med Biol (Oct 2024)*
4. **Technical Note: Comparison of secondary radiation dose contribution between pencil beam scanning, scattered proton and VHEE radiotherapy.** MG Ronga, F Gesualdi, A. Bonfrate, A. Patriarca, R. Ferrand, G. Créhange, I. Buvat, L De Marzi. *Soumis dans Med Phys (oct 2024)*

#### 2023

5. **Characterization of Ultra-High-Dose Rate Electrons Beams with ElectronFLASH Linac.** Giuliano L, Franciosini G, Palumbo L, Aggar L, Dutreix M, Faillace L, Favaudon V, Felici G, Galante F, Mostacci A, Migliorati M, Pacitti M, Patriarca A, Heinrich S. *Applied Sciences*. 2023, 13(1), 631; <https://doi.org/10.3390/app13010631>.
6. **Radiation-induced immune response in novel radiotherapy approaches FLASH and spatially fractionated radiotherapies.** Bertho A, Iturri L, Prezado Y. *Int Rev Cell Mol Biol*. 2023;376: 37-68.
7. **Secondary radiation dose modeling in passive scattering and pencil beam scanning very high energy electron (VHEE) radiation therapy.** Deut U, Ronga MG, Bonfrate A, De Marzi L. *Med Phys*. 2023 Jul;50(7): 4491-4504. doi: 10.1002/mp.16443. Epub 2023 May 25. PMID: 37227704
8. **Very high-energy electron dose calculation using the Fermi-Eyges theory of multiple scattering and a simplified pencil beam model.** Ronga MG, Deut U, Bonfrate A, De Marzi L. *Med Phys*. 2023 Dec;50(12): 8009-8022. doi: 10.1002/mp.16697. Epub 2023 Sep 20. PMID: 37730956
9. **Chapter Two - Radiation-induced immune response in novel radiotherapy approaches FLASH and spatially fractionated radiotherapies.** Bertho A, Iturri L, Prezado Y. *International Review of Cell and Molecular Biology*. Volume 376, 2023, Pages 37-68.
10. **Lung Organotypic Slices Enable Rapid Quantification of Acute Radiotherapy Induced Toxicity.** Dubail M, Heinrich S, Portier L, Bastian J, Giuliano L, Aggar L, Berthault N, Londoño-Vallejo JA, Vilalt, M, Boivin G, Sharma RA, Dutreix M, Fouillade C. *Cells* 2023, oct 11, 12, 2435. <https://doi.org/10.3390/cells12202435>

#### 2022

11. **Radiobiology of the FLASH effect.** Friedl AA, Prise KM, Butterworth KT, Montay-Gruel P, Favaudon V. *Med Phys*. 2022 Mar;49(3): 1993-2013.
12. **Model studies of the role of oxygen in the FLASH effect.** Favaudon V, Labarbe R, Limoli CL. *Med Phys*. 2022 Mar;49(3): 2068-2081.

13. **Combining FLASH and spatially fractionated radiation therapy: The best of both worlds.** Schneider T, Fernandez-Palomo C, Bertho A, Fazzari J, Iturri L, Martin OA, Trappetti V, Djonov V, Prezado Y. *Radiother Oncol*. 2022 Aug 8; S0167-8140(22)04226-8.
14. **A Comprehensive Analysis of the Relationship Between Dose Rate and Biological Effects in Preclinical and Clinical Studies, From Brachytherapy to Flattening Filter Free Radiation Therapy and FLASH Irradiation.** Beddok A, Lahaye C, Calugaru V, De Marzi L, Fouillade C, Salvador S, Fontbonne JM, Favaudon V, Thariat J. *Int J Radiat Oncol Biol Phys*. 2022 Aug 1;113(5): 985-995.
15. **Practice-oriented solutions integrating intraoperative electron irradiation and personalized proton therapy for recurrent or unresectable cancers: Proof of concept and potential for dual FLASH effect.** Calvo FA, Ayestaran A, Serrano J, Cambeiro M, Palma J, Meiriño R, Morcillo MA, Lapuente F, Chiva L, Aguilar B, Azcona D, Pedrero D, Pascua J, Delgado JM, Aristu J, Prezado Y. *Front Oncol*. 2022 Nov 14;12: 1037262.
16. **Perspectives in linear accelerator for FLASH VHEE: Study of a compact C-band system.** Faillace L, Alesini D, Bisogni G, Bosco F, Carillo M, Cirrone P, Cuttone G, De Arcangelis D, De Gregorio A, Di Martino F, Favaudon V, Ficcadenti L, Francescone D, Franciosini G, Gallo A, Heinrich S, Migliorati M, Mostacci A, Palumbo L, Patera V, Patriarca A, Pensavalle J, Perondi F, Remetti R, Sarti A, Spataro B, Torrisi G, Vannozzi A, Giuliano L. *Phys Med*. 2022 Dec;104: 149-159.

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