RÉPUBLIQUE FRANÇAISE
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INSTITUT NATIONAL DU CANCER

APPEL À CANDIDATURES 2022

Structuration de la recherche -
Labellisation d'un réseau national de recherche pré-clinique en radiothérapie 2022-2025

RTH2022

Dossier de candidature / descriptif du projet

DATE LIMITE DE SOUMISSION DES CANDIDATURES : **4 novembre - 17h00**

Soumission en ligne du dossier électronique :
https://www.e-cancer.fr/Institut-national-du-cancer/Appels-a-projets/Appels-a-projets-en-cours/RTH2022

Candidat-e	
N° du dossier : Veuillez indiquer le n° de dossier attribué par le portail PROJETS (Menu "Dépôt de projets")	**Radio22-002**
Acronym :	RadioTransNet 2.0
Nom du réseau de recherche pré-clinique en radiothérapie : Name of the Radiotherapy preclinical research network:	**Radiotherapy Translational and Preclinical Research Network**
Coordonnateur principal du réseau (NOM, Prénom, email et affiliation principale) / *Main coordinator (NAME, First name, email and affiliation)*	MAINGON Philippe philippe.maingon@aphp.fr UPMC Sorbonne Université 91 Bd de l'Hôpital 75013 Paris APHP Paris. GHU La Pitié Salpêtrière Charles Foix ; 47/83 Bd de l'Hôpital, 75013 Paris MARCHESI Vincent v.marchesi@nancy.unicancer.fr Institut de Cancérologie de Lorraine Avenue de Bourgogne, CS 30519 54519 VANDŒUVRE-LÈS-NANCY Cedex
Budget demandé à l'INCa */Requested budget to INCa*	400 000€

Partie I/Part 1

Organismes membres du réseau[1]/ Members of the network

Nom de l'organisme	Adresse	Nom du directeur/président ou du représentant légal	Nom du responsable scientifique
UNICANCER INSERM	Radiation Oncology - ICM Montpellier - 208 Avenue des Apothicaires, 34298 Montpellier	Pr. Marc YCHOU	David AZRIA
UNICANCER	Radiotherapy Department - Centre François-Baclesse - 3 Avenue du Général Harris, 14000 Caen	Pr. Marc-André Mahé	Jacques BALOSSO
IRSN	Institut de Radioprotection et de Sûreté Nucléaire - 31 Avenue de la Division Leclerc, 92260 Fontenay-aux-Roses	M. Jean-Christophe NIEL	Marc BENDERITTER
UNICANCER INSERM	IUCT-Oncopole de Toulouse -CRCT- Av. Irène Joliot-Curie, 31100 Toulouse	Pr. Jean-Pierre DELORD	Elisabeth COHEN-JONATHAN MOYAL
SFPM UNICANCER	Institut de Cancérologie de l'Ouest - Site Nantes René Gauducheau - Bd J. Monod 44805 Saint-Herblain	Pr. Mario CAMPONE	Gregory DELPON
UNICANCER INSERM	Radiation Oncology Department – Gustave Roussy - 114 Rue Edouard Vaillant, 94800 Villejuif	Pr. Fabrice BARLESI	Eric DEUTSCH
Institut Curie INSERM - CNRS	Institut Curie – Centre Universitaire - 91405	Pr. Alain PUISIEUX	Marie DUTREIX

[1] Les organismes membres du réseau devant désigner l'organisme porteur de la candidature et le coordonnateur peuvent appartenir aux organismes suivants : organismes publics de recherche (EPST) ; établissements d'enseignement supérieur ; organisations à but non lucratif (associations, sociétés savantes, fondations, ...) ; établissements de santé (CHU, CLCC, CH). Ces établissements doivent être autorisés à traiter des patients en cancérologie (chimiothérapie et chirurgie et radiothérapie) ; entreprises privées (industriels, cliniques, CH privés à but lucratif ou non).

	Orsay Cedex		
SFPM UNICANCER	Service de Physique Médicale - Centre Oscar LAMBRET - 3 Rue Frédéric Combemale, 59000 Lille	Pr. Eric LARTIGAU	Thomas LACORNERIE
APHP	Radiation Oncology Department – GHU Pitié-Salpêtrière- Charles Foix – 47/83 bld de l'hôpital, 75013 Paris	Mme Christine WELTY	Philippe MAINGON
SFPM UNICANCER	Service de Physique Médicale - Institut de Cancérologie de Lorraine - 6 Avenue de Bourgogne, 54519 Vandœuvre-lès-Nancy	Pr. Thierry CONROY	Vincent MARCHESI
CEA	CEA – DRF - Centre d'études de Saclay-91191 Gif sur Yvette cedex	Mme Elsa CORTIJO	Paul-Henri ROMEO

Organisme porteur de la candidature (bénéficiaire de la subvention) [2]/ Funding beneficiary institution

Nom de l'organisme bénéficiaire de la subvention */funding beneficiary* : **Représentant légal** (ou personne dûment habilitée)[3] / Legal representative : **Nom prénom-Titre et fonction : Adresse :**	Société Française de Radiothérapie Oncologique GIRAUD Philippe, président de la SFRO 47 rue de la Colonie, 75013 PARIS
Nom et prénom de la personne chargée du suivi administratif du dossier : Adresse de correspondance : E-mail : Téléphone :	BAYART Emilie 47 rue de la Colonie, 75013 PARIS Eb.RadioTransNet@gmail.com 0660808074

Résumé du projet / Project summary

Attention, ce résumé est obligatoirement bilingue et indispensable pour l'expertise de votre projet / Warning, this summary is essential for the evaluation of your project

Titre du projet
Renouvellement de la labellisation du réseau national de recherche préclinique en radiothérapie : RadioTransNet
Mots-clés principaux
Oncologie-radiothérapie, recherche préclinique translationnelle, imagerie, dosimétrie, biologie, pharmacologie
Résumé scientifique du projet (max. 3500 caractères espaces compris)
Le projet RADIOTRANSNET est une initiative ayant pour vocation la structuration de la recherche préclinique et translationnelle en radiothérapie oncologique au niveau national. Lancé fin 2018, l'ambition du réseau RADIOTRANSNET est de proposer une méthodologie robuste afin de construire un consortium national de recherche dédié à la radiothérapie préclinique et contribuer à coordonner les efforts nationaux de recherche fondamentale et translationnelle dans ce domaine. Les activités du réseau sont organisées autour de 4 axes qui sont : la définition des volumes cibles, les interactions des irradiations avec les tissus sains, l'apport des thérapies combinées et les approches modernes des calculs de dose. A ces axes sont associés différents objectifs concernant la radiobiologie fondamentale, les études d'implémentation de nouvelles drogues en préclinique, l'apport de l'imagerie dans cette problématique, la recherche en physique médicale, en intégrant une dimension transversale intéressant l'oncologie médicale, la radiologie médicale, la médecine nucléaire, sans oublier les considérations de coût/efficacité. Durant sa première phase d'activité, 4 workshops, sur le modèle des réunions consensus à l'interface de la radiothérapie et de la radiobiologie et portant sur les thématiques des 4 axes majeurs identifiés, ont été organisés. Ils ont permis de dégager des priorités de recherche et conduit à la rédaction d'une

[2] Les organismes suivants sont éligibles à être organisme porteur de la candidature : organismes publics de recherche (EPST) ; établissements d'enseignement supérieur ; organisations à but non lucratif (associations, sociétés savantes, fondations, ...) ; établissements de santé (CHU, CLCC, CH). Ces établissements doivent être autorisés à traiter des patients en cancérologie (chimiothérapie et chirurgie et radiothérapie).

[3] Personne habilitée à signer les conventions

feuille de route afin de définir une stratégie de recherche.
Les thèmes retenus constitueront la base des projets qui seront étudiés et développés dans la deuxième phase d'exercice du réseau RadioTransNet en faisant appel, au sein du réseau aux compétences complémentaires de tous les partenaires et toutes les plates-formes impliquées. Ils devront également servir de base de propositions d'appels d'offres qui seront soumises à l'INCa et aux différentes associations académiques, pour financer les moyens humains et techniques nécessaires à conduire, dans les meilleures conditions, cette recherche préclinique et translationnelle en radiothérapie.
En plus de workshops et de webinaires sur des thématiques ciblées du réseau, RadioTransNet se propose de mettre en place un congrès annuel de radiothérapie préclinique faisant intervenir des experts évoluant au niveau international et incluant une restitution des avancées du réseau à ses partenaires. Le réseau ambitionne également de développer un Observatoire de la Recherche en Radiothérapie Préclinique, complémentaire de l'Observatoire de la Radiothérapie clinique déjà existant, qui permettra de dresser un panorama de la recherche dans le domaine sur le territoire national.
Les activités de RadioTransNet sont organisées sous la supervision d'un Conseil Scientifique (dirigé par un coordinateur et un co-coordinateur respectivement désignés par la SFRO et la SFPM). Ce Conseil Scientifique a désigné, pour chacun des 4 axes précédemment nommés, trois coordinateurs (un oncologue-radiothérapeute, un physicien médical et un biologiste,) chargés assurer l'animation scientifique au sein de chaque axe de recherche. Conseil de surveillance incluant des membres de la SFRO, de la SFPM, de la SFR, de la SFMN et d'un représentant des associations de patients supervisera également les activités du réseau.
L'ensemble des travaux du réseau sera publié, diffusé sur les réseaux scientifiques et sociaux, ainsi que sur le site web développé pendant la première phase d'exercice du réseau et dédié à ses activités.

Project title

Renewed accreditation for the French radiotherapy translational and preclinical research network: RadioTransNet

Principal keywords

Radiation oncology, preclinical translational research, imagery, dosimetry, biology, pharmacology

Scientific abstract (Max. 3500 characters)

The RadioTransNet project is an initiative structuring preclinical and translational research in radiation therapy for cancer at national level.
Launched in late 2018, RadioTransNet's ambition is to propose a robust methodology building a national research consortium dedicated to radiation oncology and contributing to organizing national efforts in fundamental and translational research in this field.
The network's activities are organized around four chosen priorities, which are: target definition, normal tissue, combined treatments and dose modelling. The sub-targets linked to these four major priorities are unlimited. They include all aspects associated with fundamental radiobiology, preclinical studies, imaging, medical physics research and transversal components clearly related to these scientific areas, such as medical oncology, radio-diagnostics, nuclear medicine and cost-effectiveness considerations.
During its first phase of activity, four workshops following the consensus conference model and based on scientific and medical state of the art in radiotherapy and radiobiology were organized on the four above mentioned objectives to identify key points. A dedicated roadmap is under production to define a strategic research agenda.
The selected priorities will form the basis of the projects to be studied and developed during the

second phase of RadioTransNet activity, drawing on the complementary skills of all partners and platforms involved in the network. They will also be the basis of proposed calls submitted to INCa and academic associations or charities to finance the human and technical resources necessary to conduct optimal translational and preclinical research in radiation oncology.

In addition to small events on targeted topics, RadioTransNet proposes to launch an annual preclinical radiotherapy conference involving international experts and including an update on network activities for its partners. The network also aims to implement a Preclinical Radiotherapy Research Observatory, complementary to the existing Clinical Radiotherapy Observatory, which will provide an overview of research in the field in France.

RadioTransNet activities are organized under the supervision of a scientific committee (led by one SFRO coordinator and one SFPM co-coordinator). It has appointed three coordinators for each main target (a radiation oncologist, medical physicist and biologist) who are responsible for scientific oversight within each research area. A steering committee, including SFRO, SFPM, SFR, SFMN and patient representatives, will also oversee the network's activities.

RadioTransNet's results will be shared through publications, social media as well as the dedicated website developed during the network's first phase and dedicated to its activities.

Budget prévisionnel / Estimated budget

Annexe budgétaire/Bugetary Annex

Veuillez compléter l'annexe budgétaire présentée dans le fichier Excel / *Refer to Excel file*

Budget/ Network financial plan

Adéquation et justification du financement demandé en cohérence avec les objectifs du projet sur la période de 48 mois. The network will develop a provisional budget for a period of four years. The applicant must specify the requested funding and justify the funding adequacy and coherence with the objectives of the project.
€400 K over four years This funding will mainly support (80%) the salary of Emilie BAYART (PhD), a senior scientist experienced in the fields of oncology, radiobiology and radiotherapy, who has been RadioTransNet's project manager since it launched. She provides support and assistance for structuring the network, events, timelines, reporting and communication. 15% will be allocated to organizing events (targeted webinars and workshops, annual meetings). 3% will be invested in upgrading the website. The remaining 2% meets overheads.

Partie II / Part 2

Missions scientifiques du réseau / Scientific missions of the network

Le projet scientifique doit être rédigé uniquement en anglais et doit exposer les points suivants/Scientific project must be written in English, and should include the following points:

The scientific missions of the network should be described precisely according to the objectives of the call*:*

- Scientific context,
- Comprehensive discussion of the overall strategy of the project,
- The network's activities must be organized around chosen themes and priorities presented in a clear and structured way, along with tasks, planning and deliverables. For each theme, describe:
  – program areas and tasks;
  – description of collaborations and synergies between team and members of the network for each theme (cf pt2 table of members);
  – general background and scientific needs;
  – main scientific objectives;
  – international relevance;
- National and international collaborations,
- Concrete actions, scientific events, meetings and workshops contributing to the structuration of radiotherapy in France,
- Expected outcomes (collaborations, synergy, visibility, attractiveness of research in French radiotherapy…)

Scientific project: max.

Four major specific challenges have been consensually identified for improving radiotherapy's therapeutic index. These challenges are clarified below. They need to bring together different disciplines including oncology, biology, pharmacy, information technology, dosimetry and medical physics. RadioTransNet is willing to propose a robust methodology of science-based consensus with the view to (i) building a national research consortium dedicated to radiation oncology, (ii) implementing a strategic research agenda based on rigorous scientific and medical state of the art in radiotherapy and radiobiology, and (iii) defining a roadmap to facilitate existing scientific and clinical interactions. This approach will contribute to organizing a high-level preclinical network that can connect research teams and technological platforms in radiation oncology and increase national and international visibility. The network's scientific missions are described in detail and a methodology for implementing this national network is proposed according to the call's objectives*.*

I. Scientific challenges

Radiotherapy has a major role in local-regional treatment for cancer patients. However, radiotherapy's antitumor efficacy must increase since about one third of cancer deaths involve local-regional failure. Finally, radiotherapy's effectiveness must be increased while its side effects on normal tissue are decreased.

RadioTransNet has identified four major strategies to improve radiotherapy's therapeutic index:

1) Optimizing the specificity of radiotherapy treatments' absorbed dose distribution to decrease the dose to normal tissues and increase the dose to the tumor. Major improvements have been obtained in this field in the last two decades, with emphasis on particle beam therapy, intensity-

modulated radiotherapy and image-guided radiotherapy. These developments, which are changing clinical practice, offer new treatment opportunities such as hypofractionation, dose painting or adaptation. Research programs aiming to study the radioresistance and genetic profile of tumoral cells are essential.

2) Combining new molecular-targeted agents and biological modifiers with radiation therapy to increase the anti-tumor efficacy and/or decrease the radiation effects on normal tissues, i.e., to extend the therapeutic ratio and enlarge the therapeutic window. The combination of a new drug with radiotherapy generally occurs relatively late in the course of drug development, although the potential clinical interest could be of major importance for patients. This outlines the major need for strong interaction between industrial and academic partners to develop combined strategies faster and earlier and to find new targets based on enhancing radiation response. The objective **of this project is to form a high-level preclinical network that can connect research teams and technological platforms to test innovative strategies in the field of radiotherapy and demonstrate their added values.**

3) Decreasing radiotherapy side effects on normal tissue. Radiotherapy fractionation is mainly based on the differential response of normal versus tumor tissues. Dose/volume constraints and tolerance doses of at-risk organs have been widely documented for "normo-fractionated" protocols. There is a very significant lack of knowledge of the biological effects associated with both high doses per fraction and high dose rates, two major parameters related to the development of radiotherapy practices / techniques. Consequently, the concept of differential responses of normal versus tumor tissues needs to be reconsidered. New normal tissue complication probabilities should be derived.

4) Predicting the response of tumors and normal tissues to ionizing radiation using new multimodal and functional imaging and/or new biological and molecular surrogates. The development and validation of novel biomarkers will then be required to develop treatment personalization approaches. Treatment personalization will increase the success of clinical transfer and justify the allocation of resources based on specific patient needs.

II. Comprehensive discussion of the overall strategy of the project

Supported by the French National Society of Radiation Oncology (SFRO) and the French National Society of Medical Physics (SFPM), two coordinators have been appointed by the two societies. A scientific community, including experts in the field and representatives of public and private research institutes (CEA, CNRS, INSERM, IRSN), healthcare professional associations (SFRO, SFPM) and federations of public and private hospitals (SNRO, CHU, Unicancer), has created networks organized around four major issues in radiation oncology clinical practice. These four areas are: target definition, normal tissue, combined treatments and dose modelling.

During the first step of the process, a project manager was recruited. She coordinated the actions decided by the Scientific Committee and first, established an exhaustive list of partners. Secondly, all such partners were questioned to identify their field of expertise in relation to the four identified challenges. All existing authorities, bodies and networks were asked to contribute to this effort. This process identified each party's resources and funding capacities. A list of potential partners willing to participate in this initiative is provided.

In the same period, the Scientific Committee appointed coordinators for each main target. A radiation oncologist, medical physicist and scientist/biologist were asked to lead one of the priorities as co-coordinators. They organized, for the four abovementioned objectives, dedicated meetings and workshops using the current possibilities offered by national scientific societies such as SFRO, SFPM, DOSEO, French Society of Cancer, etc. All existing research networks were involved in this task (CEA, IRSN, CNRS, INSERM and SIRICs…).

III. Network Activities

1) The first taskforce is dedicated to "Target volume definition".

The workshop was held at La Pitié-Salpêtrière University Hospital in July 2019 and was led by Vincent Grégoire, Charlotte Robert and Benjamin Lemasson.

- General background and scientific needs:

The last two decades have seen the development of imaging modalities and RT treatment techniques. 3D and 4D imaging modalities make it possible to describe tumor and normal tissues and their motions. However, radiotherapy's anti-tumor efficacy must increase since about one third of cancer deaths involve local-regional failure. That fact demonstrates the need to better define the target.

- Main scientific objectives:

With modern imaging modalities and registration software, spatial definition of the macroscopic target can be achieved. From a biological point of view, different phenomena should be included in definition of the target. Hypoxia, vascularization and other processes related to the microenvironment should be known at least at the voxel scale. From an anatomical point of view, delineation is still a time-consuming operator-dependent action. Automation should be added to produce more consistent volumes irrespective of the clinician and to pave the way for adaptive radiotherapy.

Functional imaging with PET and MRI should provide specific sequences or radiopharmaceuticals to derive biological sub-volumes representative of a biological phenomenon able to help define the target volume or prescribed dose. Additionally, biological sub-volumes should be spatially registered to the planning images to define planning volumes. Research should be conducted to better understand the biological mechanisms and pathways needed to improve the sensibility and specificity of imaging exams that can derive accurate and quantitative hypoxia, tumor vascularization or other biomarker maps defining criteria for radioresistance. As biological mechanisms occur at cellular scale and imaging modalities use comparatively large voxels, studies should also consider this multiscale problem to fully exploit biological findings. In addition, quantitative imaging should make it possible to convert the detected signal into a required dose to prescribe for these sub-volumes. Such quantitative imaging is a prerequisite for developing treatments using dose painting by contours or by numbers.

These steps are fundamental to pave the way for adaptive radiotherapy. Indeed, adaptive radiotherapy is limited due to the necessary interventions of different operators. Fully adaptive radiotherapy could be developed only if progress is made in automation. Many algorithms already exist and prove satisfactory for some organs, especially when contrast is high. However, they still fail in some situations and always require expert validation. Research should continue, including by exploring neural networks and machine learning.

- Program areas and tasks:

The RADIOTRANSNET consortium identifies as a collective goal the progressive implementation of a strategic research agenda for optimizing radiation exposure and standardizing practices in radiotherapy. The "Target Volume Definition" research topics considered necessary and most urgent for effective medical care and efficient radiation protection are outlined below:

A. BIOLOGY-DRIVEN IMAGE ACQUISITION

To develop and validate new *in vivo* imaging strategies reflecting tumor biology and microenvironments in order to personalize radiotherapy planning. The long-term goal of the methods developed will drive future clinical trials validating multiparametric imaging's contribution to improving tumor control and/or reducing the toxicities of treatments. Therefore, research should focus on the following issues:

– Preclinical and/or clinical development and validation of new tracers (PET, SPECT) or NMR sequences to assess the tumor's heterogeneity and microenvironment (e.g., inflammatory infiltrate and its characterization).

– Preclinical validation of imaging modalities (already used in clinical practice or in development) on adapted animal models (e.g., collaboration with veterinary schools for studies on large animals) with suitable imaging systems (e.g., micro-CT, micro-PET, micro-NMR) is mandatory to better characterize the sensitivity and specificity of the imaging modalities, define biological significance (comparison with anatomopathological data) and assess the relationship with tumor heterogeneity.

– Evaluation of the interdependence of these multiparametric imaging modalities using AI, e.g., to transfer the result of one imaging modality to another.

B. EXTRACTION METHODS FOR MULTIPARAMETRIC IMAGING-BASED TARGET VOLUME(S) DELINEATION

– Development and validation of segmentation methods to extract relevant imaging information for target volume delineation; various approaches could be used, e.g., comparison with a ground truth (prostate, larynx) or pattern of local recurrences, to validate the use of these imaging modalities.

– Assessment of the segmentation methods' influence on dose distribution using both photons and proton beams.

– To evaluate the segmentation methods' robustness with images acquired during radiotherapy treatment in the framework of adaptive planning.

– Development of models for the automatic selection and delineation of the microscopic infiltration around the gross tumor volume (GTV) and in the drainage lymph nodes, e.g., Bayesian models of lymph node infiltration, AI-based delineation of clinical target volume (CTV).

– Development of OAR segmentation methods to account for the difference in function between various subareas of a given organ, e.g., lung, parotid glands.

C. VALIDATION OF THE CONCEPTS OF PERSONALIZED IMAGE-GUIDED RADIATION THERAPY

In the era of personalized medicine, new radiation therapy concepts have been proposed, including dose painting, i.e., modulation of the prescribed dose on a subregion or voxel scale, and adaptive radiation therapy, which tailors the treatment plan to the anatomy of the day and could also benefit from daily dose adjustment. Today, the clinical impact of these concepts has yet to be validated. To do this, the following research is proposed:

– Definition of the optimal scale of tumor heterogeneity characterization affecting the variation of dose distribution in photon and hadron beams and on patients' clinical response based on preclinical and clinical models.

– Characterization of the variation in tumor heterogeneity during treatment for different tumor locations (preclinical and clinical) to provide recommendations on which criteria a decision for treatment adaptation should be based.

– Development of preclinical models on large animals (e.g., in collaboration with veterinary schools) to validate the concept of adaptive radiotherapy and dose painting.

– Development of planning tools making it possible to calculate the "dose of the day" based on the consideration of positioning variations as well as intrinsic variations of target volumes (GTV and CTV) and at-risk organs.

– Adaptation of target volume selection/delineation in the framework of combined modality treatments, e.g., should we decrease target volumes in combined immunotherapy/radiation therapy strategies?

D. IMAGING DATABASES FOR TARGET VOLUME DEFINITION

Robust evaluations of any new personalized imaging-based radiation therapy are required prior to use

in clinical practice. Such evaluations need large, structured databases (images and biological data) dedicated to radiation therapies. Moreover, the variability of images between centers is one of the major issues in multicenter studies.

– Creation of preclinical and/or clinical image databases to facilitate validation of the use of multimodal imaging. Proposals should not only aim to collect raw data, but also to propose the development of one or more automated data pre-processing modules in order to standardize the images, resample them, readjust, etc. and make them insofar as possible "ready to use" to answer various clinical questions. This initiative will build on existing initiatives and institutions such as ONCOshare (Rennes), Shanoir, HealthDatahub and France Life Imaging. The databases could be prospective or retrospective on preclinical or clinical data.

– Propose methods of standardizing clinical practices in image acquisition, reconstruction and segmentation and developing a "best practice guide". These proposals should be based on collaborations between experts (pathologists, radiologists, physicists, radiation oncologists) as well as on various ongoing international initiatives such as QIBA, EIBALL, etc.

- Description of collaborations and synergies between the teams and members of the network for each theme:

To ensure open and inclusive research, contributions from a large number of scientists, clinicians, physicists and patient associations are needed. Many RadioTransNet partners involved in such research topics are also members of the France Life Imaging Network (FLI, www.francelifeimaging.fr) coordinated by CEA.

Indeed, research progress, and thus cancer treatment improvement, may benefit from contributions from advanced dosimetry, radiobiology, systems biology, physics and mathematics developments. Scientific expertise is available in several research centers and collaboration will be encouraged. This could benefit from coordination, guidance and support. The development of a network of centers sharing tools, methods and outcome data would facilitate and accelerate implementation of findings.

- International relevance:

Synergy between advanced dosimetry, radiobiology, systems biology, physics and mathematics will enhance clinical practice and radiation protection in the medical field. International collaboration will be encouraged. Moreover, SFPM organizes annual international workshops for young scientists. This topic is consistent with the European Horizon program supporting “Scaling up multi-party computation, data anonymization techniques, and synthetic data generation” (HORIZON-HLTH-2022-IND-13-02) and the European Cancer Imaging initiative.

2) The second taskforce is dedicated to “ionizing radiation interaction with normal tissues”.

The workshop on this topic was held in Fontenay-aux-Roses in December 2019 under the auspices of IRSN. This taskforce is led by François Paris, Carmen Villagrassa and Renaud de Crevoisier. They were assisted by Fabien Millat and Thomas Lacornerie since François Paris and Renaud de Crevoisier could not attend the workshop because of widespread strikes.

- General background and scientific needs:

Considerable progress towards reducing the toxicity of radiation therapy has been made by the introduction of so-called “dose-sculpting” treatment techniques. High-tech RT enables precise beam delivery that closely follows the shape of tumors, yielding an improved efficacy/toxicity ratio. Identification of the molecular and cellular basis of radio-induced side effects could help define new therapeutic strategies to prevent them and improve the quality of life of patients who receive radiotherapy.

- Main scientific objectives:

Reducing the risk of sequelae and second cancer occurrence was identified as one of the seventeen objectives of the French “Plan Cancer 2014–2019” and was also a priority of the last ten-year national program. It will be a key point of the next Cancer Plan. Reducing adverse effects represents a major

challenge for better quality of life for long-term cancer survivors. Preclinical research investigating the mechanistic processes of normal tissue response will pave the way for optimizing radiation exposure and reinforcing the emergence of new therapeutic approaches to cancer treatment.

- Program areas and tasks:

The RADIOTRANSNET consortium identifies as a collective goal the progressive implementation of a strategic research agenda for the optimization of radiation exposure and standardization of radiotherapy practices. The research topics on "normal tissue" considered necessary and most urgent for effective medical care and efficient radiation protection are summarized in six main areas:

A. CLINICAL OBSERVATION - CORRELATION TO DOSE

Patients' individual tissue response may be considered in the choice of therapeutic strategies. This can be based on intrinsic factors (age, gender, genomics/epigenomics…) of the normal tissues, but also on concomitant diseases impacting the general or specific normal tissue tolerance. Patients with a high risk for certain severe normal tissue responses may require a change in dose distribution or treatment strategy. Follow-up protocols may need to be adjusted to the individual morbidity risk pattern based on early predictive molecular or functional marker expression. New predictive tests for individual susceptibility and response to normal tissue toxicity will contribute to developing personalized cancer treatment. The key points to explore are:

– Implementation of a robust methodology to standardize input dosimetric data and standardized registers allowing correlation to the deterministic effects observed
– Development of artificial intelligence models or deep-learning methods to utilize these data and find correlations
– Identification of biomarkers associated with late complications and related quantitative imaging biomarkers (e.g., sarcopenia, heart calcification)
– Evaluation of the effects of confounding factors and reirradiation when studying correlations
– Development of preclinical radiomics approaches.
Further development of NTCP models is required and needs standardized input data, delivered dose data and not only planned dose data.

B. TISSUE RESPONSE RELATIONSHIP WITH HIGH DOSE, HIGH DOSE/FRACTION AND HIGH DOSE RATES

Radiation therapy treatments are mainly delivered by high-energy photon beams produced by linear accelerators according to conventional fractionation. The development of hypofractionated radiotherapy treatments requires a new determination of normal tissue complication probabilities. The biological mechanisms involved after high dose per fraction are controversial. Dose/volume constraints and tolerance doses of at-risk organs have been widely documented for "normo-fractionated" protocols. There is a very significant lack of knowledge on the biological effects associated with both high doses per fraction and high dose rates. The relative biological effectiveness (RBE) concept of normal tissue response to new radiation modalities must be reconsidered. Preclinical research studies must be conducted to optimize new irradiation schemes.
In addition, the use of proton or carbon ion beams makes it possible to reduce the number of beams necessary to deliver highly conformal plans. The biological mechanisms involved after particle beam therapy differ from photon therapy. Consequently, radiobiological studies should consider the particle's impact on normal tissue side effects.

The identified goals are:

– Define a "safe" dose level: optimal and validated dose constraints to be used in the optimization process?
– Where can we get reliable evidence to spare one structure (or sub-structure) over another?

– How can we anticipate real clinical benefit from new advanced radiotherapy technology?
– Investigate the patient susceptibility effect
– Combine effects between organs
– Investigate severe hypofractionation and normal tissue responses
– Explore FLASH protection mechanisms
– Evaluate the irradiation of large volumes at low dose with respect to stochastic risks (IGRT)
– Move RBE concepts forward in line with the development of new techniques and practices in radiotherapy (FLASH electrons, FLASH protons, heavy ions, effects of high dose rate, therapeutic nuclear medicine)
– Initiate preclinical projects investigating reirradiation's consequences.

C. RESPONSES TO TARGETED RADIONUCLIDE THERAPY

Among the innovations developing targeted and personalized therapy, radionuclide/vectorized therapy is very promising. Methodologies like those previously described need to be adapted to radionuclide and vectorized therapy in order to investigate this field and develop new radioisotopes and vectors.

D. VALIDITY OF THE TRANSPOSITION OF THE "SMALL ANIMAL" MODEL TO HUMANS

Radiation-induced morbidity may be observed early (< three months) or late (several months or years) after cancer treatment. Emerging knowledge at the frontier between biology, chemistry and physics is required to better anticipate the risk of new treatment protocols such as hypofractionated schemes and stereotactic approaches. Exploring the role of tissue microenvironments is required to better characterize the normal tissue versus tumor response, with a system radiobiology approach making it possible to identify new molecular pathways of normal tissue response. Current morbidity risk models and normal tissue complication probability (NTCP) models are largely phenomenological in nature and aim to select a data-driven parsimonious correlation between the clinical, dosimetric and biological data with an observed treatment outcome with no assumed damage development processes or evidence of a mechanistic basis. Systems/computational radiobiology approaches and the use of up-to-date localized preclinical modeling as well as transgenic models able to elucidate the role of different cellular compartments will help address the problem. Preclinical models may help us implement NTCP models. The tasks to perform in priority are:

– Introduce relevant preclinical models using adapted irradiation tools
– Validate models for acute and mainly long-term effects
– Introduce preclinical models to study both healthy tissue and tumor cell effects, i.e., develop preclinical models of healthy tissue damage with implanted tumors
– Promote the standardization of preclinical models between different teams
– Introduce relevant preclinical models in large animals (pigs or others).

E. MOLECULAR AND CELLULAR MECHANISMS INVOLVED IN NORMAL TISSUE INJURY

Understanding the molecular and cellular mechanisms and pathways involved in normal tissue injury is a prerequisite to determining new irradiation schemes and therapeutic approaches to prevent and reduce irradiation side effects and improve patient wellbeing. Therefore, the following tasks have been deemed priorities:

– Preclinical research projects on at-risk organs such as the lung, heart, brain, digestive tract and bone
– Study the effects of high doses by fraction and decipher the molecular and cellular mechanisms by *in vitro* / *in vivo* approaches
– Develop systems biology projects applied to radiobiology: radiobiology–molecular biology–mathematics–bioinformatics interface, and share resources and skills on these integrated approaches
– Determine the role of different cell types in the initiation and progression of lesions in healthy tissues after irradiation: vascular compartments, immune cells, stem cell compartments, specialized cell types according to the organs
– Study the different cell fates of normal cells after radiation: type of cell death, senescence,

differentiation, autophagy…
– Decipher senescence's role in the responses of tumors and healthy tissues: beneficial and deleterious effects
– Study dose–response relationships in line with modern molecular concepts (cGAS/STING activation, IFNg, activation…)
– Promote preclinical projects to better study combinations of radiotherapy / targeted therapies / immunotherapy / chemotherapy and their effects on toxicity in healthy tissue
– Develop *in vitro* 3D organoid/spheroid models applied to normal tissue radiobiological studies.

F. THERAPEUTIC STRATEGIES TO PREVENT, LIMIT AND TREAT NORMAL TISSUE DAMAGE

The future challenge in the biological response of normal tissues will be to identify 1) key compartments/processes and 2) sequences of action for temporal therapeutic intervention. Clarification of these mechanisms will help develop specific strategies for protection, mitigation or management of severe radiation side effects to the at-risk organ. The identified priority actions are:

– Develop relevant preclinical models to test therapeutic strategies to prevent and limit severe damage to healthy tissue after radiation therapy
– Develop original and modern therapeutic approaches (stem cell therapy, new pharmacological drugs) applied to normal tissue toxicity
– Study the role of microbiota and microbiota-based therapeutic approaches in RT-induced tumor response and normal tissue injury.
Preclinical research requires dedicated radiation facilities with configurations representative of clinical use for cancer treatment. Specific action for the identification and networking of the whole national infrastructure will be necessary to facilitate joint efforts for the upgrading of and open access to dedicated platforms for preclinical radiotherapy research. Several radiation facilities specializing in preclinical research for radiation oncology, including image-guided small animal irradiators, medical linear accelerators, proton and carbon beams, are already installed and could be used. Numerous platforms have already been organized into different networks. Also, management of dose/volume constraints for preclinical modeling would be necessary (ablative doses, low doses on large volumes…) to develop standardized preclinical models with high clinical significance. These aspects are common to some WP4 and are also developed in the corresponding section.

- Description of collaborations and synergies between the teams and members of the network for each theme:

This topic relies on multidisciplinary collaboration: scientists specialized in radiobiology, immunology, functional genetics, systems biology, methodologists, radiation oncologists, imaging specialists, pathologists, etc. The scientific expertise is available from the RadioTransNet network as identified partners are already working on the topic, such as IRSN, Gustave Roussy or Institut Curie. This would benefit from coordination and funding support.

- International relevance:

Synergy between advanced dosimetry, radiobiology, systems biology, physics and mathematics will enhance clinical practice and radiation protection in the medical field. International collaboration will be encouraged. Moreover, SFPM organizes annual international workshops for young scientists. Moreover, these topics are major concerns for the EURAMED and MEDIRAD European consortia and are consistent with the 'Better Life for Cancer Patients Initiative' underpinning Europe's Beating Cancer Plan.

3) The third taskforce is dedicated to "Combined Treatments".

The workshop on this topic was held through a virtual symposium in December 2020 as a pandemic

precaution. This taskforce is led by Stéphane Supiot, Jean-Noël Badel and Sophie Pinel.

- General background and scientific needs:

The large number of preclinical data concluding that *in vitro* or *in vivo* experiments suggest a potential for clinical benefit in radiotherapy contrasts with the fact that very few new drugs were approved for concurrent radiotherapy administration in the last fifteen years.

It seems obvious that there might have been several gaps between experimental models and clinical reality. Only a minority of various preclinical experiments with targeted therapies and radiotherapy studied these combinations' impact on normal tissue response. The transition to the targeted therapies era has profoundly challenged the value of preclinical models. We propose focusing on few combinatory strategies, which should contribute to producing significant advances and novelty in the field; key aspects will be outlined.

- Main scientific objectives:

One important aspect is to focus on very few key combined strategies among the broad spectrum of potential approaches, based on several selection criteria at both preclinical and clinical levels and the availability of industrial support. With that aim, we propose developing a strategy to enhance the anti-tumor effect of radiotherapy, focusing on various aspects of the combinatory approach such as targeting the tumor cells' intrinsic signals, DNA damage and response pathways involved in resistance to radiation, the interplay between the tumor and vascular network, the cellular dynamics, motility and plasticity involved in resistance to radiation, and the interplay of the cancer cell and immune host.

The choice of a preclinical focus is relevant **in defining how preclinical evaluation of novel combinations would be performed in a network**. We will focus on the major dose-limiting organs; in particular, we will develop and make available to the consortium models of lung, bowel and brain late toxicities.

In addition, the emerging concepts of radiotherapy's immune effects require the development of and access to relevant murine models to evaluate its systemic immune effects. Response to highly specific targeted agents often relies on pre-existing mutations. The molecular profiling of tumors plus data from the TCGA are underscoring the emerging needs for more relevant tumor models reflecting the diversity of molecular subtypes. In the same way, patient cellular models that are fully characterized in terms of genomic profile and clinical response to irradiation will be used to study the efficacy of targeted drugs directed against the activated pathways involved in these models' radio-resistance and irradiation.

- Program areas and tasks:

The project greatly depends on the involvement of partners in imaging, radiotherapy and the pharmaceutical industry.

The potential benefits of the planned structure are the following:

− Faster and earlier testing in combination with RT of some drugs in the development pipeline based on scientific rationale (preclinical data showing that the drugs' target is of interest as well as clinical data showing that it has clinically significant relevance in terms of radiation response)

− Access to a preclinical and clinical platform and network of excellence in the field, incorporating the latest advances in the molecular classification of tumors

− Better identification of unmet clinical needs, which could lead to faster registration of the drugs in combination with RT, ultimately benefiting patients.

The network would select the drugs of interest and suggest the appropriate methodology, including access to technological platforms according to the potential selected targets. The role of each platform was defined during the dedicated workshop on this topic, under the three coordinators' supervision.

The selection of candidates to be transferred into the clinic will incorporate translational molecular, genomic and imaging data demonstrating target engagement to ensure the clinical relevance of the hypothesis and optimize patient population selection for clinical transfer. Candidate targets and agents will encompass various fields such as oncogene addiction, DNA damage repair and signaling, metabolism, tumor stroma and vasculature and immunotherapy.

Results will be presented during international meetings held by NCI-AACR-EORTC, ESTRO, ASTRO and AACR. Translational research and clinical research will be performed under the umbrella of collaborative groups such as EORTC and UNICANCER and organ-oriented groups such as GERCOR, FFCD, GORTEC, IFCT, etc. There will be a yearly meeting in the form of a specific session during the SFRO annual conference.

A specific SRA for this area is presented below:

A. IMPROVING PRECLINICAL TESTING

The relevance and predictive value of preclinical trials are often challenged because of various scientific, methodological, technical and ethical limitations and biases.

- Concerted guidelines for good practice are needed to standardize and coordinate preclinical studies. The future guidelines should address the following issues:
  - Defining the scope of preclinical research: Does the "preclinical field" include cognitive research in radiation physics and biology? Is the "preclinical field" limited to translational/clinical questions?
  - Prioritizing the radiation therapy fields affected by combined therapies: conventional radiotherapy versus new irradiation modalities (FLASH RT, hadrontherapy, etc.)
  - Referencing the *in silico*, *in vitro* and *in vivo* models currently used for combined treatment research (state of the art and critical analysis) + highlighting their respective advantages/interests and drawbacks/limitations, and positioning them in the development chain.
  - Validating the design of preclinical studies according to the scientific or clinical questions addressed: irradiation (radiation equipment, doses and fractionation), delivery of the combined molecule (route of administration, doses, schedules), therapy scheme (neoadjuvant, concomitant or adjuvant drug…)
  - Defining the most relevant methods and tools (imaging monitoring, biomarkers…) and setting the required criteria to evaluate combined treatments' efficacy in preclinical trials: the best balance will have to be found between the possibility of applying these tools and criteria in preclinical studies and the possibility of translating them into clinical practice.

Many technical and ethical limitations stem from the use of small rodents (mice and rats) for preclinical experiments in radiation therapy. Immunocompetent or immunodeficient rodents are easy to use and well known in preclinical oncology but (i) the tumor microenvironment is not fully representative (ii) significant adaptations are needed for targeted irradiation and imaging and for collecting blood samples (detection of biomarkers).

- Promoting research on new preclinical models dedicated to combined "drug and radiotherapy" treatments;
- Facilitating the development and/or access to technical tools adapted to small animals;
- It would be useful to consider the use of larger animals (such as minipigs or dogs) to overcome the limitations. Two questions need to be addressed: is it scientifically and clinically relevant (i.e., will results obtained from big animals have a better predictive value)? is it technically and ethically feasible in France (i.e., are there sufficient infrastructures and know-how to conduct

combined therapy trials using big animals)?

Researchers working in the field of "preclinical studies for combined radiotherapy and drug regimens" regret that access to new molecules is difficult, uncertain and often delayed, probably because pharmaceutical and biotech industries are reluctant. Worse, in some cases, combination therapies are applied in clinical practice without an established preclinical rationale.

- Facilitating partnerships with industry by creating the conditions for trust is urgent.

B. DIRECT RADIOSENSITIZATION

Three priorities are identified: delivery of the treatment, prediction and effects of radiation therapy, and the transfer of preclinical results to clinical practice.

- Treatment delivery raises questions about dose per fraction, standardization of irradiation protocols and access to linear accelerators for preclinical research.
  - The dose per fraction, particularly the effect of ultrahigh dose rate or FLASH irradiation, combined with nanoparticles such as radio sensitizers should be investigated. Moreover, the impact of hypofractionated treatment must be considered and studied.
  - The lack of standardized irradiation protocols is still a real problem because irradiation techniques cannot be compared between them. It would be very useful to form a working group to develop a standard irradiation protocol.
  - Researchers have limited access to linear accelerators for preclinical research, making it difficult to organize experimental measurements and wasting time. Financing solutions must be found to improve the conditions for implementing experimental measurements. The creation of specific calls for tender would be a solution.
- Prediction and effects of radiation therapy are essential in the study of direct radiosensitization. These require the implementation of preclinical imaging, research on dose calculation methods at cellular level and the choice of evaluation criteria.
  - Preclinical imaging is an essential tool to evaluate and understand the biodistribution of nanoparticles, particularly small-animal PET/MR imaging, for which further research on sensitivity and specificity is needed. Scintigraphic imaging (PET, SPECT) is another modality to be developed for the quantification of biodistribution and pharmacokinetics of radiolabeled nanoparticles.
  - Knowledge of the absorbed dose at cell level is essential to quantify the effect of interactions between radiation and nanoparticles. Research on calculation and simulation methods must be reinforced.
  - Consideration should be given to the selection of simple common endpoints to assess tumor control, preservation of healthy tissue and activation of the immune system.
- Transfer from the preclinical to clinical stage requires an evaluation of preclinical results.
  - Standard criteria for evaluating preclinical results should be developed. A working group could be formed to propose this standard.
  - The framework of partnerships to evaluate molecules with manufacturers must be reviewed.

C. RADIOSENSITIZATION BY TARGETING THE MICROENVIRONMENT

To carry out this work, the choice of tumor models respecting the tumor microenvironment, particularly the immune one, is essential.

– The use of sequential biopsies or samples after preoperative radiotherapy should be encouraged to better characterize radiotherapy's interactions with molecules targeting the microenvironment. Mathematical modeling of these interactions will make it possible to better anticipate the clinical protocols that will emerge from these preclinical results. Evaluation of the tumor response by specific imaging will make it possible to transpose preclinical experiments to clinical practice.

– The microenvironment is composed of cells of multiple types and origins, such as vascular cells

(endothelial, lymphatic, pericytes, etc.), immune cells (lymphocytes, macrophages, MDSC, DC, etc.), or stromal cells (CAF, adipocytes, etc.). It is necessary to better characterize the cell subtypes forming this microenvironment. There are few data on the plasticity of the tumor microenvironment subjected to irradiation. One population of the microenvironment cannot be isolated from others and interaction between all the cell types that make up the microenvironment makes multiparametric analysis of these interactions essential.

– Many communication routes need to be explored in the specific context of irradiation, whether the role of substances released into the microenvironment (proinflammatory cytokines, extracellular vesicles, microRNA, pro-angiogenic / antiangiogenic substances, paracrine hormonal signaling, particularly in the bone microenvironment, etc.) or direct communications by intercellular junctions / desmosomes. In particular, the neoangiogenesis or neovascularization mechanisms and inflammatory responses occurring after irradiation require particular analysis.

– The physical parameters of this microenvironment (degree of oxygenation, pressure and acidity) require precise analysis. Studying radiotherapy's effects on the microenvironment's metastatic permissiveness would make it possible to determine new therapeutic targets. Questions relating specifically to the radiotherapy technique's influence on the tumor microenvironment can be asked: influence of fractionation, dose rate and type of particles. The sequence of administration of molecules targeting the microenvironment with radiotherapy is worth investigating. Joint analysis of the tumor's molecular characteristics and relationship to those of the microenvironment will be an essential step in implementing treatment personalization approaches.

- Description of collaborations and synergies between the teams and members of the network for each theme:

This topic relies on multidisciplinary collaboration: small animal modeling, immunology, pharmacology, biomathematics, experimental therapeutics, medical physics for local dose enhancement, etc. Many actors from the Nanotherad initiative are working on these topics and considering combined treatments with drugs or nanoparticles. Partners like Gustave Roussy have developed strong industrial partnerships to investigate drug combinations with radiotherapy. Startups like NhTheraguix have fostered powerful collaboration throughout the country to evaluate the AguIX nanoparticles' potential.

- International relevance:

In accordance with European Directive 2010/63/EU on the protection of animals used for scientific purposes, the topics aim at improving the relevance and predictive value of preclinical trials based on good practice guidelines and improving animal models and dedicated tools for experiments. This topic also fits with the European horizon program supporting the preclinical development of next-generation immunotherapies for diseases with unmet medical needs (HORIZON-HLTH-2022-DISEASE-06-02).

4) The fourth taskforce is dedicated to "Dose Modelling"

The workshop on this topic was held in Paris in September 2019. This taskforce is led by Ludovic De Marzi, David Pasquier and Etienne Testa.

- General background and scientific needs:

Radiotherapy treatments are mainly based on single *in silico* tridimensional dose calculation using patient-specific CT images and contours. Indeed, dose modelling by advanced statistical methods is of great interest in some circumstances. Monte Carlo (MC) simulations seem to meet the expressed needs well: they accurately compute organ doses for every patient using computational 3D models based on their CT images.

However, dose distributions are usually calculated on a snapshot of the living and breathing patient. It is necessary to move from planned dose maps to delivered dose maps. This issue is of major interest

in the context of stereotactic ablative radiotherapy, reirradiation, adaptive radiotherapy and clinical outcomes in order to derive dose–response relationships. However, scientific problems are still unsolved, especially validation of deformable registration algorithms, measurement or computation of the daily dose and dose accumulation.

Because reducing the risk of sequelae and cancer in irradiated areas is an objective of RadioTransNet, the use of MC simulations could help to address various issues related to the radiotherapy field and associated imaging techniques (kV- and MV-imaging, radiology), as well as out-of-field dose estimation or the determination of patient dosimetry caused by imaging CT examinations for treatment preparation, delivery and follow-up. Dose calculation is important to better understand the dose–carcinogenic effect based on CT images because a simple relationship between material density and Hounsfield Units is taking into account patient heterogeneities. However, the perspectives of an increased role of MRI in radiotherapy encourage to led researches on dose calculation on MR images instead of CT images.

Dose modelling will make it possible to estimate accurately for each patient and each treatment, the out-of-field doses delivered by the therapeutic beam and the imaging positioning procedure used for IGRT.

Finally, dose modelling using MC calculation will be used to answer current questions such as simulation of innovative treatments like:

- ultra-high dose rate (Flash) or mini-beam radiotherapy (MBRT) for which accurate dosimetry is currently limited using standard methods and dose incertitude will have more impact on patients compared to current radiotherapy protocols,
- ions beams, as an example, in the case of protons the appearance of necrosis just behind Bragg Peak deposition has to be elucidated to prevent associated sequelae,
- nanoparticles, radionuclide or vectorized: by, for example, determining the local dose enhancement factor is crucial for the optimization of protocol.

- <u>Main scientific objectives:</u>

There are no internationally recognized recommendations/protocols on how to plan radiotherapy to minimize the risk of cancer in irradiated tissue. Indeed, during the entire treatment, dose to patient is not always recorded and calculated due to different diagnostic procedures. Moreover, the addition of physical doses from orthovoltage and megavoltage energy beams is controversial. Thus, new models of biologically effective doses are required to accumulate doses and consider previously absorbed doses in cases of reirradiation.

The developments of innovative techniques such as nanoparticles/vectorized, flash therapy or MBRT stress the need for the development of new tools for dose measurement and calculation. Furthermore, it also exists a gap between dose deposition and biologically effective dose which is currently unsolved. This gap has expanded considering these new irradiating techniques for which the linear-quadratic model is far from sufficient.

The RadioTransNet consortium's main ambitions for this purpose are: to calculate delivered dose to patients instead of planned dose to derive dose–response relationships; to develop new and reliable built-in software tools to estimate accurately and rapidly imaging and out-of-field doses; to develop tools and methods for accurate dose measurement and calculation dedicated to innovative beams; to develop mathematical models to sum biological doses or calculate biologically effective doses delivered by various beams.

- <u>Program areas and tasks:</u>

The RadioTransNet consortium identifies as a collective goal the progressive implementation of a Strategic Research Agenda (SRA) for the optimization of radiation exposure and standardization of radiotherapy practices. The research topics on "Dose Modelling" could be summarized as follows:

The primary goal of RT is to reach tumor control by minimizing healthy tissue complications. During the last decade, intensive research was performed to quantify the out-of-field doses produced by scattered radiations, which are known to enhance the risk of inducing a secondary cancer and complications of the cardiovascular and central nervous systems, fertility problems and other

toxicities, for pediatric and young adult populations. Research should also include proton and carbon ions beams.
In addition to out-of-field doses, we should also examine additional doses delivered by X-ray imaging systems used in image-guided RT for patient positioning, known as imaging doses. The RadioTransNet consortium will focus on assessing out-of-field doses and concomitant doses due to positioning imaging procedures during radiotherapy.
The quantity used at present for clinical prescriptions in radiotherapy deliveries is absorbed dose to water. Therefore, for several radiotherapy modalities, such as ion beams, treatment planning is based on the product of the absorbed dose and a weighting factor accounting for the relative biological effectiveness of the respective radiation type. The question is how characteristics of the track structure can be used to predict the biological outcome expected for a given irradiation. It has been shown that nanodosimetric quantities derived from ionizing radiation track structures in mixed radiation fields are directly related to the biological outcome of the mixed field. They can be the basis for future treatment planning systems with biological optimization based on nanometric characteristics of particle track structures.
Only 3% of adult patients are included in clinical studies, which take a long time to initiate, and clinical results are difficult to register. Finally, the results are often irrelevant considering the development of practice and knowledge. Therefore, it is necessary to use treatment data from all patients to determine feedback and improve clinical practice. The main barrier to creating a machine-learning database is the poor quality of data, which are not standardized. To build an efficient clinical decision support system and radiotherapy that can correlate toxicities and tumor control probability to treatment data, actually delivered doses are required. Functional imaging after or during treatment will improve disease response assessment and registering these images with dose distribution is an active area of research. Such registrations are necessary to enable quantitative evaluation of the tumor or normal tissue response to radiation.
The dose accumulation during overall treatment is of major importance to derive dose–response relationships, tumor control probabilities and normal tissue complication probabilities. However, this concept only considers physical dose. Modified fractionations or modified treatment modalities make it necessary to consider biologically effective doses. In clinical practice, the linear-quadratic model and the equivalent dose to 2 Gy fractions (EQD2) are used to compare different fractionations. There is a strong need for mathematical models that can accommodate modern radiotherapy cancer care. Models aiming to derive dose/volume constraints in a context of reirradiation are essential. These investigations should also consider relative biological effectiveness according to the linear energy transfer of particles.
The taskforce's SRA is presented below:

A. DOSE CALCULATION

Dose calculations are the key component of treatment planning systems (TPS) that ensure proper tumor irradiation while sparing insofar as possible healthy tissues and at-risk organs. Such calculations must, therefore, be able to estimate doses in both tumor volumes and healthy tissues (out-of-field doses). Moreover, doses induced by imaging, especially during image-guided radiotherapy (IGRT), must be accurately considered, which is not the case currently. Finally, the impact of treatment uncertainties must be minimized with improvements in each treatment step (imaging, planning and delivery). Monte Carlo (MC) simulations are the gold standard in terms of precision and are extensively used in research to improve estimates of any kind of dose (transversal research focus). The main research areas identified are the following:

- Monte Carlo (MC) simulations
  - Key role in the connection between physical dose calculation and biological endpoint predictions (e.g., Tumor Control Probability and Normal Tissue Complication Probability)

using biophysical models
    - Use of AI for computing time acceleration. If direct predictions of dose distributions can be considered as science fiction, AI might replace MC methods to predict some probability distributions, boosting the computing time efficiency
    - Modeling of MRI-guided linear accelerators (MRI-LINAC) for precise physical (and biological) dose predictions
- Modeling of out-of-field doses
    - Need for improved experimental data (for model validation) and beam models
    - Need for patient data standardization
- Modeling of doses induced by imaging, especially during image-guided radiotherapy (IGRT)
    - Need for patient data standardization
- Robust treatment planning to consider treatment uncertainties and organ motion. Main areas:
    - Active motion management (e.g., breath control)
    - Probabilistic treatment planning methods
- Improved tissue characterization (dual-energy computed tomography, MRI, proton tomography...)

B. ADAPTIVE RADIOTHERAPY

The dose accumulation during overall treatment is of major importance to specify dose–response relationships, tumor control probabilities and normal tissue complication probabilities. Nevertheless, the clinical benefit and benefit/cost ratio have yet to be demonstrated. Many biological parameters related to the biological effect (fractionation, treatment duration) must be taken into account. There is no consensus on the appropriate manner of accumulating the dose. We lack robust validation of dose accumulation algorithms based on elastic registration and also robust parameters to decide on new planning. In addition, more and more patients benefit from reirradiations and clinicians need to know how to consider previously absorbed doses.

– Adaptive radiotherapy implies research in the following areas: auto-segmentation, deformable registration, automated planning, advances in workflows (off and online), anatomical and functional imaging, and evidence of benefit in clinical sites.

– All of these main adaptive radiotherapy components: delineation, deformable registration, planning and decision-making may benefit from AI-based algorithms.

– MR-LINAC machines are particularly suitable for adaptive radiotherapy due to high contrast for soft tissues. Adapting the treatment (volume, dose) to the changing signal (diffusion, perfusion...) during radiotherapy courses should be areas of preclinical and clinical investigation. Adaptive radiotherapy according to the changing PET signal could also be studied.

– The development of an image and dosimetric database is suggested. This large-scale database would make it possible to link outputs (tumor control, toxicity) to the accumulated dose.

C. INNOVATIVE RADIATION THERAPY TECHNIQUES

A main limitation of RT remains that the dose delivered to a tumor is conditioned by how the surrounding normal tissues will tolerate it. Consequently, the treatment of radioresistant tumors (e.g., gliomas), tumors close to a sensitive structure (e.g., the spinal cord) and pediatric cancers is limited. Finding new approaches or innovative techniques to shift the normal tissue complication probability (NTCP) curve towards higher doses is therefore a priority in RT today.

Spatial fractionation (micro, grid or minibeam radiation therapy) is a RT technique derived from synchrotrons (x-rays) that combines the use of spatial fractionation of the dose with submillimetric field sizes. This approach can, in particular, be developed with protons or electrons to partner the inherent physical advantages of charged particles for radiotherapy with the gain in normal tissue preservation observed when irradiated with narrow spatially fractionated beams. Several studies evidence a very significant increase of mean survival time in preclinical investigations with MBRT, this significant increase of the therapeutic window could provide real hope may open new treatment

strategies for high-grade glioma patients.

FLASH radiotherapy, a new treatment modality and irradiation technology currently being developed by several groups, involves the ultrafast delivery of radiation treatment at dose rates several orders of magnitude greater than routine clinical practice. It has recently been shown that FLASH with electrons, photons or protons is as effective as conventional irradiation for tumor inhibition while dramatically less damaging for healthy tissue. While the mechanisms underlying the biological effects remain to be elucidated, the FLASH effect has been very recently demonstrated in the first human patient with promising results, supporting further studies.

Recently, several studies showed significantly enhanced biological effects when human tissues were treated with nanoparticles before being irradiated. The use of boron-containing compound is an example with protons or neutrons: thermal neutron interactions can result in the production of energetic charged particles with high relative biological effectiveness (called boron neutron capture therapy, BNCT) as well as in proton boron capture therapy (pBCT), where low-energy alpha particles with high RBE can be generated. These kinds of techniques could be used during the treatment of radioresistant cancers. Although the increased effectiveness was proven experimentally, the exact mechanisms behind this effect remain a source of debate and have still not been elucidated.

D. NEW TOOLS DEVELOPMENT FOR RADIOBIOLOGICAL DOSE MODELING

Despite multiple simulations, some radio-induced responses still do not fit with models, such as dose enhancement with nanoparticles. The biological mechanisms of chemo-radio-induced responses in tumors and neighboring tissues are very complex and vary between different signs (age, gender, genomics, proteomics) and symptoms of morbidity (e.g., reduced lung/liver tolerance due to smoking and alcohol consumption) or previous/parallel treatments. A contemporary view of radiation-induced responses involves multiple cell compartments that interact in a complex sequence of events following the radiation insult. Adaptive and innate immune systems, vascular networks, mesenchymal and epithelial cells and even microbiomes can contribute to the radio-induced response. Moreover, radio-induced response results from various biological cascades at numerous levels (molecules, cells, organs…). All these parameters should be considered for accurate *in silico* modeling.

The following research is proposed:
- Database creation to collect preclinical (chemicals, *in vitro* and *in vivo* models) and clinical data and improved access to Biological Resource Centers (BRC) to facilitate the use of these data by computational tools.

- Structured analyses: creation of facilities dedicated to complex analyses, recruitment of qualified staff (biostatisticians, bioinformaticians and bioanalysts) to perform such deep analyses; creation of a working group on preclinical radiotherapy: definition of clear and common annotations, definition of minimal endpoints and analyses, definition of processes for improving data quality control and traceability.

- Generation of radiobiological data following the working group's recommendations for data standardization and using the various beams available in the RadioTransNet network (i.e., beams from ResPlaNdIr) to evaluate radiobiological responses depending on beam parameters (particles, energy, dose rate, fractionation…), in combination or not with nanoparticles.

- Identification and improvement of existing mathematic models as well as development of new computational tools for radiation biology modelling. Absorbed dose is a macroscopic average quantity, while the biological effects of ionizing radiation are known to be related to the pattern of radiation interactions on the micro- and nanoscopic subcellular scales.

- <u>Description of collaborations and synergies between the teams and members of the network for each theme:</u>

This work package relies on multidisciplinary collaboration: engineering, physics, dosimetry, medical physics, biomathematics and data processing. As mentioned above, identified RadioTransNet partners are already working on this topic, i.e., members of the ResPlaNdIr network, IRSN and teams from the Nanotherad–Paris Saclay consortium. The topics will also benefit from the Nanox project emerging from M. Beuve's team (Lyon).

- International relevance:

Many parties and projects have already secured support from the European Commission in these areas, for example through the H2020 program (e.g., European Federation of Organizations for Medical Physics EFOMP and European networks for metrological support such as PTB and NPL). There are few platforms developed in close cooperation with all stakeholders (clinical, industry, regulatory and research) that can specialize in studying these effects. The topics of this work package are consistent with the European programs EURADOS and MEDIRAD, with which RadioTransNet is already connected. They also fit with the European Horizon program supporting R&D for the next generation of scientific instruments, tools and methods (HORIZON-INFRA-2022-TECH-01-01).

5) Conclusions from the Feedback Workshop: Standardization and Database Implementation

A feedback workshop was held in Paris on 22 October 2021. A major point, which has been underlined in each work package's roadmap, is the strong need to standardize and share data. This specific topic will receive particular attention as it is a crucial point for structuring research and standardizing practices within the network. The development and implementation of databases for clinical or preclinical data collection and sharing will help us fully use existing ones, avoiding wasting time repeating what has already been done and defining common ways to generate new datasets. Moreover, database implementations are required for the development of and training on, especially in the case of artificial intelligence, new tools for simulating radiotherapy's efficacy and predicting associated adverse effects.

This database implementation could be inspired by the infrastructure developed in the context of lymphoma research, which brings together the consortium's clinical professionals, researchers, data collections, biological resources and platforms (https://experts-recherche-lymphome.org/). These developments could rely on the existing and sustainable UNITRAD infrastructure. Depending on the type of data, specific needs and annotations will have to be defined by the "producers" as well as the users. Database development could benefit from the MED-OSIRIS initiative, a computational model based on data sharing developed to facilitate personalized medicine, which is currently being implemented in a radiotherapy-compatible way. These partnerships will allow close collaboration between clinical and preclinical research and so ensure clinical-orientated preclinical research.

This topic is wholly compatible with the European Horizon program supporting initiatives helping to generate global standards, specifications and recommendations for open sharing of FAIR research data, publications and software (HORIZON-INFRA-2022-EOSC-01-04).

IV. National and international collaborations

The RadioTransNet project will be highly interconnected thanks to the preselected members of the Scientific Committee and their respective affiliations in European medical and scientific associations. It will build upon or create synergies with numerous international, European and national projects. Our initiatives will be opened to international collaborations with ESTRO, EPT, Enlight, PTCOG, CERN and other dedicated scientific networks including other specialists. Also, interaction with existing EU research platforms including EURADOS, EURAMET and EURAMED will be developed to anchor the national view of preclinical research for radiation oncology in the European landscape. This will increase RadioTransNet's impact, avoid duplicating efforts and improve our dissemination and consensus-building efforts. All of these have been described in the relevant section and each partner's involvement in the four work packages are listed in the annex.

V. Concrete actions, scientific events, meetings and workshops contributing to structuring radiotherapy in France

RadioTransNet proposes to set up small events on targeted topics as well as an annual preclinical radiotherapy conference. RadioTransNet, through its numerous partners, will contribute to the development of dedicated teaching and training. The network also aims to implement a Preclinical Radiotherapy Research Observatory.

1) Scientific coordination

To facilitate scientific reflexion, digital and physical events such as webinars and workshops are held on targeted topics within RadioTransNet's research program. The French Society of Ionizing Radiation Biology (SFBR) launched this summer. It aims to support and promote research in the field of ionizing radiation biology and its transfer to human health. Since SFBR and RadioTransNet share common orientations, they plan to work in close collaboration and organize joint events. Moreover, RadioTransNet will also strengthen its relationship with Canceropôles to promote local actions. As an example, it is already planned that RadioTransNet will partner Canceropôle Normandie to organize in 2022 a physical event dedicated to hadron therapy, from bench to bedside. Targeted events will be planned at least once a year.

Last but not least, RadioTransNet aims to create a large and recurrent (annual) national event dedicated to research in preclinical radiation oncology involving international experts and providing an update on network activities for its partners. This event will include several sessions on overlapping topics from each work package and also one to inform patient associations on advances in research and how patient wellbeing is central to the projects. This specific session could follow the model of QP2R events (Quand le Patient Rencontre la Recherche) co-organized by laboratories from the PRIMES and DEVweCAN labExs (Lyon) and Europa Donna association.

2) Teaching

SFRO (SFjRO) and SFPM are involved in organizing several education and training activities respectively in brachytherapy, radiographic anatomy, radiophysics and radiobiology for SFjRO and at least three postgraduate education programs per year for SFPM. Several parties have already organized teaching and training activities relating to radiotherapy and involving other partners to this consortium, many of which are listed here http://sirlaf.free.fr/liens/cours.htm):

- DU (Diplôme Universitaire) de radiobiologie et radioprotection (Univ. Paris Sud)
- DU de radiobiologie et radioprotection (Univ. Lille2)
- DU de radiobiologie et radioprotection (Univ. Lyon)
- DU Curiethérapie (Univ. Paris Sud)
- DU Innovation thérapeutique (Univ. Paris Sud)
- DU radiothérapie ORL (Univ. Paris Sud)
- DIU (Diplôme inter universitaire) Radiologie interventionnelle oncologique (31 French universities)
- Diplôme de qualification en Physique radiologique et médicale (DQPRM) (INSTN)
- Master de cancérologie (Univ. Paris Sud): 4 teaching modules, 80 hours dedicated to radiation biology
- International Master of Oncology, (Univ Montpellier)
- Master de physique médicale (Univ. Paris Sud)
- Master Européen de Radioprotection (Univ. Grenoble)
- DIU radioanalyse et radiobiologie (Lyon)
- DIU radiothérapie externe haute technicité (Univ. Lille2)
- DIU Thyroïdologie / DIU tumeurs endocrines (Univ. Paris Sud/Univ. Lille2)

Moreover, many of RadioTransNet's institutional partners give access to e-learning, MOOC and seminar retransmissions. In this way, SFRO is also building a digital platform that will group all the

video content produced by SFRO, SFjRO, AFCOR and RadioTransNet together.
The educational and training program to be associated with RadioTransNet's second phase would be planned and organized with AFCOR, which oversees the training of French radiation oncologists, in close liaison with the four main areas' moderators. AFCOR will appoint one corresponding member who will coordinate the program.

3) Training

Several national incentives for biological physics education will support students, such as the Maurice Tubiana grant from SFRO, and, at local level, specific PhD grants from institutions like IRSN, CEA, Curie, Gustave Roussy, Fondation de France, ARC…
Training possibilities will be increased and supported by call proposals from RadioTransNet orientations based on the SRA. RadioTransNet is working to launch an annual call, like the Maurice Tubiana grant from SFRO, to support at least one student's studies on project topics. RadioTransNet is also negotiating with industry (i.e., AstraZeneca) to increase student support opportunities. These joint calls will focus on targeted topics within the work package's themes.

4) Preclinical Radiotherapy Research Observatory

The network also aims to implement a Preclinical Radiotherapy Research Observatory. It will complement the existing Clinical Radiotherapy Observatory, supervised by INCa in close collaboration with SFRO, SNRO and SFPM. The Preclinical Radiotherapy Research Observatory will provide an overview of research in the field in France, help partners connect and may join the RadioTransNet initiative for standardization and harmonization of preclinical research practice. The Scientific Committee will also establish an inventory of the different funding instruments able to support the RadioTransNet research program.

VI. Expected outcomes (collaborations, synergy, visibility, attractiveness of research in French radiotherapy…)

Several reports and specific meetings aiming to identify French research's strengths in radiation oncology pointed out the dynamism and originality of research achievements in radiobiology and medical physics. The major weaknesses are well known, such as the shortage of human and technical resources and the lack of funding and dedicated academic or industrial calls, particularly in translational and preclinical research. In this context, the initiative taken by the French National Society for Radiation Oncology (SFRO) and French National Society for Medical Physics (SFPM) for all partners and structures involved in this purpose is a major opportunity to structure translational research in radiation oncology through large studies aiming to benefit patients. Reducing the risk of sequelae and second cancer occurrence was identified as one of the seventeen objectives of the French "Plan Cancer 2014–2019" and the future INCa funding SEQ21 "Limiter les séquelles et améliorer la qualité de vie" and PREVBIO2021 "Recherche en Prévention : apport de la biologie".

A large scientific community, including experts in the field and representatives of research institutes (CEA, CNRS, INSERM, IRSN), healthcare professional associations (SFRO, SFPM) and federations of public and private hospitals (SNRO, FHF, Unicancer), will create networks organized around the four major issues facing clinical practice in radiation oncology: target definition, normal tissue, combined treatments and dose modelling. The sub-targets linked to these four major priorities are unlimited. They include all aspects associated with fundamental radiobiology, preclinical studies, imaging, medical physics research and transversal aspects clearly related to these scientific areas, such as medical oncology, radiology, nuclear medicine and cost-effectiveness considerations. A bottom-up process under the supervision of steering and scientific committees is outlined in the RadioTransNet proposal to promote interdisciplinarity, unite existing national research initiatives, further synergies and facilitate connections between research groups and technological platforms.

As described above, active collaboration between relevant clinical and scientific parties will drive implementation of the SRA in the four major identified areas. Synergy between advanced dosimetry, radiobiology, systems biology, physics and mathematics will enhance clinical practice and radiation protection in the medical field. This should also allow for standardization and harmonization of

methods and endpoints. The research program will be open access on the RadioTransNet website for widespread consultation and implementation. Moreover, publication of RadioTransNet reports and recommendations on good practice for better radiation oncology and communications during national and international congresses will increase RadioTransNet's impact.
RadioTransNet's final objective is to give itself the means to develop new strategies for better patient care with radiotherapy. As well as structuring the scientific and medical community, RadioTransNet aims to increase partnerships with pharma to facilitate drug development for combined therapy and clinical trial initiation.

To achieve the project's objectives and maximize the expected impact, RadioTransNet will follow a well-defined dissemination, exploitation and communication strategy. The following main groups will be targeted by the dissemination: scientific community (researchers, students, research organizations in the field of radiobiology, oncology, physics…), national and international platforms (EURADOS, EURAMED, MELODI, EURAMET…), medical community (clinicians, including oncologists, radiation oncologists, medical physicists, specialists in cardiology, pneumology, neurology, general practitioners), national and European medical scientific societies (SFRO, ESTRO, SFPM, EFOMP…), and healthcare authorities and regulators (DGS, ASN…), patients and patients' organizations (ARC, LNCC, European Patients' Forum…).

Missions d'organisation et de gouvernance/ Organization and management of the network

Organization of the network

The application must present well-defined and detailed governance, in which responsibilities and tasks are clearly described.
The application should present:
a coordinator with recognized scientific and managerial skills. The coordinator organizes and supervises the activities of the network. The coordinator's commitment will be crucial to the achievement of the network's objectives. The coordinator shall present his skills and expertise in order to demonstrate his abilities and availability to organize the network.

- a steering Committee which defines the strategy, and ensures coordination with all participating teams;
- a scientific Committee;
- an understandable organizational scheme and a network operating charter;
- a charter of ethics common to the network, signed by its members.

The scientific managers of the team members of the network must describe precisely their commitment in the network according to their skills, expertise and availability.

I. Organization of the network

The application is led by one coordinator from SFRO and one co-coordinator from SFPM. During RadioTransNet's first phase, coordination was managed by Professor Philippe MAINGON and Vincent Marchesi, who were respectively chairmen of the French Society of Radiation Oncology (SFRO) and the French Medical Physics Society when it launched. They organize and supervise the Scientific Committee's activities. They will manage the network for at least two more years to oversee the actions before SFRO and SFPM assign new coordinators. The coordinators' backgrounds and CVs are detailed in the "Skills and expertise" section of this application.

1) Coordinator

During his chairmanship of the Radiation Oncology Department at Centre Georges-François Leclerc in Dijon, the coordinator developed several preclinical research activities in the field of imaging. He worked on researching the immunology of environmental normal tissue. He coordinated the SARI national PHRC project studying the clinical, biological and dosimetric predictive factors associated with the occurrence of sarcoma in irradiated areas.
He was chairman of the Radiation Oncology Group of the European Organization for Research and Treatment of Cancer (EORTC) from 2012 to 2015. During his chairmanship, he launched the STAR initiative (Synergy of Targeted Agent Research) aiming to promote and support the early development of combined modality treatments including radiation therapy. This initiative gave pharmaceutical companies the opportunity to study in a select network of institutions working in the fields of radiobiology, radiosensitivity of tumor cells, radio-resistance and interactions with normal tissue during the early introduction of combined treatments for various tumor locations in which chemo-radiation demonstrated superiority over radiotherapy alone.

2) Co-coordinator

The co-coordinator has been a Medical Physicist in the Radiation Oncology Department of the Institut de Cancérologie de Lorraine in Nancy for twenty years. He has been a coordinator of the GORTEC working group's Medical Physicist Group. This group defined recommendations on QA procedures for new radiotherapy techniques such as IMRT at a time when no guidelines were published by scientific

societies. During his chairmanship, the group also performed a multi-institutional study based on an external audit of IMRT procedures for French and Belgian centers (work mentioned in the ICRU 83 report).
The Co-coordinator is a member of the Editorial Board of the Cancer Radiotherapie scientific journal and a reviewer for many journals on medical physics or radiation therapy (IJROBP, Radiother/Oncology, Medical Physics, Cancer/Radiother…).

3) Steering Committee

The Steering Committee has a supervisory role in defining the topics developed by the network. The new SFRO Steering Committee will have to reappoint representatives of the Society to that role in the next two years. Three SFRO representatives, one for Unicancer, one for the CHU and one for private practice, and three SFPM representatives to be named will be committee members. Other national medical societies such as the French Radiology Society or the French Nuclear Medicine Society will each appoint one representative. One representative of "end users", Marie-Sophie Gannac, has been invited to join the Steering Committee. The chair and/or co-chair of the Scientific Committee are invited, as are INCa representatives, to be observers. It will check whether the Scientific Committee's activities are running as expected by the SFRO and SFPM boards. It reviews the use of the funding provided by INCa to ensure that RADIOTRANSNET is following the program's guidelines and meets every year. All members will be appointed for two years. Their term can be renewed only once.

4) Scientific Committee

The Scientific Committee develops and promotes a research program relevant to preclinical research for radiation oncology and based on the roadmap resulting from consensus conferences. In the framework of RADIOTRANSNET, a scientific committee has been created to answer the first INCa call on behalf of SFRO and SFPM and propose continuing its activities. It comprises experts in radiation oncology, biology and medical physics. The members are Philippe MAINGON (coordinator), Vincent MARCHESI (co-coordinator), David AZRIA, Jacques BALOSSO, Marc BENDERITTER, Elizabeth COHEN-JONATHAN MOYAL, Gregory DELPON, Eric DEUTSCH, Marie DUTREIX, Thomas LACORNERIE and Paul-Henri ROMEO (respective affiliations are listed in the section "Members of the network").

- The Scientific Committee has formulated the final version of the SRA and associated roadmap on the basis of four workshop reports.
- At the beginning of RadioTransNet's second phase, a kick-off meeting will allow the Scientific Committee to define in more detail the priority objectives within the roadmaps produced for each main focus, in collaboration with the work package's moderators, and accurately define the methodology used to standardize the network's activities. The format of the deliverable (workshops, webinars, congresses, calls and reports) will also be defined. A list of partners is provided in the "Partnerships" section of the application. This list remains open to any new partner wishing to join the network.
- The Scientific Committee has appointed moderators, including a medical doctor, biologist and physicist for each identified work package who are responsible for its scientific coordination. The Scientific Committee arranges measures for receiving the moderators' feedback on the research programs, which will be submitted to INCa and academic institutions and charities.
- Implementation of participative web consultations (through the RADIOTRANSNET website) helps us gather feedback from members of the network.

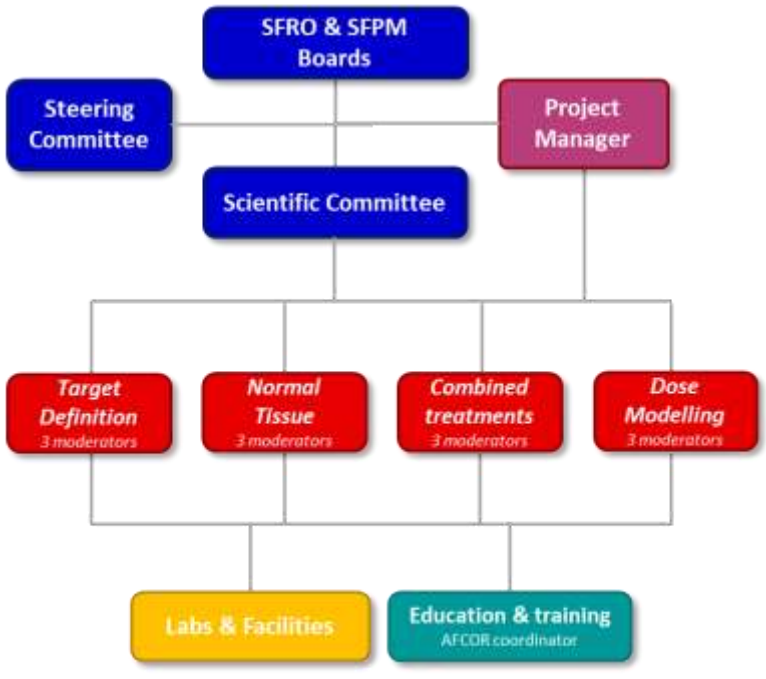
The term of Scientific Committee members will last two years. After this period, the Scientific Committee will be renewed. New coordinators will have to be appointed respectively by SFRO and SFPM. Members of the French Society of Ionizing Radiation Biology will also be invited to join the Scientific Committee. They will both have to revise the list of Scientific Committee members.

5) Project Manager

The project manager provides support and assistance for coordinating and structuring the network, maintains contact with scientific societies and partners, and assists the project coordinators for their reporting to INCa. Emilie BAYART was recruited as the RadioTransNet project manager when it officially launched.

- The project manager pays particular attention to the project's timelines, particularly for organizing events and implementing the strategic research agenda. She helps the area coordinators arrange scientific events.
- The project manager also promotes interactions between (radio)biology, imaging modalities and dosimetry within each defined research area and between the four areas.
- The project manager ensures dissemination through social media and the RadioTransNet website (www.radiotransnet.fr). This website facilitates web consultations at every stage of the project.
- The project manager organizes all RadioTransNet meetings, with at least one meeting per year. There will also be specific annual meetings organized by the WP moderators around certain themes (DNA repair, nanoparticles, mice models, preclinical irradiators and imaging, computing …).
- The project manager facilitates formal liaisons and communications at European level with ESTRO and EORTC, with the EU platform including EURADOS, EURAMED and MEDIRAD, and also with similar European incentives and networks (UK: CR-Rad, Germany: DKTK, etc.).

The major weaknesses of such a network includes the scarcity of human and technical resources, which could complicate communication between partners and the standardization of methods. However, the bottom-up organization should help the RADIOTRANSNET coordinators circumvent these bottlenecks. Regular SWOT analyses will help counteract emerging difficulties and facilitate the network's transparency, interactions and efficiency. It will provide relevant tools and arguments to the Scientific Committee for the development and implementation of the strategic research agenda.



Organizational scheme of the RADIOTRANSNET network

Coordinators	Time commitment
Philippe MAINGON	15%
Vincent MARCHESI	15%
Scientific Committee	
David AZRIA	5%
Jacques BALOSSO	5%
Marc BENDERITTER	5%
Elisabeth COHEN- JONATHAN MOYAL	5%
Gregory DELPON	5%
Eric DEUTSCH	5%
Marie DUTREIX	5%
Thomas LACORNERIE	5%
Paul-Henri ROMEO	5%
Project Manager	
Emilie BAYART	100%

6) Working groups

As described previously, moderators have been appointed to manage activities within each work package and are listed in the following table. Four exploratory workshops bringing together experts representing a wide range of disciplines have been organized by these moderators to explore the four key scientific questions raised by challenging innovative radiotherapy treatments, to identify the most promising

preclinical research lines and to provide recommendations for the future. All existing research Institutes (CEA, IRSN, CNRS, INSERM) and networks (DOSEO, Cancéropôles and ongoing SIRIC partners) including radiobiology in their field of interest (Curie, Gustave Roussy, La Pitié-Salpêtrière, Montpellier…). Moderators also select scientific and medical experts to ensure that the areas addressed by the four work packages are fully represented and to keep the scientific level of the conference as high as possible. Young scientists, including post-doc, PhD and MD students, are invited to participate in the framework of AFCOR and SFjRO (French Society of Young Radiation Oncologists).

Based on the roadmap, the work will be planned in working groups with the experts distributed to ensure the balance of skills. Each working group allocates the necessary tasks to working subgroups to answer the questions defined by the roadmap. This step-by-step approach will make it possible to perform the necessary research on the four previously described topics, supported by INCa calls, to improve radiation oncology's therapeutic index. Each working group's progress will be published on the RadioTransNet website.

Target Definiton	Normal Tissue	Combined Treatment	Dose Modelling
Vincent Grégoire (OR) Centre Léon Bérard - Lyon	**François Paris** (CB) Centre de Recherche en Cancérologie et Immunologie Nantes-Angers	**Stéphane Supiot** (OR) Centre René-Gauducheau - Nantes	**Ludovic De Marzi** (PM) Centre de Protonthérapie - Institut Curie - Orsay
Charlotte Robert (PM) Gustave Roussy - Villejuif	**Carmen Villagrassa** (PM) IRSN - Fontenay-aux-Roses	**Jean-Noël BADEL** (PM) Centre Léon Bérard - Lyon	**David Pasquier** (OR) Centre Oscar Lambret - Lille
Benjamin Lemasson (CB) Grenoble Institut Neuroscience	**Renaud De Crevoisier** (OR) Centre Eugène Marquis - Rennes	**Sophie Pinel** (CB) Centre de Recherche en Automatique de Nancy	**Etienne Testa** (CB) Institut de Physique Nucléaire - Lyon

II. Ethics

RadioTransNet wished to adopt an ethics charter that embodies the principles to which it adheres. With that charter, the radiotherapy transnational network seeks to affirm its commitment to perform research according to the ethical guidelines recognized by the national community. The network is at the interface of research, public health, radiation therapy, teaching, training and patients. Research undertaken within RadioTransNet extends to many different fields in both basic research and its application. RadioTransNet emphasizes the need to situate transnational research and the resulting progress in a rigorous ethical framework that contributes to enforcing ethical guidelines for research and living subjects and to respecting human dignity and human rights. All human research is subject to protections established by the international community. Furthermore, all research must comply with current laws and regulations where it is conducted (Jardé's law). This charter aims to define the legal and regulatory documents that various internal departments must maintain to ensure that all parties remain well informed. As patient safety must always be the primary concern for doctors and/or scientific researchers, the interests of research participants must always take precedence over the interests of science and society. In this regard, the benefit obtained through research must be compared against the risks assumed by all parties, irrespective of whether the research subjects are in good or bad health and whether the staff are scientific, medical or paramedical. All structures involved in the preclinical or transnational research promoted by RadioTransNet give staff guidance on legislative and regulatory directives applicable to research using human biological samples. These texts protect both the person from whom samples were taken with respect to the inventory maintained by health and research authorities and the staff working on them. French laws and regulations impose strict procedures for informing patients and obtaining their consent or non-opposition. Moreover, a sample may not be used for research purposes if the person from whom the sample was gathered is expressly opposed to its use for that purpose.

Research studies using human stem cells of embryonic or fetal origin must adhere strictly to legislation and regulatory statutes. A person whose genetic characteristic is to be examined must be informed prior

to giving his or her consent, which staff must respect. Moreover, RadioTransNet would like to draw the teams' attention to the ethical questions that often arise in the course of research on genetic predispositions and vulnerabilities.

The use of live vertebrates in biochemical research is currently supervised by European Directive 86-609, which was transposed into French law in 1987. This directive was revised in 2010 and its transposition is under preparation. The use of animal models for biochemical research is an essential step in scientific activities, preceding research on human subjects. RadioTransNet research in the scope of this charter should be consistent with the regulatory text currently in force. The French text requires that all facilities performing animal experimentations are approved, that lead investigators in charge of the protocol are authorized to perform that experiment and that all persons involved receive appropriate training. Certain protocols must be declared and justified at the prefecture before any research can begin. Finally, any person possessing nondomestic species must have a certificate of capacity. Moreover, the RadioTransNet Scientific Committee expects staff working with animals to be aware of good practices in developing research protocols for use on vertebrates.

- Statutory operating procedures

Members of the RadioTransNet network pledge to respect the following statutes, which may be supplemented with internal rules of procedure or another document:

- Creating a steering committee coordinating SFRO, SFPM and other authorities and bodies throughout the transnational and preclinical research in radiotherapy project.
- Launching teaching and training programs for translational and preclinical research in radiotherapy.
- Facilitating the contribution or participation of all members willing to promote, support and participate in the design and implementation of preclinical research protocols.
- The SFRO/SFPM Steering Committee pledges to implement procedures that ensure the independence of Scientific Committee members, transparency and management of conflicts of interest.
- All members working in this RadioTransNet network pledge to respect the following principal: no executive operations will be paid; no profits of any kind will be directly or indirectly distributed; no group members will receive any assets.
- Effective management.

RadioTransNet commits to optimizing the use of funding allocated for research. In this context, it will implement procedures and checks ensuring appropriate and effective management of the operational research structures. It will be objective as possible in its choice of service providers and suppliers.

- Academic communication of all results:

Members of the RadioTransNet network commit to the goal of publishing progress in medical research by conducting research projects. All results from their research projects, even if negative, must be published and brought to the attention of the scientific community, institutions and public. RadioTransNet is responsible for communicating on its activities in a way that is academic, transparent, and as widely and easily accessible as possible. Every publication should mention the role of INCa in the process. The coordinator will have to relay this request to all project coordinators and leaders. The study's principal investigator is responsible for all scientific uses of data.

- Financial transparency:

Members of the RadioTransNet network pledge to produce annual accounts and summary documents and to respond to authorities and bodies.

- Roles and responsibilities of the Scientific Committee:

The role of RadioTransNet's Scientific Committee is to provide effective independent leadership by supervising the network. The Scientific Committee's responsibilities include: adopting a strategic planning process and following that procedure for the management of research. It should renew and approve an annual operating plan and budget.
The Scientific Committee will adopt measures for receiving feedback from coordinators on research

programs, which will be submitted to the Scientific Committee.
The Scientific Committee will have to submit to INCa and other funding bodies' research programs aiming to provide researchers, resources and funding programs.

- Health democracy:

The network is committed to involving patient representatives in a relevant, regular and effective way at all levels of its actions: governance, research areas and dissemination. To do this, RadioTransNet will liaise with patient associations and the SFRO Ethics Commission, which also works in close collaboration with patient associations on health democracy (T. Haaser et al., 2020) and whose operating charter is given in the annex 3.

Partnerships and relations between the partners: Added value of the network

The application must provide a thorough discussion of the strategic arguments supporting the network designation:
quality of the network (description of each team, nature and interest of grouping together different teams);

national scale of the teams within the network;

added-value of the network (synergy, complementarities, etc.);

relevance, originality of the network;

cooperation and collaboration of the network (past, actual, expected).

Partnerships:
Please refer to the annex 4 to have a complete overview of the partnership available with RadioTransNet, including orientations of the partners in the four major topics, expertise, available equipment's, ongoing collaborations (national, international, academic and/or industrial) and funding.

I. Quality of the network:

RadioTransNet aim to unite radiation oncology stakeholders at all institutional levels.

- At the time of this application, RadioTransNet accounts for over ninety research teams included in about seventy research groups or units. It comprises experts in the field and representatives of public and private research institutes (CEA, CNRS, INSERM, IRSN, universities), federations of public and private hospitals (SNRO, CHU, CRLCC, Unicancer) and several specific institutions such as Cancéropôles, SIRIC and IRBA, which are already well interconnected.
- RadioTransNet is supported by the French National Society of Radiation Oncology (SFRO) and the French National Society of Medical Physics (SFPM). Many identified members are affiliated with healthcare professional associations or other academic societies in the field (DOSEO, French Society of Cancer, SFBR, etc.).
- Additionally, many of these groups' activities are supported and accredited by patient associations (LNCC, ARC, FRM, Fondation de France, etc.), showing that those associations are aware of some radiation oncology issues. That will facilitate their participation in the review and discussion of the topics to be supported as a priority and how to finance them.

For this second phase of RadioTransNet activity, the network will rely particularly on several partners:

– **DOSEO (annex 1):** an experimental platform developed by the French Alternative Energies and Atomic Energy Commission (CEA) for research in radioprotection and radiotherapy. There are four areas of expertise at CEA in the use of ionizing radiation in health: i) study of ionizing radiation's effect on health, ii) metrology of ionizing radiation, iii) physics of ionizing radiation and iv) ionizing radiation measurements. DOSEO is one of two existing CEA platforms. It encompasses two medical accelerators representative of French equipment, an HD scanner for spectral and 4D imaging, a technical facility dedicated to brachytherapy, a ^{60}Co irradiator, instrumentation laboratories and many dosimetry resources. It is available to all operators in radiotherapy and radioprotection. Accessible by day, its technical platform allows manufacturers, researchers and hospital practitioners to benefit from the technological equipment and expertise of its teams. CEA resources and expertise in the area of ionizing radiation in health are detailed in the annex 1.

– **UNITRAD (annex 2)**: launched in 2014, UNITRAD is a radiotherapy working group supported by Unicancer and led by radiation oncologists, medical physicists, dosimetrists, radiobiologists, nuclear physicians, methodologists and quality control managers. The Unitrad philosophy is to optimize radiotherapy and radiotherapy combined treatments to improve prognosis and quality of life for

cancer patients (http://www.unicancer.fr/recherche/les-groupes-recherche/unitrad-groupe-recherche-en-radiotherapie-oncologique). The main objective of this group is to facilitate clinical research and accelerate progress in radiation oncology to benefit as many people as possible. Unitrad activities are subdivided into five working groups, which are i) artificial intelligence in imaging and radiomics, ii) radiobiology for immunotherapy, radiosensitivity and radiopotentiation, iii) innovative technologies and physical developments, iv) quality aassurance and radiotherapy safety and v) PROMs and real-life data. Unitrad relies on its working group to promote multicentric national and international clinical trials involving academic and industrial (big pharma, AI startups, manufacturers, etc.) collaborations. It collects and shares data from trials to develop new therapeutic strategies, standardize practices, optimize quality control and develop predictive models. Collaboration with RadioTransNet is a unique opportunity to promote translational research and facilitate its transfer to the patient. Unitrad has already built its own sustainable infrastructure to collect and share data, which could help RadioTransNet implement data collection from the network.

– **MED-OSIRIS**: OSIRIS is a data model corresponding to a minimum dataset for data sharing and interoperability in oncology (JCO Clinical Cancer Informatics, Volume 5, March 2021). Because of precision medicine initiatives in oncology, a large amount of clinical and genomic data is being produced. In this context, a French taskforce, supported by INCa and composed of Integrated Cancer Research Sites (SIRICs), comprehensive cancer centers from the Unicancer network, and university hospitals, launched an initiative to improve and accelerate retrospective and prospective clinical and genomic data sharing in oncology. The group used a multidisciplinary approach to foster a national consensus on a minimal dataset of clinical and genomic data that can be used to accelerate oncology data sharing. The model relies on clear and formally defined terminologies and, as such, may benefit the larger international community (JCO Clinical Cancer Informatics, Volume 5, March 2021). This working group is now extending the model to radiotherapy and proposing specific terminology and agreements for data sharing. OSIRIS is a tool for implementing an interoperable dataset between projects, institutes and/or teams and providing the structuring, coherence and data quality essential for data aggregation, data science and artificial intelligence. RadioTransNet's collaboration with OSIRIS working groups is a unique opportunity to define interoperable datasets and to build the databases required by the different work packages of the RadioTransNet roadmaps.

– **GdR CNRS MI2B**: the GDR 20917 MI2B (https://www.mi2b.fr/) is a CNRS working group focused on the development of tools and nuclear methods for cancer treatment. It brings together researchers with expertise in physics, medical physics, mathematics, dosimetry and radiobiology. It is coordinated by D. Dauvergne, a physicist from the CNRS IN2P3 Department (National Institute for Nuclear and Particle Physics), M. Dutreix, a radiobiologist affiliated to CNRS INSB (National Institute for Biological Sciences), and S. Chiavassa, who is the current SFPM representative. The GDR MI2B encompasses 36 teams who are also RadioTransNet partners and aim to promote, within CNRS, research in five areas, which are: i) tools and physical methods for innovative radiotherapy, ii) methods and instruments in biomedical imaging, iii) tools, methods and simulations for radiobiology, iv) radionuclides for imaging and therapy, and v) physicochemical and biological characterization. These topics fit perfectly with those of RadioTransNet, which welcomes this CNRS initiative of great interest for structuring radiotherapy preclinical research.

– **SFBR**: SFBR (https://sfbr.fr/) is the French Society of Ionizing Radiation Biology. It launched this summer to take over the activities of SiRLAF. SFBR aims to support and promote research in the field of ionizing radiation biology and its transfer to human health, being representative of all the institutions involved (INSERM, CNRS, CEA, IRSN, CLCC, universities, etc.), to facilitate exchanges between its members and to enhance radiobiology's visibility at national level. These actions will be performed in close collaboration with other national (SFRO, SFPM) and international (ERR, EANM, RRS) societies as well as national networks (RadioTransNet, GDR MI2B). This partner will be of

particular interest to organize events.
The network's activities should lead to innovative strategies and subsequent Phase I and II trial proposals. The project greatly depends on the involvement of industrial partners in imaging, radiotherapy and the pharmaceutical industry. Many teams have developed partnerships with dozens of manufacturers (as listed in the provided annex) at individual level. RadioTransNet's structure and the convergence of priorities should reinforce industrial partnerships at the all-network level, allowing for better promotion of early clinical trials.

II. National and international scale:

The RadioTransNet network aims to involve stakeholders at all territorial levels. The scientific community already identified (hospitals, research institutes and platforms) is spread across France. A summary of each team is given in the table provided in the annex, where they are ranked by location in France, showing that all regions are represented. Existing local, regional or national groupings or identified, and often accredited, collaborations are mentioned and summarized in the annex. Several regional collaborations are currently ongoing, in particular thanks to Cancéropôles network, and RadioTransNet will also rely on them, showing the growing importance of collaboration. The national and international scale of some teams is obvious given their existing collaborations, which are detailed. RadioTransNet will use this ongoing dynamic to reach its own goal of federation on a national scale, liaising with national authorities (INCa, Ministry of Higher Education and Research, Ministry of Health and associated funding instruments). This is an invaluable chance to bring together all the RadioTransNet network quickly at an international standard of quality and visibility. In addition to the existing collaboration, this will rely on participation in recognized international congresses, such as ESTRO, ASTRO, AACR and PTCOG, and on liaison and communication with EORTC and similar international incentives and networks (CR-Rad, DKTK, EURATOM, LIFE SCIENCE, EURAMET…).

III. The added value of the network:

Through the active synergies and complementarities, the network's added value will be easy to establish since this near-exhaustive overview of the French teams active in the preclinical research field shows the similarities and complementarities related to radiation oncology: radiotherapy, chemotherapy, targeted therapy, radiobiology, radiopathology, genetics, systems biology, stem cell biology, immunology, vascular biology, physics, dosimetry, imaging, mathematics, machine learning, etc. The similarities will urge us to work together to build critical mass in critical areas and converge on specific tasks. The complementarities will make it possible to strengthen multidisciplinary fields and here also to gain critical mass to succeed in the collaborative activities. The provided table is the initial tool used by teams joining RadioTransNet to structure the network to meet its scientific objectives.

IV. Relevance, originality of the network:

The project aims to form a high-level preclinical network that can connect research teams and technological platforms to test innovative strategies in the field of radiotherapy. The originality of the network comes from the fact that the RadioTransNet initiative is driven by healthcare professional associations. This organization highlights the critical issues related to radiation oncology which the medical community and patients face during cancer treatment. All identified partners will have to take part in the projects by using the existing expertise and relevant platforms on a complementary basis within the network. Many teams have added originalities, particularly regarding their specific equipment (imaging equipment, source types, preclinical facilities, equipment for specialized biological analyses, simulation algorithms) and local collaborations. In particular, the very multidisciplinary nature of preclinical research in radiotherapy is largely demonstrated by the participation of all French scientific bodies. This network will facilitate the development of collaboration that will often be the extension of pre-existing collaborations. The organization and depth of RadioTransNet should make it possible to implement high-quality and efficient preclinical research.

Calendrier et étapes clés du projet / Schedule and milestones

1) Members of the **RadioTransNet Steering Committee** will be appointed to supervise the Scientific Committee's activities.
2) The Scientific Committee will first **establish an inventory** of the different **funding instruments** able to support the research programs defined by each work package's roadmaps.
3) The Scientific Committee will launch the **Preclinical Radiotherapy Research Observatory** to provide an **overview of research in the field** in France and **help partners connect**.
4) The Scientific Committee will launch a **call for student research fellows** every year.
5) The first **RadioTransNet targeted workshop** will be held in the first half of 2022.
6) The **annual feedback meeting** at the end of 2022 and every other year on RadioTransNet activity.
7) The annual **Congress of Preclinical Radiotherapy Research** will be held during the second year after RadioTransNet's accreditation is renewed.
8) RadioTransNet aims to begin launching dedicated **Databases** during this second phase of activity.

Adéquation et justification du calendrier proposé au regard des objectifs du projet / justification and coherence of the proposed schedule with the objectives of the project

Etapes /key steps	Calendrier /schedule	Justification /justification
Application to INCa	4 November 2021	Defined by INCa
Appointment of **Steering Committee members** by the Scientific Committee	End of February 2022	One month required for appointing moderators after RADIOTRANSNET renewed accreditation from INCa
Establishment of an **inventory of existing calls** to fund RadioTransNet research programs	March 2022	One month required to identify and list the funding instruments able to support preclinical radiotherapy research
Implementation of the **Preclinical Radiotherapy Research Observatory**	April–May 2022	One or two months required to define data to be collected from the team and the dedicated form to be shared and completed
Launch of the **call for student research fellows**	First half of 2022	1–3 months required to finalize call definition and fellow selection procedures
Organization of the first **RadioTransNet targeted workshop**	First half of 2022	2–4 months required to organize the workshop with expert partners
Feedback meeting	November 2022	Feedback will be given during the general assembly (annual meeting) at the end of each year
Organization of the annual **Congress of Preclinical Radiotherapy Research**	2023	At least one year to plan sessions and find sponsors to organize this annual congress. If possible, it will be held each year
Implementation of the **RadioTransNet Database**	Before 2025	Several years required to find and fund housing infrastructures as well as to define adapted datasets before data collection and sharing

Exploitation et valorisation des résultats du projet / Exploitation and dissemination of the results

Valorisation envisagée pour le projet /Valorisation plan
– *Communication scientifique / Scientific communication*
– *Communication auprès du grand public/communication towards general public*
– *Retombées scientifiques, organisationnelles, de santé publique, .../ scientific, organizational, public health impacts*

Dissemination will be made through **social media**, the currently available **website** (monitored by the project manager) linked to the SFRO and SFPM websites and **email newsletters** (several have been published during the network's initiation).

There will be at least **one annual feedback meeting** and a **general assembly** including the Steering Committee. The Scientific Committee is expecting to organize one annual congress on the topic of radiobiology to standardize and coordinate the activities of the project's various partners.

The INCa **health democracy representative** will **be invited** to attend the next **meetings and congresses** to be part of the discussions and decisions. During these events, a **dedicated session** aiming to involve patients in RadioTransNet's aims will be organized to improve public knowledge of radiotherapy in order to optimize treatment delivery and patient outcomes. She will contribute to the strategic decisions taken by the Steering and Scientific Committees over the following four years.

There will be specific annual meetings organized by the WP leaders around certain themes (DNA repair, nanoparticles, mice models, preclinical irradiators and imaging, computing…). There will be formal liaison and communication at European level with ESTRO and EORTC and with similar European incentives and networks (UK: CR-Rad, Germany: DKTK, etc.).

An annual report will be provided to the Steering Committee and shared with INCa after validation. It will be **published and made available** to public health authorities on the RadioTransNet, SFRO, SFPM and SFRB websites.

There will be a yearly meeting in the form of a specific session during the SFRO annual meeting and SFPM international meetings. Altogether, the actions taken by RadioTransNet, through **structuring a network focused on radiotherapy challenges**, should lead to the **synergistic activity of contributors from many disciplinary fields**: dosimetry, radiobiology, systems biology, physics and mathematics. RadioTransNet aims to **reinforce existing collaborations** and **federate new ones** in order to develop new strategies for better cancer management with radiotherapy. This should result in **increased scientific production** and lead to **scientific and medical publications**, **patent registrations** and, hopefully for patients, **clinical trial initiations**.

Compétences et expertises /Skills and expertises

Coordonnateur / Coordinator

CV complet du coordonnateur y compris les différentes fonctions dans lesquelles il est impliqué/Full CV of the coordinator **(sans publication)**

Philippe MAINGON
February 9th, 1957, Reims, France

ACADEMIC TITLE
Professor in Radiation Oncology
Sorbonne University, Paris, France

ADDRESS
Radiation Oncology Department
APHP. Sorbonne University
47-83, boulevard de l'hôpital
Pavillon Antonin Gosset, 75013 Paris

PRESENT POSITION
Radiation Oncologist

Medical Director of Medical Oncology, Radiation Oncology, Clinical Hematology and Supportive Care Units of the Medical Universitary Department of APHP. Sorbonne University

EDUCATION
1987 Graduation in Radiotherapy - Dijon University
1988 Medical Doctor - Dijon University
1991 Master degree in Cellular and Molecular Biology - Dijon & Besançon Universities
1999 Accreditation for Research Supervision - Dijon University
2000 Professor in Radiation Oncology - Dijon University
2016 Professor in Radiation Oncology – Sorbonne University - Paris

POSTGRADUATE EDUCATION/SPECIALIZATION/TRAINING
1986 Graduation in Human General and Experimental Biology in Oncology - Paris XI University
1987 Graduation in Clinical Oncology - Paris XI University
1988 Graduation in Statistics and computerized data management for clinical research in medicine - Besançon University
1988 Graduation in Head-and-Neck Oncology - Paris XI University

PREVIOUS APPOINTMENTS
1989 - 1991 Assistant Physician - Dijon University Hospital.
Appointed at Centre Georges-François LECLERC / Radiotherapy Department
1992 - 2000 Radiation Oncologist in the Radiotherapy Department
Centre Georges-François LECLERC
2000 - 2010 Head of Radiotherapy Department
Centre Georges-François LECLERC, Dijon, France
2016- 2019 Head of Radiotherapy Department
HU La Pitié Salpêtrière Charles Foix
2018- 2021 Head of the ORPHé Department Oncology, Hematology and Supportive Care
HU La Pitié Salpêtrière Charles Foix

ADMINISTRATIVE APPOINTMENTS

2021 Head of the International Committee of SFRO
2020 - Member of the Radiation Oncology Safety and Quality Committee of ESTRO
2020 Past-President of the French National Society of Radiation Oncology
2019-2021 Co-Chairman of RadioTransNet National network for pre-clinical translational research
2018 -2019 President of the French National Society of Radiation Oncology (SFRO)
2017 President-elect of the French National Society of Radiation Oncology (SFRO)
2012 - 2015 EORTC ROG Chairman / Member of the EORTC Board
2009 - 2011 EORTC ROG Treasurer
2003 - 2015 EORTC ROG quality assurance working party
2006 - 2008 EORTC ROG - Chairman gastro-intestinal working party
2003 - 2006 EORTC ROG Co-Chairman Genito-Urinary working party
2002 - 2016 Steering and Executive Committees of EORTC Radiation Oncology Group (ROG)
2012 - 2017 Vice-General Secretary of the French Society for Radiation Oncology
2003 - 2017 Member elect of the Steering Committee of the French Society for Radiation Oncology
2013 - 2021 Medical Expert in Radiation Oncology for Dijon Appeal Court
2013 - 2021 Medical Expert for ONIAM
2002 - 2013 Medical Expert for the Cassation Court
2005 - 2011 Medical Expert in the National Committee (CN5) for ARC (Cancer Research Association)
1999 - 2002 Secretary of the Scientific Steering Committee (Centre Georges-François LECLERC – Dijon)
2007 - 2011 EQUAL Scientific Advisor
2008 - 2018 Steering Committee member of the GI tract National Thesaurus
2010 - 2016 Medical advisor for the Health, Security and Care Department of the Human Rights Counsel
2011 - 2014 Quality Assurance in Radiation Therapy Steering Committee Member (QART) of EORTC ROG
2013 Expert for the Transparency Commission of the HAS
2015 - 2021 Editorial Board Member for Radiotherapy & Oncology
2015 - 2021 Editorial Board Member for Frontiers Head and Neck Cancer

CLINICAL ACTIVITIES

1990 Patients treated in a clinical research protocols: 950
1999 - 2012 Member of the Scientific Committee of the French foundation: Fondation Française de Cancérologie Digestive (FFCD)
2010 - 2015 Investigator in clinical research protocol: 30 studies
Number of patients included: 275
Principal investigator at Centre Georges-François LECLERC: 25 studies
National and international coordinator: 3 studies
Coordinator of national PHRC: 3
2011 -2016 Medical Expert member of the Scientific Commission of the Belgium National Federation of Scientific Research (FNRS)
2013 Expert for the Swiss National Foundation
2013 Expert for the Research Foundation – Flanders
2014 Expert for Cancer Research UK National Foundation
2016 Expert for the European Commission (European Research Council – ERC)

EDUCATIONAL ACTIVITIES

2020 - Member of the Radiation Oncology Safety and Quality Committee of ESTRO
2000 - 2016 Head of Burgundy University and Research program in radiation oncology.
1999 - 2005 ESTRO teaching course instructor: physics for clinical radiotherapy
2008 - 2010 ESTRO teaching course instructor: from 2D to IMRT
2004 - 2009 Dijon VARIAN IMRT School Medical Coordinator: European School for Intensity

Modulated Radiation Therapy
2010 - 2016 Dijon VARIAN Advanced Techniques Clinical School (IMRT/IGRT/RapidArc). Medical Coordinator
2013 - 2018 Co-Director of ESTRO Teaching Course 'Quality Management in Radiation Therapy'
2015 ESTRO teaching course instructor: Upper GI tract tumor.

Member of ERASMUS, ESTRO and ASTRO teaching programs.

Reviewer for:
International Journal of Oncology Biology Physics, Radiotherapy and Oncology, European Journal of Cancer, Cancer Treatment Review, Radiation Oncology, Bulletin du Cancer, Journal of Thoracic Oncology, Acta Oncologica, Critical Review in Oncology and Hematology, The Oncologist, Prescrire, Journal of Gastroenterology and Hepatology, World Journal of Surgery, Targeted Oncology, Head & Neck, Plos One, Jama, New England Journal of Medicine.

Member of the Editorial Board of Radiotherapy&Oncology

ICH GCP training validated on 1999, 2013, 2015 and 2019.

Principales publications du coordonnateur du projet attestant de son expertise dans le domaine concerné au cours des cinq dernières années

Major scientific publications of the project coordinator demonstrating his/her expertise in the project field during the last five years

1. Head and neck proton therapy in France: A missed opportunity or a challenge in front of us? Thariat J, Calugaru V, Aloi D, **Maingon P**, Grégoire V.Cancer Radiother. 2021 Oct;25(6-7):537-544. doi: 10.1016/j.canrad.2021.06.018. Epub 2021 Jul 14.PMID: 34272183

2. High seroconversion rate but low antibody titers after two injections of BNT162b2 (Pfizer-BioNTech) vaccine in patients treated with chemotherapy for solid cancers.
Palich R, Veyri M, Vozy A, Marot S, Gligorov J, Benderra MA, **Maingon P**, Morand-Joubert L, Adjoutah Z, Marcelin AG, Spano JP, Barrière J.Ann Oncol. 2021 Oct;32(10):1294-1295. doi: 10.1016/j.annonc.2021.06.018. Epub 2021 Jun 22.PMID: 34171494

3. Short Androgen Suppression and Radiation Dose Escalation in Prostate Cancer: 12-Year Results of EORTC Trial 22991 in Patients With Localized Intermediate-Risk Disease.
Bolla M, Neven A, **Maingon P**, Carrie C, Boladeras A, Andreopoulos D, Engelen A, Sundar S, van der Steen-Banasik EM, Armstrong J, Peignaux-Casasnovas K, Boustani J, Herrera FG, Pieters BR, Slot A, Bahl A, Scrase CD, Azria D, Jansa J, O'Sullivan JM, Van Den Bergh ACM, Collette L; EORTC Radiation Oncology Group.J Clin Oncol. 2021 Sep 20;39(27):3022-3033. doi: 10.1200/JCO.21.00855. Epub 2021 Jul 26.PMID: 34310202

4. Dosimetric study between a single isocenter dynamic conformal arc therapy technique and Gamma Knife radiosurgery for multiple brain metastases treatment: impact of target volume geometrical characteristics.
Chea M, Fezzani K, Jacob J, Cuttat M, Croisé M, Simon JM, Feuvret L, Valery CA, **Maingon P**, Benadjaoud MA, Jenny C.Radiat Oncol. 2021 Feb 27;16(1):45. doi: 10.1186/s13014-021-01766-w.

Principaux articles publiés et répertoriés dans des revues à comité de lecture international ou toutes autres publications significatives au cours des cinq dernières années, max 10 (*titres et références*)
Mettre en caractères gras les publications réalisées avec le concours financier de l'Institut National du Cancer,
Major scientific publications in indexed journals and peer-reviewed with international committees or any other significant publications during the last five years for the

consortium, 10 max (titles and references)

1. Head and neck proton therapy in France: A missed opportunity or a challenge in front of us? Thariat J, Calugaru V, Aloi D, **Maingon P**, Grégoire V.Cancer Radiother. 2021 Oct;25(6-7):537-544. doi: 10.1016/j.canrad.2021.06.018. Epub 2021 Jul 14.PMID: 34272183

2. High seroconversion rate but low antibody titers after two injections of BNT162b2 (Pfizer-BioNTech) vaccine in patients treated with chemotherapy for solid cancers.
Palich R, Veyri M, Vozy A, Marot S, Gligorov J, Benderra MA, **Maingon P**, Morand-Joubert L, Adjoutah Z, Marcelin AG, Spano JP, Barrière J.Ann Oncol. 2021 Oct;32(10):1294-1295. doi: 10.1016/j.annonc.2021.06.018. Epub 2021 Jun 22.PMID: 34171494

3. Short Androgen Suppression and Radiation Dose Escalation in Prostate Cancer: 12-Year Results of EORTC Trial 22991 in Patients With Localized Intermediate-Risk Disease.
Bolla M, Neven A, **Maingon P**, Carrie C, Boladeras A, Andreopoulos D, Engelen A, Sundar S, van der Steen-Banasik EM, Armstrong J, Peignaux-Casasnovas K, Boustani J, Herrera FG, Pieters BR, Slot A, Bahl A, Scrase CD, Azria D, Jansa J, O'Sullivan JM, Van Den Bergh ACM, Collette L; EORTC Radiation Oncology Group.J Clin Oncol. 2021 Sep 20;39(27):3022-3033. doi: 10.1200/JCO.21.00855. Epub 2021 Jul 26.PMID: 34310202

4. Dosimetric study between a single isocenter dynamic conformal arc therapy technique and Gamma Knife radiosurgery for multiple brain metastases treatment: impact of target volume geometrical characteristics.
Chea M, Fezzani K, Jacob J, Cuttat M, Croisé M, Simon JM, Feuvret L, Valery CA, **Maingon P**, Benadjaoud MA, Jenny C.Radiat Oncol. 2021 Feb 27;16(1):45. doi: 10.1186/s13014-021-01766-w.

5. **Genomic and transcriptomic comparison of post-radiation versus sporadic sarcomas.**
Lesluyes T, Baud J, Pérot G, Charon-Barra C, You A, Valo I, Bazille C, Mishellany F, Leroux A, Renard-Oldrini S, Terrier P, Le Cesne A, Laé M, Piperno-Neumann S, Bonvalot S, Neuville A, Collin F, Maingon P, Coindre JM, Chibon F.Mod Pathol. 2019 Dec;32(12):1786-1794. doi: 10.1038/s41379-019-0300-2. Epub 2019 Jun 26.PMID: 31243333

6. Mismatch Repair System Deficiency Is Associated With Response to Neoadjuvant Chemoradiation in Locally Advanced Rectal Cancer.
Meillan N, Vernerey D, Lefèvre JH, Manceau G, Svrcek M, Augustin J, Fléjou JF, Lascols O, Simon JM, Cohen R, **Maingon P**, Bachet JB, Huguet F.Int J Radiat Oncol Biol Phys. 2019 Nov 15;105(4):824-833. doi: 10.1016/j.ijrobp.2019.07.057. Epub 2019 Aug 9.

7. **RILA blood biomarker as a predictor of radiation-induced sarcoma in a matched cohort study.**
Mirjolet C, Merlin JL, Truc G, Noël G, Thariat J, Domont J, Sargos P, Renard-Oldrini S, Ray-Coquard I, Liem X, Chevreau C, Lagrange JL, Mahé MA, Collin F, Bonnetain F, Bertaut A, Maingon P.EBioMedicine. 2019 Mar;41:420-426. doi: 10.1016/j.ebiom.2019.02.031. Epub 2019 Mar 1

Co-Coordonnateur / Co-Coordinator

CV complet du coordonnateur y compris les différentes fonctions dans lesquelles il est impliqué/**Full CV of the coordinator** (sans publication)

Vincent MARCHESI
Physicien médical

Institut de Cancérologie de Lorraine – Unité de RadioPhysique Médicale 6 avenue de bourgogne - CS 30519 - 54519 Vandoeuvre-les-Nancy Cedex
03.83.59.85.36
v.marchesi@nancy.unicancer.fr

FONCTIONS PROFESSIONNELLES
Responsable de l'Unité de Radiophysique médicale de l'Institut de Cancérologie de Lorraine

Responsable de l'activité de Physique médicale au Centre Hospitalier Emile Durkheim d'Epinal

FORMATION

2003 Doctorat en Physique Radiologique et Médicale au CLCC Alexis-Vautrin / Institut National Polytechnique de Lorraine (Nancy, 54).

2001 Diplôme de Qualification en Physique Radiologique et Médicale, à l'Institut National des Sciences et Techniques Nucléaires, CEA (Saclay, 91).

1999 DEA Rayonnements et Imagerie en Médecine, option Physique Radiologique et Médicale à l'Université Paul Sabatier (Toulouse, 31).

1999 Diplôme de l'École Supérieure d'Ingénieur de Luminy (ESIL), département Génie Biomédical (Marseille, 13).

ACTIVITES SCIENTIFIQUES (EXTRAIT)

Président de la Société Française de Physique Médicale de 2016 à 2019.
Vice-président de la Société Française de Physique Médicale de 2011 à 2016 et de 2019 à 2021
Co-coordonateur du réseau de recherche préclinique en radiothérapie RadioTransnet depuis novembre 2018 www.radiotransnet.fr
Membre du Conseil d'Enseignement de la Société Française de Physique Médicale depuis 2009.
Membre du Comité de rédaction de la revue Cancer/Radiothérapie.
Reviewer pour les revues scientifiques : Cancer/Radiothérapie, European Journal of Medical Physics, International Journal of Radiation Oncology Biology and Physics, Medical Dosimetry.

Responsable du Conseil Scientifique du Congrès SFPM 2016 à Nancy
Membre du Conseil Scientifique des Congrès SFPM 2011 (Nantes), 2015 (Lille), 2017 (Lyon), 2021 (Rennes) Membre du Conseil Scientifique d'Enseignements Post-Universitaires :
- Radiothérapie Conformationnelle avec modulation d'instensité, Nancy, 9 sessions (2004-2009)
- Formation Nationale SFPM/SFRO/AFCOR sur la RCMI, Paris, 2011, 2012, 2013
- Formation Nationale SFPM/SFRO/AFCOR sur la radiothérapie stéréotaxique, Paris, 2013, 2014
- EPU SFPM RCMI sur les accélérateurs linéaires d'électrons, Rennes, 2011, 2012, 2013, 2014, 2016
- EPU SFPM Radiothérapie Stéréotaxique, Rennes, 2018 (2 sessions), 2019, 2021

ACTIVITES D'ENSEIGNEMENTS (EXTRAIT)

Membre du bureau exécutif du Diplôme de Qualification en Physique Radiologique et Médicale depuis janvier 2014.
Chargé d'enseignements à l'INSTN Saclay, Diplôme de Qualification en Physique Radiologique et Médicale
Chargé d'enseignements à l'Université Paul Sabatier de Toulouse, Master 2 UE 52 EI9RAMBM « Dosimétrie pour les applications médicales » (Parcours spécifique Radiophysique Médicale)
Chargé d'enseignements à l'Université de Lorraine, Faculté de Pharmacie DFG-SP2 - UEL « Instrumentation et techniques médicales pour le diagnostic et la thérapie
Chargé d'enseignements à l'Université de Lorraine, Master "Sciences de la vie et de la santé", option Ingénierie biomédicale et radiothérapie – Module Technologies Médicales Hospitalières TMH
Chargé d'enseignements Institut de Formation de Manipulateurs en Electro-radiologie médicale de Nancy
5 co-encadrement de Thèse de Doctorat en Physique Médicale entre 2002 et 2013
14 encadrements de stage de Masters 2 en Physique Médicale depuis 2002.

Principaux articles publiés ou travaux du responsable scientifique de l'organisme membre du réseau attestant de l'expertise dans le domaine concerné au cours des cinq dernières années

Major scientific publications and other publications of the scientific manager of the network members demonstrating its expertise in the project field over the last five years

1. Cancer/Radiothérapie 23 (2019) 609–616.
RadioTransNet, the French network for preclinical research in oncological radiotherapy
E. Bayart, D. Azria, J. Balosso, M. Benderitter, E. Cohen-Jonathan Moyal, G. Delpon, E. Deutsch, M. Dutreix, T. Lacornerie, P.H. Romeo, V. Marchesi, P. Maingon

2. Radiother Oncol. 2021 Jun;159:241-248. doi: 10.1016/j.radonc.2021.03.024. Epub 2021 Apr 8.PMID: 33838170 Radiotherapy and Oncology, 2019, vol. 131, pp. 93–100
Intensity-modulated radiation therapy of anal squamous cell carcinoma : Relationship between delineation quality and regional recurrence.
N Rouard, D Peiffert, E Rio, M-A Mahé, G Delpon, V Marchesi, A Falk, J Salleron, A-A Serre.

3. Marchesi V, Huger S : La radiothérapie conformationnelle par modulation d'intensité.
in Mazeron JJ (ed): Techniques d'irradiation des cancers, 3ème édition. La radiothérapie conformationnelle, Editions Maloine, 2018, pp 145-158.

4. Journal of Thoracic Disease, 2018 vol. 10(8), pp. 4976-4984
Cyberknife stereotactic radiation therapy for stage I lung cancer and pulmonary metastases: evaluation of local control at 24 months
M Khadige, J Salleron, V Marchesi, G Oldrini, D Peiffert, V Beckendorf.

5. Radiation Oncology, 2017, 12:99
Intensity-modulated radiation therapy from 70Gy to 80Gy in prostate cancer: six- year outcomes and predictors of late toxicity.
M Jolnerovski, J Salleron, V Beckendorf, D Peiffert, A-S Baumann, V Bernier, S Huger, V Marchesi, C Chira

6. Journal of Applied Physics, 2015, 118, 234507
Why diamond dimensions and electrode geometry are crucial for small photon beam dosimetry
F. Marsolat, D. Tromson, N. Tranchant, M. Pomorski, C. Bassinet, C. Huet, S. Derreumaux, M. Chea, K. Cristina, , G. Boisserie, I. Buchheit, V. Marchesi, S. Gaudaire-Josset, A. Lisbona, D. Lazaro, R. Hugon, and
P. Bergonzo

Responsables scientifiques impliqués dans l'organisation du réseau (Missions scientifiques ou missions d'organisation et de gouvernance) / Scientific managers of the Network members implicated in the scientific missions or organization and management of the network

CV court de chaque responsable scientifique / *Short CV of each scientific manager (max 2 pages sans publication)*

David AZRIA

ICM Val d'Aurelle
Département de Radiothérapie Oncologique
208 rue des apothicaires
Parc Euromédecine
34298 MONTPELLIER Cedex
Tel: +33 (0) 4 67 61 85 79
email: David.Azria@icm.unicancer.fr
Numéro RPPS : 10003248779
Numéro CNOM: 34/10740
Date de naissance: 30/04/1971 à Castres (Tarn); Marié; 3 enfants

Position Actuelle

Montpellier-Nîmes:
Professeur d'Oncologie Radiothérapie à la Faculté de Médecine de Montpellier-Nîmes (Première Classe) Coordonnateur du département de Radiothérapie Oncologique de l'ICM (2012 – en cours) Coordonnateur de la Fédération Universitaire d'oncologie radiothérapie d'Occitanie Méditerranée, ICM – ICG (2019 – en cours) Co-chef d'équipe radiobiologie INSERM U1194 (2021 – en cours) Directeur scientifique de l'ICM (2016 – en cours)

Département de l 'Hérault :
Expert près la cour d'Appel de Montpellier (2020 - en cours)

Région:
Coordonnateur régional du DES Oncologie option précoce « radiothérapie » (2018 – en cours) Président élu du réseau régional de cancérologie Onco-Occitanie (2018 – en cours)

France:
Membre élu du bureau de la Société Française de Radiothérapie Oncologique (SFRO) (2011–en cours)

International:
Clinicien coordonnateur du programme européen FP7 REQUITE de radiotoxicité (2012 – en cours) Membre actif du consortium international de radiogénomique (RGC) (2010 – en cours)

Education et Positions Passées

I – Formations Médicales

A – Etudes médicales

EXTERNAT
Stages de médecine (Toulouse, Rangueil, France) **LAUREAT DE L'UNIVERSITE Médaille d'argent 1993 LAUREAT DE L'UNIVERSITE Médaille d'or 1994 LAUREAT DE L'UNIVERSITE Médaille d'or 1995**

INTERNAT
1 CRLC - MONTPELLIER - FRANCE
Département de Radiothérapie Oncologique
2 LAPEYRONIE HOSPITAL - MONTPELLIER - FRANCE
Unité d'Hématologie et d'Oncologie médicale

3 CRLC - MONTPELLIER - FRANCE
Département de Radiothérapie Oncologique
4 NIMES HOSPITAL - FRANCE
Département de Radiologie
5 CRLC - MONTPELLIER - FRANCE
Département de Radiothérapie Oncologique
6 CRLC - MONTPELLIER - FRANCE
Département d'Oncologie médicale
7 CRLC - MONTPELLIER - FRANCE
Département de Radiothérapie Oncologique
8 CRLC - MONTPELLIER - FRANCE
Département de Radiothérapie Oncologique

B – Formations post-internat

ASSISTANT RECHERCHE A L'INSTITUT CURIE
Institut Curie, Paris (1999)
QUALIFICATION EN CANCEROLOGIE (DESC)
ICM Montpellier (2001)

C – Mobilité étrangère
Université de Lausanne, Suisse 2001-2002

D – Prix
1. Prime d'Enseignement et de Recherche (PEDR) : MESRI (depuis 2016)
2. Lauréat i-lab2016, Ministère de l'Enseignement et de la Recherche
3. American Society for Radiation Oncology (ASTRO) Abstract Award 2015, San Antonio
4. Prevot Fondation Award, Geneva 2013, Switzerland
5. Prevot Fondation Award, Geneva 2012, Switzerland
6. Prevot Fondation Award, Geneva 2011, Switzerland
7. Prevot Fondation Award, Geneva 2010, Switzerland
8. The Swiss Society of radiobiology and Medical Physics (Varian Award), December 2008
9. Research in Radiobiology Award, Paris, November 2008, France
10. Research in Radiobiology Award, Paris, June 2007, France
11. Prevot Fondation Award, Geneva 2004, Switzerland
12. Research in Radiobiology Award, Paris, June 2004, France
13. GEFLUC Clinical Research Award, Montpellier 2003, France
14. Breast Research Award, Journées Françaises de pathologies mammaires, Nice 2002, France.
15. Lilly Oncologie 2002 Award Special Mention, Eurocancer, France
16. Médaille d'or Université Paul-Sabatier Toulouse 1995
17. Médaille d'or Université Paul-Sabatier Toulouse 1994
18. Médaille d'argent Université Paul-Sabatier Toulouse 1993

E – Positions passées
Président du registre des tumeurs de l'Hérault (2016-2021)
Président élu du Collège National des Enseignants en Cancérologie (CNEC) (2016-2019) Membre du comité national de recherche Clinique en cancérologie (PHRC-K) (2015-2017) Membre du comité national du programme de recherche PAIR pédiatrie (INCa) 2016
Président-Fondateur élu du Groupe de recherche et de développement de radiothérapie oncologique d'UNICANCER (UNITRAD) (2015-2018)
Président de la CME de l'ICM (2012-2016)
Président du comité national de recherche Clinique en cancérologie (PHRC-K) (2011)

II – Formations scientifiques

Faculté de Médecine, Montpellier – France
Faculté de Médecine Kremlin-Bicêtre, Paris XI – France

A. **MASTERE BIOLOGIE SANTE**
Faculté de Médecine de Montpellier (1997-1999) Certificat d'hématologie
Certificat de radiologie

B. **DIPLOME D'ETUDES APPROFONDIES DE RADIOBIOLOGIE**

Institut Curie
Faculté de médecine Kremlin-Bicêtre, PARIS (1999-2000) MAJOR MENTION TRES BIEN

C. **DOCTORAT DE SCIENCES (PHD)**
BIOLOGIE-SANTE
Faculté de Médecine, Montpellier (2000-2004)

D. **HABILITATION A DIRIGER DES RECHERCHES (HDR)**
Faculté de Médecine, Montpellier (2006)

III – Formations dommages corporels et représentants patients

E. **DIPLOME UNIVERSITAIRE DE REPARATION JURIDIQUE ET DU DOMMAGE CORPOREL**
Faculté de Médecine de Montpellier, 2018-2019

F. **REPRESENTANT MEDICAL DE L'ICM LORS DES PROCEDURES DE CRCI**

G. **PRESIDENT DE LA CME (2012-2016) ET ES QUALITE REPRESENTANT DE L'ASSURANCE QUALITE DES PARCOURS PATIENT ET DU DOMMAGES CORPOREL POTENTIEL**

H. **EXPERTISE DES DOMMAGES CORPORELS DU RADON EN FRANCE : COMITE EXPERT DE L'INCA**

Affiliations

Membre de : SFRO, ESMO, ESTRO, ASCO, ASTRO

Membre des comités éditoriaux : Cancers, Radiation Oncology, Cancer Radiothérapie

Membre du groupe des relecteurs scientifiques : The Lancet, The Lancet Oncology, EbioMedicine, Journal of Clinical Oncology, International Journal of Radiation Biology Physics, Annals of Oncology, European Journal of Cancer, British Journal of Cancer, Radiotherapy and Oncology, Cancers, Frontiers in Oncology

Publications

319 publications peer-review référencées dans PubMed
50 chapitres de livre
Conférences invitées : 40 en radiothérapie, oncologie générale, radiobiologie

Principaux articles publiés ou travaux du responsable scientifique de l'organisme membre du réseau attestant de l'expertise dans le domaine concerné au cours des cinq dernières années
Major scientific publications and other publications of the scientific manager of the network members demonstrating its expertise in the project field over the last five years

1. A data science approach for early-stage prediction of Patient's susceptibility to acute side effects of advanced radiotherapy.
Aldraimli M, Soria D, Grishchuck D, Ingram S, Lyon R, Mistry A, Oliveira J, Samuel R, Shelley LEA, Osman S, Dwek MV, Azria D, Chang-Claude J, Gutiérrez-Enríquez S, De Santis MC, Rosenstein BS, De Ruysscher D, Sperk E, Symonds RP, Stobart H, Vega A, Veldeman L, Webb A, Talbot CJ, West CM, Rattay T; REQUITE consortium, Chaussalet TJ. Comput Biol Med. 2021 Aug;135:104624.

2. Development of a method for generating SNP interaction-aware polygenic risk scores for radiotherapy toxicity.
Franco NR, Massi MC, Ieva F, Manzoni A, Paganoni AM, Zunino P, Veldeman L, Ost P, Fonteyne V, Talbot CJ, Rattay T, Webb A, Johnson K, Lambrecht M, Haustermans K, De Meerleer G, de Ruysscher D, Vanneste B, Van Limbergen E, Choudhury A, Elliott RM, Sperk E, Veldwijk MR, Herskind C, Avuzzi B, Noris Chiorda B, Valdagni R, Azria D, Farcy-Jacquet MP, Brengues M, Rosenstein BS, Stock RG, Vega A, Aguado-Barrera ME, Sosa-Fajardo P, Dunning AM, Fachal L, Kerns SL, Payne D, Chang-Claude J, Seibold P, West CML, Rancati T; REQUITE Consortium Collaborators. Radiother Oncol. 2021 Jun;159:241-248. doi: 10.1016/j.radonc.2021.03.024. Epub 2021 Apr 8.PMID: 33838170

3. A Deep Learning Approach Validates Genetic Risk Factors for Late Toxicity After Prostate Cancer Radiotherapy in a REQUITE Multi-National Cohort.
Massi MC, Gasperoni F, Ieva F, Paganoni AM, Zunino P, Manzoni A, Franco NR, Veldeman L, Ost P, Fonteyne V, Talbot CJ, Rattay T, Webb A, Symonds PR, Johnson K, Lambrecht M, Haustermans K, De Meerleer G, de Ruysscher D, Vanneste B, Van Limbergen E, Choudhury A, Elliott RM, Sperk E, Herskind C, Veldwijk MR, Avuzzi B, Giandini T, Valdagni R, Cicchetti A, Azria D, Jacquet MF, Rosenstein BS, Stock RG, Collado K, Vega A, Aguado-Barrera ME, Calvo P, Dunning AM, Fachal L, Kerns SL, Payne D, Chang-Claude J, Seibold P, West CML, Rancati T. Front Oncol. 2020 Oct 15;10:541281. doi: 10.3389/fonc.2020.541281. eCollection 2020.PMID: 33178576

4. Higher Anti-Tumor Efficacy of the Dual HER3-EGFR Antibody MEHD7945a Combined with Ionizing Irradiation in Cervical Cancer Cells.
Bourillon L, Demontoy S, Lenglet A, Zampieri A, Fraisse J, Jarlier M, Boissière-Michot F, Perrochia H, Rathat G, Garambois V, Bonnefoy N, Michaud HA, Chardès T, Tosi D, Pèlegrin A, Azria D, Larbouret C, Bourgier C. Int J Radiat Oncol Biol Phys. 2020 Apr 1;106(5):1039-1051. doi: 10.1016/j.ijrobp.2019.12.020. Epub 2020 Jan 17.PMID: 31959545

5. Use of genomics to balance cure and complications.
Azria D, Rosenstein BS. Nat Rev Clin Oncol. 2020 Jan;17(1):9-10. doi: 10.1038/s41571-019-0306-1.PMID: 31784674

CV court de chaque responsable scientifique / *Short CV of each scientific manager (max 2 pages sans publication)*

CURRICULUM VITAE du Pr JACQUES BALOSSO

Né le 10 décembre 1960
ADRESSE PROFESSIONNELLE:
j.balosso@baclesse.unicancer.fr

NATIONALITE: française
Service de Radiothérapie
CRLCC François Baclesse
3 rue du Gral Harris ; F-14000 CAEN

N° RPPS : 10000537505 N° CNOM : 14/6469 Tél: 02 31 45 50 50 poste 5845

FORMATION et POSITION UNIVERSITAIRE:
- Mars 1986: Nomination à l'**Internat** de Montpellier, inter-région Sud, 2/167;
- Octobre 1988: **D.E.A.** des "Bases fondamentales de l'oncogenèse",
- Septembre 1990: **Thèse de doctorat de Médecine** à Montpellier.
- Octobre 1990: **Diplôme d'Etudes Spéciales** d'Oncologie option Radiothérapie.
- 1er Novembre 1990: **Chef de clinique assistant** à la Faculté St-Antoine (Paris 6) et l'Hôpital Tenon, Paris.
- Octobre 1996: **Diplôme d'Etudes Spéciales Complémentaires** de Cancérologie.
- Octobre 1997: **Doctorat es Sciences** l'Université Paris VII.
- Novembre 2001 : **Habilitation à diriger des Recherches, Université Joseph Fourier, Grenoble1 (UJF)**
- Septembre 2003 : **Professeur des Universités en cancérologie radiothérapie à l'UJF**
- Septembre 2017 : **Détachement à temps complet auprès du Centre François Baclesse à Caen**

EXPERIENCE SCIENTIFIQUE ET DIRECTION DE PROJET:

Un an de laboratoire à l'**Institut Curie**, Unité INSERM 350, 1988-89 pour le DEA, étude des interactions Chimiothérapie- Irradiation. Poursuite dans ce laboratoire des travaux au retour des USA. Séjour de 2 ans, nov.1991 - oct.1993, dans le laboratoire de Radiobiologie de la **Harvard School of Public Health**, Prf. J.B.Little, Boston, U.S.A. Poursuite des travaux de radiobiologie à l'Institut Curie jusqu'en 1997.
Activités d'évaluation scientifique: **membre nommé de la Comm. Scientif. Spé. n°2** de l'INSERM, 1995-98.
Coordonne depuis 1999 la thématique « radiothérapie expérimentale » de l'EA « RSRM » à l'ESRF devenue Unité INSERM en 2003, actuellement **GIN/U836/E6 INSERM** dirigée par le Dr François ESTEVE.
Directeur du Groupement de coopération sanitaire **GCS-ETOILE** (2007-2014) (www.centre-etoile.org)
Fondateur et coordonnateur de l'infrastructure nationale de recherche ***France HADRON*** (2013…)
Coordonnateur scientifique du **projet ARCHADE** de recherche en hadronthérapie (lettre de mission, 8 mars 2018)

ACTIVITES HOSPITALIERES ACTUELLES

- PU-PH Cancérologie-radiothérapie au CHU de Grenoble depuis sept. 2003. **Chef de service** de sept 2010 à août 2017.
Recherche en radiobiologie et recherche clinique en carcinologie digestive: **essais multicentriques** de phase II et III pour le traitement des cancers de l'**œsophage**, du **pancréas** et du **rectum**.
Coordinateur de l'infrastructure nationale de recherche ***France HADRON*** (2013…)
Coordonnateur des activités scientifiques en **hadronthérapie** à Caen (CFB, Archade)

Expert national pour l'hadronthérapie pour la CNAM
Chef du Service de Radiothérapie-Protonthérapie du Centre F. Baclesse (depuis le 1/11/2019…)

PRINCIPALES CHARGES D'ENSEIGNEMENTS

Direction universitaire du Master français de Radioprotection (Coop : CEA/INSTN, IRSN, UJF ; 1999-2008)
Création du Master 2 (R et P) de physique-médicale à l'UJF à Grenoble (Coop initiale UCBL – UJF ; 2003 …)
Coordonnateur universitaire du Master Européen de Radioprotection (F, UK, Cz) : EMRP, 2008-2019

PUBLICATIONS : 119 publications internationales depuis 1991)

64: Obeid L, Deman P, Tessier A, **Balosso J**, Estève F, Adam JF. Absolute perfusion measurements and associated iodinated contrast agent time course in brain metastasis: a study for contrast-enhanced radiotherapy. J Cereb Blood Flow Metab. 2014 Apr;34(4):638-45.
60: Pittet P, Ismail A, Ribouton J, Wang R, Galvan JM, Chaikh A, Lu GN, Jalade P, Giraud JY, **Balosso J.** Fiber background rejection and crystal over- response compensation for GaN based in vivo dosimetry. Phys Med. 2013 Sep;29(5):487-92.
58: Rodriguez-Lafrasse C, **Balosso J.** [From the carbon track to therapeutic efficiency of hadrontherapy]. Can Rad. 2012 Feb;16(1):16-24.

Caen le 25 octobre 2021:

Principaux articles publiés ou travaux du responsable scientifique de l'organisme membre du réseau attestant de l'expertise dans le domaine concerné au cours des cinq dernières années
Major scientific publications and other publications of the scientific manager of the network members demonstrating its expertise in the project field over the last five years

1. Verry C, Dufort S, Villa J, Gavard M, Iriart C, Grand S, …, Deutsch E, Loeffler M, Le Duc G, Tillement O, **Balosso J**. Theranostic AGuIX nanoparticles as radiosensitizer: A phase I, dose-escalation study in patients with multiple brain metastases (NANO-RAD trial). Radiother Oncol. 2021 May 4:S0167-8140(21)06219-8.

2. Chaikh A, Calugaru V, Bondiau PY, Thariat J, **Balosso J**. Impact of the NTCP modeling on medical decision to select eligible patient for proton therapy: the usefulness of EUD as an indicator to rank modern photon vs proton treatment plans. Int J Radiat Biol. 2018 Jun 7:1-26.

3. Eling L, Bouchet A, Ocadiz A, Adam JF, Kershmiri S, Elleaume H, Krisch M, Verry C, Laissue JA, **Balosso J**, Serduc R. Unexpected Benefits of Multiport Synchrotron Microbeam Radiation Therapy for Brain Tumors. Cancers (Basel). 2021 Feb 24;13(5):936.

4. COPERNIC project investigators, Granzotto A, Benadjaoud MA, Vogin G, …. **Balosso J**, Foray N. Influence of nucleoshuttling of the ATM Protein in the healthy tissues response to radiation therapy: toward a molecular classification of human radiosensitivity. Int J Radiat Oncol Biol Phys. 2016 Mar 1;94(3):450-60.

5. Laprie A, Hu Y, …, **Balosso J**; radiotherapy committee of SFCE and France Hadron. Paediatric brain tumours: A review of radiotherapy, state of the art and challenges for the future regarding protontherapy and carbontherapy. Cancer Radiother. 2015 Dec;19(8):775-89.

CV court de chaque responsable scientifique / *Short CV of each scientific manager (max 2 pages sans publication)*

BENDERITTER Marc

01 58 35 91 36

marc.benderitter@irsn.fr
IRSN, Pôle santé-Environnement, 31, avenue de la Division Leclerc, BP17, 92262 Fontenay aux Roses
www.irsn.fr

Cursus

1999| Habilitation à Diriger des Recherches, spécialité Biologie Moléculaire
1995| Doctorat de Biologie, spécialité Physiopathologie-Pharmacologie

Expérience

Chef de Service ***2017*** (radiobiologie et médecine régénérative)

IRSN | Fontenay aux Roses
Chef de Service ***2013*** – 2016 (radiobiologie et épidémiologie)
IRSN | Fontenay aux Roses
Chef de Laboratoire ***2002*** – 2012 (radio pathologie et thérapie cellulaire)
IRSN | Fontenay aux Roses

Compétences

- Management d'équipes de recherche
- Recherche en Radio pathologie-Radiobiologie (H-index 35, 125 publications)
- Pilotage de projets scientifiques nationaux et européens
- Evaluation de projets scientifiques nationaux et européens
- Expert auprès de l'AIEA (Missions d'assistance médicale internationale - accidents radiologiques)
- Expert auprès de l'OMS (Responsable IRSN du WHO-Collaborating Center en Radioprotection)

Contrat de recherche (3 dernières années)

- WP leader du projet européen MEDIRAD (2017-2022) "Implication of Medical Low dose radiation exposure", Task leader du projet européen EURAMED-Rocc-n-Roll (2019-2023) "European Medical application and radiation protection concept: Strategic research agenda and roadmap interlinking to health and digitization aspects".
- Pilote du projet PIA3-ANR/RSNR : PRIODAC (2016-2022) " Prophylaxie répétée par l'iode stable et contre-mesures innovantes en situation accidentelle", Membre du conseil scientifique du projet INCA RADIOTRANSNET (2018-2021) "Réseau national de radiothérapie oncologique préclinique".

Principaux articles publiés ou travaux du responsable scientifique de l'organisme membre du réseau attestant de l'expertise dans le domaine concerné au cours des cinq dernières années

Major scientific publications and other publications of the scientific manager of the network members demonstrating its expertise in the project field over the last five years

1. Hematopoietic Recovery using Multi-Cytokine Therapy in 8 Patients Presenting Radiation-Induced Myelosuppression after Radiological Accidents. **Benderitter M**, Herrera-Reyes E, Gigov Y, Souleau B, Huet JC, Trompier F, Fagot T, Grégoire E, Malfuson JV, Konopacki-Potet J, Buglova E, Lataillade JJ, Tamarat R, Gourmelon P, de Revel T. Radiat Res. 2021 Sep 23. doi: 10.1667/RADE-21-00169.1. Online ahead of print. PMID: 34554263

2. The stromal vascular fraction mitigates radiation-induced gastrointestinal syndrome in mice. Bensemmane L, Squiban C, Demarquay C, Mathieu N, **Benderitter M**, Le Guen B, Milliat F, Linard C. Stem Cell Res Ther. 2021 May 29;12(1):309. doi: 10.1186/s13287-021-02373-y. PMID: 34051871

3. HGF and TSG-6 Released by Mesenchymal Stem Cells Attenuate Colon Radiation-Induced Fibrosis. Usunier B, Brossard C, L'Homme B, Linard C, **Benderitter M**, Milliat F, Chapel A. Int J Mol Sci. 2021 Feb 11;22(4):1790. doi: 10.3390/ijms22041790. PMID: 33670243

4. Evaluation of the Effectiveness of Mesenchymal Stem Cells of the Placenta and Their Conditioned Medium in Local Radiation Injuries. Brunchukov V, Astrelina T, Usupzhanova D, Rastorgueva A, Kobzeva I, Nikitina V, Lishchuk S, Dubova E, Pavlov K, Brumberg V, **Benderitter M**, Samoylov A. Cells. 2020 Nov 29;9(12):2558. doi: 10.3390/cells9122558. PMID: 33260310

5. Effect of repetitive potassium iodide on thyroid and cardiovascular functions in elderly rats. Lebsir D, Cantabella E, Cohen D, Sache A, Ebrahimian T, Kereselidze D, Amine Benadjaoud M, Maurisier FC, Guigon P, René Jourdain J, **Benderitter M**, Lestaevel P, Souidi M. Biochem Biophys Rep. 2020 Sep 30;24:100816. doi: 10.1016/j.bbrep.2020.100816. eCollection 2020 Dec. PMID: 33024842

6. Extracellular vesicles derived from mesenchymal stromal cells mitigate intestinal toxicity in a mouse model of acute radiation syndrome. Accarie A, l'Homme B, Benadjaoud MA, Lim SK, Guha C, **Benderitter M**, Tamarat

R, Sémont A. Stem Cell Res Ther. 2020 Aug 27;11(1):371. doi: 10.1186/s13287-020-01887-1. PMID: 32854778

7. Effects of repetitive Iodine thyroid blocking on the foetal brain and thyroid in rats: a systems biology approach. Cohen DPA, Benadjaoud MA, Lestaevel P, Lebsir D, **Benderitter M**, Souidi M. Sci Rep. 2020 Jul 2;10(1):10839. doi: 10.1038/s41598-020-67564-8. PMID: 32616734

CV court de chaque responsable scientifique / *Short CV of each scientific manager (max 2 pages sans publication)*

Prof. Elizabeth Cohen-Jonathan, M.D., Ph.D.
Married Name: Moyal
Head of the Radiation Oncology department of IUCT-O, France
Head of the translational research team Radiotherapy Optimization "RADOPT", INSERM UMR1037, CRCT, Toulouse,France

Office Address: Department of radiation Oncology-IUCT-Oncopole-1 avenue Irene Joliot Curie-31059 Toulouse Cedex-France
Email : moyal.elizabeth@iuct-oncopole.fr

RPPS : 10004898135

Education

1982 – 1988 M.D. Université Paul Sabatier, Faculté de Médecine Purpan, Toulouse, France 1993 Specialization in Radiation Oncology-France
1996 Complementary diploma in Medical Oncology-France
1993-1997 Ph.D. in Radiobiology, *Summa Cum Laude*. Université Paul Sabatier, Toulouse, France 1999 ECFMG certification-USA

Post-graduate Training and Fellowship Appointments

1989 - 1994 Resident in Radiotherapy-Centre Claudius Regaud, Toulouse, France
1997 - 1999 Post-Doc researcher and instructor in the Radiation Oncology Laboratory and Radiation Oncology department (Pr McKenna)- University of Pennsylvania-Philadelphia-USA.

Faculty Appointments

1994 - 1997	Assistant Professor in the Radiation Oncology Department , Institut Claudius Regaud, Toulouse, France
1998 - 1999	Instructor in the Radiation Oncology Department –University of Pennsylvania, Philadelphia, USA
2000	Radiation Oncologist in the Radiation Oncology Department , Institut Claudius Regaud, Toulouse, France
2001	Associate Professor in Radiation Oncology , Université de Médecine Toulouse Purpan ; Department of Radiation Oncology- Institut Claudius Regaud Toulouse, France
2005 to present	Full Professor in Radiation Oncology (Classe exp 2 since 2020) Université de Médecine Toulouse Purpan ; Department of Radiation Oncology-Institut Claudius Regaud Toulouse, France

Professional activities

-Head of the Radiotherapy department of the Cancer University Institute (IUCT), Toulouse, France (since 2014)
-Head of the team Radiation Optimization (RADOPT) INSERM U1037, CRCT, Toulouse, France
-Head of the Brain tumor committee of the Cancer University Institute (IUCT), Toulouse, France
-Head (For the French Nuclear Safety agency ASN) of the Gammaknife Unit, CHU Toulouse, France
-Head of the Neurooncology Committee, IUCToulouse,France
-Head of the Oncology teaching for the students in School of medicine
-Head of the regional teaching for the residents in Radiation Oncology (2001-2017)
-National and local teaching for students in Biology (Master, PhD) (supervisor of at least 7 PhD thesis; and 7 MD thesis, several M2R students)
-National Teaching for students in neuro-oncology

Scientific and administrative functions

▪Elected Member of the Executive board of the European Neuro-Oncology society (EANO) (2015-2018)
▪Member of the EANO Scientific committee (since 2018)

▪Member of the National scientific committee (CSS2) of the French National institute for medical research (INSERM) (2012-2016)
▪Member of the national scientific committee of the Foundation for Cancer Research (ARC) (2012-2017)
▪Member of the Executive board of the UNICANCER radiotherapy group (UNITRAD).
▪Member of the board of direction of the Toulouse Research Cancer Center (CRCT)
▪Member of the medicine faculty council of Toulouse Purpan (2012-2017)
▪Member of the scientific committee of the Comprehensive Cancer Center Claudius Regaud, France
▪Member of the ESMO scientific committee meeting section « new drugs » and "Neuro-oncology"
▪Member of the AACR-EORTC scientific committee meeting section « new drugs » and "Neuro-oncology"

▪Expert in Neuro-oncology and radiotherapy for the French national cancer institute (INCA) and the French Research agency (ANR).
▪Expert at the AERES (National agency for research team evaluation)
▪Member of the regional scientific committees of « la Ligue contre le cancer »
▪Coordinator of the National MoGlimaging consortium on tumor heterogeneity ITMO Cancer Aviesan.

Founding member and Chairman of an ESTRO Radio-Chemotherapy international meeting

- Creation and Organization (Founding member and Chairman) of the ESTRO international meeting in translational research in radiotherapy, "**Novel targeting drugs and radiotherapy : from the bench to the clinic**"-Toulouse, June 2005, June 2007, june 2010, September 2012

Chairman of the ESTRO FORUM Target meeting (Barcelone) 2015
Co-Chairman of the ESO-EANO Masterclass in Neurooncology (Lugano)2016
Member of the scientific committee of the EANO winter masterclass Athens 2018
Member of the scientific committee of the EANO (organization of the scientific program of the annual EANO meetings)

Patents:

· Method for predicting the responsiveness of a patient affected with an osteosarcoma to a chemotherapy. EP11305809.3
· Continuous administration of integrin ligands for treating cancer . Patent with Merck kGa
·Methods for predicting the survival time of patient suffering from a Gliobastoma » EP12305996.6
· New method for treating resistant glioblastoma PCT/IB2016/000626,International patent

·Methods for the prognosis and the treatment of Glioblastoma":N° 18305148.1

Coordination and design of national clinical trials and research programs:

- Phase I-II clinical trial associating the farnesyltransferase inhibitor Zarnestra with radiotherapy in de novo Glioblastoma
- Phase I clinical trial associating continuous infusion of Cilengitide with radiochemotherapy in patients with stade III NSCLC
- STEMRI trial : Study of the capacity of the MRI spectroscopy to define the tumor area enriched in glioblastoma stem cells
- STERIMGLI phase I-II trial: study of the radiosensitizing effect of the anti-PDL1 Durvalumab in combination with stereotactic re-irradiation in recurrent glioblastoma.
- SI2GMA (ARC foundation Sign'it national program (5 teams)) : study of predictive factors of response to stereotactic hypo-fractionateded re-irradiation and immunotherapy in patients with recurrent gliobalstoma
- National MoGLImaging program (8 teams): Modeling of Glioblastoma treatment-induced resistance and heterogeneity by multimodal imaging
- National SILK Phase II trial: study of the radiosensitizing effect of the anti-PDL1 Durvalumab in combination with stereotactic irradiation in NSCLC Metastases.
- PI of the international GBM AGILE Global Adaptive Study Master Protocol: An International, Seamless Phase II/III Response Adaptive Randomization Platform Study Designed To Evaluate Multiple Therapies In Newly Diagnosed and Recurrent Glioblastoma (GBM)
- Coordinator for France of the international trial Trident (EF-32) : A pivotal randomized, open-label study of OPTUNE (TTFields, 200KHZ) concomitant with radiation therapy and temozolomide for treatment of newly diagnosed glioblastoma.
- Precinical studies on radiosensitizing effects of inhibitors of the FGFR and Tie 2 pathways in glioblastoma models: Contracts with Bayer and with Incyte.
- Preclinical studies of TTF resistance : contract with Novocure

Lectures by invitation (since 2010)
· Invited to more than 55 national and international conferences (SFRO; ESTRO; ECCO-ESMO; EANO; ICTR)

Advisory boards
International and national advisory boards member for Roche, Astra-Zeneca, Merck-Serono, Accuray, Novocure.

Grants :
-More than 5.5 M€ grants since 2009.

Publications:
-More than 100 publications

Principaux articles publiés ou travaux du responsable scientifique de l'organisme membre du réseau attestant de l'expertise dans le domaine concerné au cours des cinq dernières années
Major scientific publications and other publications of the scientific manager of the network members demonstrating its expertise in the project field over the last five years

1. Evaluation of two modalities of perioperative treatment in the management of extremity and truncal soft tissue sarcomas: neoadjuvant concurrent chemoradiotherapy and sequential treatment. Attal J, Cabarrou B, Valentin T, Nesseler JP, Stoeckle E, Ducassou A, Filleron T, Le Guellec S, Boulet B, Vogin G, Ferron G, Moyal EC, Delannes M, Chevreau C. Strahlenther Onkol. 2021 Oct 21

2. Intracranial Treatment in Melanoma Patients with Brain Metastasis Is Associated with Improved Survival in the Era of Immunotherapy and Anti-BRAF Therapy. Dalmasso C, Pagès C, Chaltiel L, Sibaud V, Moyal E, Chira C, Sol JC, Latorzeff I, Meyer N, Modesto A. Cancers (Basel). 2021 Sep 6;13(17):4493

3. The Impact of Surgery on the Survival of Patients with Recurrent Glioblastoma. Sacko O, Benouaich-Amiel A, Brandicourt P, Niaré M, Charni S, Cavandoli C, Brauge D, Catalaa I, Brenner A, Moyal EC, Roux FE. Asian J Neurosurg. 2021 Feb 23;16(1):1-7

4. Characteristics of diffuse hemispheric gliomas, H3 G34-mutant in adults. Picart T, Barritault M, Poncet D, Berner LP, Izquierdo C, Tabouret E, Figarella-Branger D, Idbaïh A, Bielle F, Bourg V, Vandenbos FB, Moyal EC, Uro-Coste E, Guyotat J, Honnorat J, Gabut M, Meyronet D, Ducray F. Neurooncol Adv. 2021 Apr 19;3(1):vdab061

5. Radiotherapy in the Era of Immunotherapy With a Focus on Non-Small-Cell Lung Cancer: Time to Revisit Ancient Dogmas? Khalifa J, Mazieres J, Gomez-Roca C, Ayyoub M, Moyal EC. Front Oncol. 2021 Apr 21;11:662236.

6. Chemotherapy and radiotherapy in locally advanced head and neck cancer: an individual patient data network meta-analysis. Petit C, Lacas B, Pignon JP, Le QT, Grégoire V, Grau C, Hackshaw A, Zackrisson B, Parmar MKB, Lee JW, Ghi MG, Sanguineti G, Temam S, Cheugoua-Zanetsie M, O'Sullivan B, Posner MR, Vokes EE, Cruz Hernandez JJ, Szutkowski Z, Lartigau E, Budach V, Suwiński R, Poulsen M, Kumar S, Ghosh Laskar S, Mazeron JJ, Jeremic B, Simes J, Zhong LP, Overgaard J, Fortpied C, Torres-Saavedra P, Bourhis J, Aupérin A, Blanchard P; MACH-NC and MARCH Collaborative Groups. Lancet Oncol. 2021 May;22(5):727-736. (E Moyal belongs to authors)

7. Radiotherapy and spinal toxicity: News and perspectives]. Peyraga G, Ducassou A, Arnaud FX, Lizée T, Pouédras J, Moyal É. Cancer Radiother. 2021 Feb;25(1):55-61.

8. Tolerance and efficacy of dose escalation using IMRT combined with chemotherapy for unresectable esophageal carcinoma: Long-term results of 51 patients. Modesto A, Dalmasso C, Lusque A, Vieillevigne L, Izar F, Moyal E, Carrère N, Guimbaud R, Rives M. Cancer Radiother. 2020 Apr;24(2):88-92.

CV court de chaque responsable scientifique / *Short CV of each scientific manager (max 2 pages sans publication)*

Grégory DELPON

Residential Address: Institut de Cancérologie de l'Ouest, Bd Jacques Monod, 44805 Saint-Herblain
Nationality: French
Date of Birth: 30/05/1975
Place of Birth: Savigny Sur Orge (91), France
Mobile Phone No.: +33.(0)6.14.09.84.91.
Email ID: gregory.delpon@ico.unicancer.fr

EDUCATION

- 2017: Habilitation to supervise research, University of Nantes
  - Topic: Image-guided radiotherapies
- 2002-2003: French Board certification for Medical Physics (2003), approved by the French Ministry of Health
- 1999-2002: PhD in Medical Physics, University of Toulouse
  - Topic: Optimization of quantitative imaging protocols for dosimetry during iodine 131 radiommunotherapy clinical trials
- 1998-1999: Master of science in medical physics, University of Toulouse

PROFESSIONAL CAREER

- 2018-Present: Head of Medical Physics Team, Institut de Cancérologie de l'Ouest Site Saint-Herblain, Nantes.
- Sept 2011-Dec 2017: Radiotherapy Medical Physicist, Institut de Cancérologie de l'Ouest Centre René Gauducheau, Nantes Saint-Herblain. Member of Team 14 INSERM U1232 Centre de Recherche en Cancérologie et Immunologie Nantes Angers.
- Mar 2004-Aug 2011: Radiotherapy Medical Physicist, Institut de Cancérologie de l'Ouest Centre René Gauducheau, Nantes Saint-Herblain.
- Jul 2003-Feb 2004: Nuclear Medicine, Radiotherapy Medical Physicist, Centre J. Bernard, Le Mans.

HONORS AND AWARDS

- 2021-2023 Principal Investigator FLASHMOD: End-to-end dosimetry for preclinical proton FLASH irradiation at ARRONAX, Projet de recherche dans le domaine de la physique, des mathématiques ou des sciences de l'ingénieur appliqués au Cancer
- 2012-2014 Principal Investigator Monte Carlo SMall Animal RadioTherapy, Projet de recherche dans le domaine de la physique, des mathématiques ou des sciences de l'ingénieur appliqués au Cancer
- 2016 Principal Investigator Objets Tests pour l'Assurance de qualité en Radiothérapie et Imagerie, Projet Ligue Contre Le Cancer (Conseil Scientifique Inter Régional Grand Ouest)
- 2012 SFPM Grant: Image-guided radiotherapy

Principaux articles publiés ou travaux du responsable scientifique de l'organisme membre du réseau attestant de l'expertise dans le domaine concerné au cours des cinq dernières années

Major scientific publications and other publications of the scientific manager of the network members demonstrating its expertise in the project field over the last five years

1. A Bongrand, C Koumeir, D Villoing, A Guertin, F Haddad, V Métivier, F Poirier, V Potiron, N Servagent,S Supiot, G Delpon, S Chiavassa. A Monte Carlo Determination of Dose and Range Uncertainties for Preclinical Studies with a Proton Beam. Cancers (Basel). 2021 Apr 15;13(8):1889. doi: 10.3390/cancers13081889.

2. S Chiavassa, R Nilsson, K Clement-Colmou, V Potiron, G Delpon, E Traneus. Validation of the analytical irradiator model and Monte Carlo dose engine in the small animal irradiation treatment planning system µ-RayStation 8B. Phys Med Biol. 2019 Dec 12. doi: 10.1088/1361-6560/ab6155.

3. C Noblet, G Delpon, S Supiot, V Potiron, F Paris, S Chiavassa. A new tissue segmentation method to calculate 3D dose in small animal radiation therapy. Radiat Oncol. 2018 Feb 26;13(1):32.

4. C Noblet, S Chiavassa, F Smekens, D Sarrut, V Passal, J Suhard, A Lisbona, F Paris, G Delpon. Validation of fast Monte Carlo dose calculation in small animal radiotherapy with EBT3 radiochromic films. Phys Med Biol.

2016 May 7;61(9):3521-35.

5. G Delpon, AM Frelin-Labalme, S Heinrich, V Beaudouin, C Noblet, M Begue, C Le Deroff, F Pouzoulet, S Chiavassa. Small animal image-guided radiotherapy: A new era for preclinical studies. Cancer Radiother. 2016 Feb;20(1):43-53.

CV court de chaque responsable scientifique / *Short CV of each scientific manager (max 2 pages sans publication)*

NAME Eric	CURRENT POSITION TITLE Chair of the radiation oncology department Chair of the INSERM1030 molecular radiotherapy Director of Gustave Roussy SIRIC program Full professor of radiation oncology
Last names DEUTSCH	
Date of Birth: 30 05 1968	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Val de Marne, 94	Baccalauréate	1986	Sciences
Paris 7 - faculty of medicine	MD	1987-2000	Medicine
Paris-Sud faculty of medecine	Master degree	1999-2000	Radiation biology
Paris-Sud University	Radiation biology	2002	Radiation Oncology
Paris-Sud University	PhD	2003	Molecular oncology
University of Pennsylvania, Phildephia, USA	Post-Doc	2005	Translational research

A. Personal Statement and keywords (present subject of interest)

Eric Deutsch is Radiation Oncologist, MD PhD with a strong background in research. He leads several clinical trials translating innovative approaches into the clinic, namely in the field of RT + immunotherapies . He leads a preclinical research group focused on immunotherapies and radiomics applied to radiotherapy. Under his leadership, he manages more than 150 people (clinic + research) as board member of GR transfer office, he is well versed into the transfer, valorization and contracting aspect of research.

B. Positions

2002-2004 Assistant professor, U. Paris-Sud, dept. oncology-radiotherapy, Gustave Roussy

2004-2005 Post-doc : University of Pennsylvania, Philadelphia USA

Since 2006 Tenure track position in radiation oncology with protected research time 2009 Creation of the INSERMU1030 unit

2010 Full professor (PUPH) in radiation oncology, U. paris-Sud Since 2011 Member of the CODIR of "Labex-LERMIT"

Since 2011 Medical director of Gustave Roussy technology and transfert office Since 2012 Head of Chair INSERM 1030 unit at Gustave Roussy

2018 Founding member of the réseau national de recherche préclinique en radiothérapie « Radiotransnet », labelised by INCA en 2018

Since 2018 Director of SIRIC « SOCRATE » program at Gustave Roussy

C. Current Research Support

INCA PL BIO 2018 (ED): Preclinical modeling of the inflammatory tumor/stroma response

after irradiation in stereotactic conditions: 600k€
ARC SIGNIT 2018 'ED): radiomics biomarkers of response to immunotherapy 600k€
ANR 2018 (to ED) : immunomodulation for lung response to IR 200K€
FRM 2017 (ED): computationnal imaging 600K€
SIRIC SOCRATES 2018 > 6.5M€: transversal program of Gustave Roussy
EDF 50k€ 2017: radiation biology of tumor response after high dose rate irradiation
EDF 50K€ 2015: radiation biology of tumor response after high dose rate irradiation
RAIDS FP7 2014 500k€: Response to radiotherapy of HPV associated tumors

D. Peer-reviewed Publications

Total number of publications: 239

Principaux articles publiés ou travaux du responsable scientifique de l'organisme membre du réseau attestant de l'expertise dans le domaine concerné au cours des cinq dernières années

Major scientific publications and other publications of the scientific manager of the network members demonstrating its expertise in the project field over the last five years

1. Low Doses of Radiation Increase the Immunosuppressive Profile of Lung Macrophages During Viral Infection and Pneumonia. Meziani L, Robert C, Classe M, Da Costa B, Mondini M, Clémenson C, Alfaro A, Mordant P, Ammari S, Le Goffic R, Deutsch E. Int J Radiat Oncol Biol Phys. 2021 Aug 1;110(5):1283-1294. doi: 10.1016/j.ijrobp.2021.03.022. Epub 2021 Mar 13. PMID: 33722770A Bongrand, C Koumeir, D Villoing, A Guertin, F Haddad, V Métivier, F Poirier, V Potiron, N Servagent,S Supiot, G Delpon, S Chiavassa. A Monte Carlo Determination of Dose and Range Uncertainties for Preclinical Studies with a Proton Beam. Cancers (Basel). 2021 Apr 15;13(8):1889. doi: 10.3390/cancers13081889.

2. Radiomics to predict outcomes and abscopal response of patients with cancer treated with immunotherapy combined with radiotherapy using a validated signature of CD8 cells. Sun R, Sundahl N, Hecht M, Putz F, Lancia A, Rouyar A, Milic M, Carré A, Battistella E, Alvarez Andres E, Niyoteka S, Romano E, Louvel G, Durand-Labrunie J, Bockel S, Bahleda R, Robert C, Boutros C, Vakalopoulou M, Paragios N, Frey B, Soria JC, Massard C, Ferté C, Fietkau R, Ost P, Gaipl U, Deutsch E. J Immunother Cancer. 2020 Nov;8(2):e001429. doi: 10.1136/jitc-2020-001429. PMID: 33188037

3. Dose escalation phase 1 study of radiotherapy in combination with anti-cytotoxic-T-lymphocyte-associated antigen 4 monoclonal antibody ipilimumab in patients with metastatic melanoma. Boutros C, Chaput-Gras N, Lanoy E, Larive A, Mateus C, Routier E, Sun R, Tao YG, Massard C, Bahleda R, Schwob D, Ibrahim N, Khoury Abboud RM, Caramella C, Lancia A, Cassard L, Roy S, Soria JC, Robert C, Deutsch E. J Immunother Cancer. 2020 Aug;8(2):e000627. doi: 10.1136/jitc-2020-000627. PMID: 32819972

4. Standardization of brain MR images across machines and protocols: bridging the gap for MRI-based radiomics. Carré A, Klausner G, Edjlali M, Lerousseau M, Briend-Diop J, Sun R, Ammari S, Reuzé S, Alvarez Andres E, Estienne T, Niyoteka S, Battistella E, Vakalopoulou M, Dhermain F, Paragios N, Deutsch E, Oppenheim C, Pallud J, Robert C. Sci Rep. 2020 Jul 23;10(1):12340. doi: 10.1038/s41598-020-69298-z. PMID: 32704007

5. Differential therapeutic effects of PARP and ATR inhibition combined with radiotherapy in the treatment of subcutaneous versus orthotopic lung tumour models. Tran Chau V, Liu W, Gerbé de Thoré M, Meziani L, Mondini M, O'Connor MJ, Deutsch E, Clémenson C. Br J Cancer. 2020 Sep;123(5):762-771. doi: 10.1038/s41416-020-0931-6. Epub 2020 Jun 17. PMID: 32546832

6. Consensus guidelines for the definition, detection and interpretation of immunogenic cell death. Galluzzi L, Vitale I, Warren S, Adjemian S, Agostinis P, Martinez AB, Chan TA, Coukos G, Demaria S, Deutsch E, Draganov D, Edelson RL, Formenti SC, Fucikova J, Gabriele L, Gaipl US, Gameiro SR, Garg AD, Golden E, Han J, Harrington KJ, Hemminki A, Hodge JW, Hossain DMS, Illidge T, Karin M, Kaufman HL, Kepp O, Kroemer G, Lasarte JJ, Loi S, Lotze MT, Manic G, Merghoub T, Melcher AA, Mossman KL, Prosper F, Rekdal Ø, Rescigno M, Riganti C, Sistigu A, Smyth MJ, Spisek R, Stagg J, Strauss BE, Tang D, Tatsuno K, van Gool SW, Vandenabeele P, Yamazaki T, Zamarin D, Zitvogel L, Cesano A, Marincola FM. J Immunother Cancer. 2020 Mar;8(1):e000337. doi: 10.1136/jitc-2019-000337. PMID: 32209603

7. Fast dose fractionation using ultra-short laser accelerated proton pulses can increase cancer cell mortality, which relies on functional PARP1 protein.
Bayart E, Flacco A, Delmas O, Pommarel L, Levy D, Cavallone M, Megnin-Chanet F, Deutsch E, Malka V. Sci Rep. 2019 Jul 12;9(1):10132. doi: 10.1038/s41598-019-46512-1. PMID: 31300704

CV court de chaque responsable scientifique / *Short CV of each scientific manager (max 2 pages sans publication)*

NAME DUTREIX Marie	POSITION TITLE Director of research (DR1) Group leader, Institut Curie
PLACE & DATE OF BIRTH Paris, France, 04/08/1955	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University Paris XI (Dr. Raymond	M2	1980	Microbiology
University Paris XI (Dr. Raymond	phD	1983	Microbiology
University Paris XI (Dr. Raymond Devoret)	Thèse d'Etat	1988	Microbiology/Genetics
Yale University, CT, USA (Department Genetics, Prof Charles Radding)	Post-doc	1988-1991	Biochemistry of homologous recombination
Institut Curie, Paris 5	Researcher	1991-1999	Radiobiology,
Institut Curie, Orsay	Team leader	1999-x	DNA repair

A. Personal Statement

All my carrier from my PhD up to now I have worked on cell response to DNA damage and genetic instability. However, my investigations have used many species (bacteria, yeast, zebrafish, rodents and patients) taking advantage of each system to address a specific question. These last decade the activity of my team has been divided between basic research and translational research on development of new therapeutic molecules and innovative instruments for treating resistant cancers with radiotherapy.

B. Actual position

Director of Research (DR1) CNRS**, Team leader** "DNA REPAIR, RADIATIONS AND INNOVATIVE CANCER THERAPIES", Institut Curie, Orsay, **Coordinator of the Medical and Scientific program** on radiation in Institut Curie

C. Awards, Fellowships and Honors

2017 Decorated Knight of the Legion of Honor **; 2003** 1st National prize of competition to help start up innovative technology companies**; 2016** Prize of the Academy of Sciences **; 2013** Biovision Next Gem Award for innovation**; 2013** Decorated Knight of the National Order of Merit **; 2005** 2nd National prize of the category "Creation - Development" of the Ministry of Industry and Research**; 2009** League Against Cancer Award, Antony Bernard Foundation Against Cancer; **2006** Prize for the promotion of research at the University of Paris XI**; 2006** Inserm-Transfert Life Science Grand Prize**; 2006** Life Science Trophy for the 8th "Tremplin Entreprise" competition organized by the Senate and ESSEC

D. Recent Memberships and professional responsabilities

Cofounder and main scientific advisor of the start-up "DNA Therapeutics" ; Coordinator of Axe V (radiobiology and radiotherapy) of the SIRIC- Institut Curie; President of the "Société Française du Cancer" ; Member of the EACR and ESTRO; Member of the scientific committee the CRUK/MRC Oxford Institute for Radiation Oncology (UK); Member of the scientific committee of the Institut Curie Hospital; Member of the scientific committee of Onxeo (SA); Coordinator of two national networks: NanoTheRad and GDR MI2B.

E. Education

Formation of 16 BTS, 7 Licences, 14 Master, 12 PhD

F. Recent patents

12 Patents (main inventor in 11)

G. Publications

95 publications in international journals, 5 book chapters, 1 cartoon explaining how act Dbaits (www.youtube.com/watch?v=95Tf4wFsK7Q)

Principaux articles publiés ou travaux du responsable scientifique de l'organisme membre du réseau attestant de l'expertise dans le domaine concerné au cours des cinq dernières années *Major scientific publications and other publications of the scientific manager of the network members demonstrating its expertise in the project field over the last five years*
1. Sofia Ferreira, Chloe Foray, Sophie Heinrich, Mihaela Lupo, Joel Mispelter, Francois Boussin, Celio Pouponnot, Marie Dutreix. Clinical Cancer research, 2021 Clin Cancer Res. 2020 Nov 1;26(21):5735-5746. doi: 10.1158/1078-0432.CCR-20-1729. Epub 2020 Sep 8. AsiDNA Is a Radiosensitizer with no Added Toxicity in Medulloblastoma Pediatric Models
2. C. Fouillade, S. Curras-Alonso, L. Giuranno, E. Quellennec, S. Heinrich, S. Bonnet-Boissinot, S. Leboucher., M. Bohec, S. Baulande, M. Vooijs, P. Verrelle, M. Dutreix, JA. Londoño-Vallejo, V. Favaudon (2020) Clin Cancer Res. 15;26(6):1497-1506.. FLASH Irradiation Spares Lung Progenitor Cells and Limits the Incidence of Radio-induced Senescence.
3. V. Favaudon, J-M. Lentz; S. Heinrich, A. Patriarca; L. De Marzi, C. Fouillade, M. Dutreix. (2019) Nuclear Inst. And Methods in Physics Research, A 944 (162537).Time-resolved dosimetry of pulsed electron beams in very high dose-rate, flash irradiation for radiotherapy preclinical studies
4. J. Biau, E. Chautard, N. Berthault, L. De Koning, F. Court, B. Pereira, P. Verrelle, M. Dutreix(2019) Frontiers in Oncology. Jun 19;9:549. doi: 10.3389/fonc.2019.00549. A preclinical study combining the DNA repair inhibitor Dbait with radiotherapy for the treatment of high grade glioma: efficacy and protein biomarkers of resistance
5. Jdey W, Kozlak M, Alekseev S, Thierry S, Lascaux P, Girard PM, Bono F, Dutreix M. (2019) Neoplasia. Jul 27;21(9):863-871. doi: 10.1016/j.neo.2019.06.006. [Epub ahead of print] PMID:31362243 AsiDNA treatment induces cumulative antitumor efficacy with a low probability of acquired resistance
6. S. Thierry , W. Jdey, S.Alculumbre, V. Soumelis, P. Noguiez-Hellin, and M. Dutreix. (2017), Molecular Cancer Therapeutics Sep 25. pii: molcanther.0405.2017. doi: 10.1158/1535-7163.MCT-17-0405. The Dbait Specificity for malignant hematologic cells in blood.
7. J. Biau, E. Chautard, L. De Koning, F. Court, B. Pereira, P. Verrelle, M. Dutreix (2017) Radiation Oncology 12:123 doi 10.1186/s13014-017-0858-0 Predictive biomarkers of resistance to hypofractionated radiotherapy in high grade glioma.
8. W. Jdey, S. Thierry, T. Popova, M-H Stern, M. Dutreix (2017) Cancer Research, Jun 6. pii: canres.2693.2016. doi: 10.1158/0008-5472.CAN-16-2693. Micronuclei frequency in tumors as a predictive biomarker for genetic instability and sensitivity to the DNA repair inhibitor AsiDNA
9. Herath N., Devun F., Hebette A., Lienefa M-C, Chouteau P., Dutreix M., Denys A. European Radiology, (2017) Apr 3. doi: 10.1007/s00330-017-4792-1 Potentiation of doxorubicin efficacy in hepatocellular carcinoma by the DNA repair inhibitor DT01 in preclinical models.
10. W. Jdey, S. Thierry, C. Russo, F. Devun, M. Al Abo, P. Noguiez-Hellin, J-S. Sun, E. Barillot, A. Zinovyev, I. Kuperstein, Y. Pommier, M. Dutreix (2016) Clinical. Canc Res. (2016) Aug 24. pii: clincanres.1193. Drug Driven Synthetic Lethality: bypassing tumor cell genetics with a combination of Dbait and PARP inhibitors.

CV court de chaque responsable scientifique / *Short CV of each scientific manager (max 2 pages sans publication)*

Nom : **Lacornerie**
Prénom : **Thomas**

Department of Medical Physics, CLCC Centre Oscar Lambret
3 rue Frédéric Combemale 59020 Lille
t-lacornerie@o-lambret.fr
https://orcid.org/0000-0001-8994-5999

Born 4th May 1968 in Strasbourg

Position: Head of Medical Physics Department

Professional experience:

2017- today Head of Medical Physics Department, Centre Oscar Lambret, Lille
2004 – 2017 Medical Physicist, Department of Medical Physics, Centre Oscar Lambret, Lille
1994 – 2003 Medical Physicist, Department of Radiotherapy, Centre Paul Strauss, Strasbourg

Scientific projects

- *Interreg CoBra (Cooperative Brachytherapy) with Lille University (2018-2022)*
- *MRI based Monte Carlo treatment planning for hypofractionated extracranial stereotactic radiotherapy* (Physicancer 2015-2017)
- *Mechanical Nanotweezeers and Microfruidic Setup for the Direct Assay of DNA* (Physicancer 2012-2014)

Education:

1991 University of Toulouse – Master of Medical Physics
2000 University of Strasbourg – Master of Computing Science

Teaching

Master of Medical Physics- University of Lille

Diploma for Qualified Medical Physicist – INSTN (French National Institute of Science and Nuclear Technics)

Scientific Societies

French Society of Medical Physics, SFPM (Vice-President and EFOMP Delegate 2013-2018, 2019-today coordinator of Scientific Committee)

European Society for Radiotherapy & Oncology, ESTRO

Associated editor of European Journal of Medical Physics (2015-2019

Reviewer

Radiotherapy and Oncology, Radiation Oncology, Cancer Radiothérapie, European Journal of Medical Physics, British Journal of Radiology, Journal of Applied Clinical Medical Physics, International Journal of Radiation Oncology, Biology, Physics, Medical Physics, Strahlen und Onkologie, Scientific Reports

Principaux articles publiés ou travaux du responsable scientifique de l'organisme membre du réseau attestant de l'expertise dans le domaine concerné au cours des cinq dernières années

Major scientific publications and other publications of the scientific manager of the network members demonstrating its expertise in the project field over the last five years

1. Crop, F., Mouttet-Audouard, R., Mirabel, X., Ceugnart, L. & Lacornerie, T. Technical note: Unexpected external markers artifact in 3D k-space based parallel imaging turbo spin-echo magnetic resonance imaging. *Phys. Medica* **90**, 150–157 (2021)

2. Tonneau, M., Lacornerie, T., Mirabel, X. & Pasquier, D. Radiothérapie stéréotaxique dans le cancer du pancréas localement avancé : revue de la littérature. *Cancer/Radiothérapie* **25**, 283–295 (2021)

3. Biston, M.-C., Chiavassa, S., Grégoire, V., Thariat, J. & Lacornerie, T. Time of PTV is ending, robust optimization comes next. *Cancer/Radiothérapie* **24**, 676–686 (2020)

4. Lebredonchel, S. *et al.* About the non-consistency of PTV-based prescription in lung. *Phys. Medica* **44**, 177–187 (2017)

5. Pasquier, D. *et al.* Radiothérapie stéréotaxique extra crânienne. Comment mieux protéger les tissus sains ? *Cancer/Radiothérapie* **23**, 630–635 (2019)

CV court de chaque responsable scientifique / *Short CV of each scientific manager (max 2 pages sans publication)*

CV Paul-Henri Romeo

PERSONAL INFORMATION
Romeo Paul-Henri
Date of birth: 03/05/1955

- **EDUCATION**

1978: Engineering graduate of the Ecole Polytechnique (the best French *Grandes Ecoles* in Science and Technology), France
1983: Ph.D. Thesis in Biochemistry
University of Paris, France

- **CURRENT POSITION(S)**

Inserm (French institute dedicated to biomedical research and human health) Exceptional Class Research Director
Head of the institute of Cellular and Molecular Radiobiology (iRCM) that is part of the Institute of Biology François Jacob of CEA. IRCM is unique in Europe and has internationally recognized research activities in radiobiology, radiotherapy, genome stability, cancer and tissue regeneration. iRCM contains 12 research teams with more than 100 permanent researchers from Inserm and CEA.

- **PREVIOUS POSITIONS**

1984-1989 CR1 Inserm
1989-1995 Director of Research Inserm
1990-2001 Professor of Biology, Ecole Polytechnique, France
1996-2001 Head of the Inserm U474 "Molecular Hematology", Hospital Henri Mondor 1996-2007 First class Director of Research Inserm, Hospital Cochin
2002-2006 Co-Director of the Cochin Institute, Inserm U567-CNRS UMR8603
2008-2014 Director of the French National Multi-Organization Institute "Immunology, Hematology and Pneumology"
2009-2018 Head of the Inserm joint research unit UMR967 CEA « Genetic Stability, Stem Cells and Radiation »

- **FELLOWSHIPS AND AWARDS**

1992 MONTYON award of the French Science Academy
1993 Ligue contre le Cancer (French anti cancer League) award 1995 Ville de Paris award
2003 Chevalier dans l'ordre des Palmes Académiques (decoration for service to research) 2008 Fondation pour la Recherche Médicale - Raymond Rozen prize
2009 Member of « Tohoku Medical Society » (Sendai, Japon)

- **COMMISSIONS OF TRUST**

President of the INSERM Scientific Commission 2
Member of the Scientific Board of the French Society of Hematology

Member of the Scientific Board of the Association for Research in Cancer (ARC)
Member of the Scientific Board of the "Fondation pour la Recherche Médicale"
Member of Scientific Board of the International Science and Technology Center (ISTC)
European Commission
Member of the Scientific Board of the French Institute for Universities (IUF)
Co-President of the Scientific Board of the Research Institute against Digestive Cancer (IRCAD)
President of one of the ARC (foundation dedicated to cancer research) Scientific Commissions

- **RELEVANT PROFESSIONAL EXPERIENCE**

Paul-Henri Romeo was the director of Inserm research units for more than 15 years and was, for 4 years, the co-director of the Cochin Institute (Paris, France) which performs both basic and clinical research and is now head of the institute of Cellular and Molecular Radiobiology (IBFJ/DRF/CEA). In 2008, he was nominated director of the French National Multi-Organization Institute "Immunology, Hematology and Pneumology" (IHP) that coordinates French research in immunology, hematology, pneumology, haemostasis, dermatology, cell and gene therapy and transplantation. IHP also strengthened European collaborations in fields dedicated to IHP and organized the 5th International Research Meetings with the Alliance for Research and Innovation in Health Industries. This event, dedicated to inflammation and inflammatory diseases, brought together academic researchers and some thirty national and international industries.

- **RESEARCH ACTIVITY**

After a Ph.D. thesis and a post-doc in USA focused hemoglobin function and regulation of PolIII transcription, Paul-Henri Romeo participated to the cloning of two genes encoding heme bio-synthetic pathways enzymes (URO-D and PBG-D). He then studied genes regulation during adult hematopoiesis and characterized cis- and trans-acting factors that regulate gene expression in normal hematopoiesis and in human leukemia. Presently, his research team focuses its research on the effects of low doses of irradiation on hematopoietic stem cells, on human radiosensitivity, on cellular therapy against the side effects of radiotherapy, on the development of new methods to characterize leukemia progression *in vivo* and on the role of TRIM33 in myeloid cells during inflammation and cancer progression.

Principaux articles publiés ou travaux du responsable scientifique de l'organisme membre du réseau attestant de l'expertise dans le domaine concerné au cours des cinq dernières années

Major scientific publications and other publications of the scientific manager of the network members demonstrating its expertise in the project field over the last five years

1. Gay D, Ghinatti G, Guerrero-Juarez CF, Ferrer RA, Ferri F, Lim CH, Murakami S, Gault N, Barroca V, Rombeau I, Mauffrey P, Irbah L, Treffeisen E, Franz S, Boissonnas A, Combadière C, Ito M, Plikus MV and Romeo PH Phagocytosis of Wnt inhibitor SFRP4 by late wound macrophages drives chronic Wnt activity for fibrotic skin healing Science Advances, 2020, 6(12):eaay3704. doi: 10.1126/sciadv.aay3704

2. Mauffrey P, Tchitchek N, Barroca V, Bemelmans A, Firlej V, Allory Y, Romeo PH, Magnon C. Progenitors from the central nervous system drive neurogenesis in cancer. Nature, 2019, 569, 672-678

3. Fortunel N, Chadli L, Coutier J, Lemaître G, Auvré F, Domingues S, Bouissou-Cadio E, Vaigot P, Cavallero S, Deleuze JF, ***Romeo PH*** and Martin M. KLF4 inhibition promotes expansion of adult human epidermal precursors and embryonic stem-cell-derived keratinocytes **Nature Biomed Eng**., 2019, 3(12), 985-997

4. Ferri F, Parcelier A, Petit V, Gallouet AS, Lewandowski D, Dalloz M, van den Heuvel A, Kolovos P, Soler E, Squadrito ML, De Palma M, Davidson I, Rousselet G, ***Romeo PH.*** TRIM33 switches off Ifnb1 gene transcription during the late phase of macrophage activation. **Nat Commun.** 2015, 6:8900.

5. Kusy S, Gault N, Ferri F, Lewandowski D, Barroca V, Jaracz-Ros A, Losson R and ***Romeo PH*** Adult hematopoiesis is regulated by TIF1repressor of TAL1 and PU.1 transcriptional activity, **Cell Stem Cell**, 2011, 4: 412-425

ANNEX

Annex 1: Expertise and experimental resources of the French Alternative Energies and Atomic Energy Commission (CEA) in the area of ionising radiation in health

Since its creation, the CEA has been involved in controlling and studying the effects of ionising radiation on living organisms, thus making it a key player in the field of radiobiology. Teams working for the CEA strive to understand the biological responses to radiation-induced stress, which includes issues such as understanding underlying molecular, cellular and tissue mechanisms, DNA damage, genome integrity and regulation of its expression, oxidative stress, etc. The CEA also plays an essential role in the control of ionising radiation in the area of health, especially through the *Laboratoire National de métrologie de rayonnements ionisants* [French Laboratory in the field of ionising radiation], but also through its simulation, modelling and artificial intelligence activities as well as the development of instruments in this field.

Its unique skills and equipment, especially the tools available on the DOSEO experimental platform for radiotherapy and radioprotection, mean it is a natural leader for the development of radiotherapy. The work of the CEA is focused on improving the therapeutic effectiveness of radiotherapy, preventing its undesirable effects, personalising treatments, optimising doses delivered to patients, determining the genetic basis of individual radiosensitivity, developing nanoparticulate radiosensitising agents, and developing new methods of irradiation.

At the CEA, there are four major areas of expertise in terms of the use of ionising radiation for health reasons: Radiobiology within the iRCM (Institute of Cellular and Molecular Radiation Biology), an institute that comes under the Fundamental Research Directorate and metrology, modelling, simulation, artificial intelligence, and instrumentation at the List Institute [Laboratory for Integration of Systems and Technology], which is part of the Technological Research Directorate. These areas of expertise use the experimental resources available on the DOSEO platform (the technology platform for radiotherapy).

Study of the effects of ionising radiation on health

The role of the *Institut de biologie François-Jacob* is to strengthen fundamental research and conduct translational and technological research in three areas including radiobiology and radiotoxicology, which is one of the core activities of the iRCM. This research institute is unique in Europe and has gained international recognition in the field of radiobiology, radiotherapy, genome stability, cancer and tissue regeneration. The iRCM relies on the creativity and risk-taking of its researchers and cutting-edge technological platforms to conduct fundamental research on model organisms, research into human diseases and their treatments and research associated with industrial developments.

At the CEA, the iRCM focuses its research on improving radiotherapy techniques, preventing the adverse effects of radiotherapy and personalising radiotherapy. In terms of improving radiotherapy, its work focuses on (i) the development of a novel irradiation method, called FLASH-RT, which uses very high dose rates thus allowing the radiation dose to be delivered in a very short time; (ii) the development of hadrontherapy, which optimises the targeting of tumours to ensure fewer deleterious effects on healthy tissues present in the irradiation field; and (iii) the development of the use of nanoparticles to increase the effectiveness of radiotherapy.

Research into the prevention of adverse effects of radiotherapy focuses on the development of cell-based therapies to protect healthy tissue from the effects of radiation. Regarding the personalisation of radiotherapy, research is focused on determining the genetic basis of individual

radiosensitivity. At the moment, as no predictive radiosensitivity tests for late adverse reactions are available, limitations are placed on the doses delivered meaning that for most patients the efficacy of the radiotherapy is decreased, despite the fact that only a small number of patients will suffer such adverse reactions. This type of research is combined with the determination of signatures to discover whether a cancer is radiation-induced or sporadic, an issue that is extremely important for both radiotherapy patients and nuclear workers.

One of the current radiotherapy projects (in the area of physics) being conducted by teams at the List Institute concerns the personalised estimation of doses delivered during on-board imaging examinations in radiotherapy and the evaluation of their impact on the function and outcome of haematopoietic stem cells in mice. The aim is to identify the risks of late-onset toxicities and radiation-induced cancers after exposure to chronic low doses delivered by imaging.

Metrology

At the CEA, the Henri-Becquerel National Laboratory (LNHB) is one of the French metrology institutes that comes under the *Laboratoire National de métrologie et d'Essais* (LNE, the French Metrology and Testing Laboratory). Its role is to implement units of the International System of Units (SI) in the field of ionising radiation and provide users with access to the metrological standards they need, within the framework of strictly established traceability, which is particularly relevant in the area of health. This role involves the development of primary measurement standards, instruments and associated methods, comparing these standards with those of similar international laboratories, their transfer to users, and the determination and/or the assessment of atomic and nuclear data, especially the data required for such measurements. The scope of the LNHB includes measurements of radioactivity (becquerel and its derivatives), neutron source emission rate ($n.s^{-1}$) and dosimetry of charged photons and particles (gray and sievert).

In terms of R&D in metrology applied to radiotherapy, its remit is:

- To improve national standards by upgrading and completing its absolute measurement resources in terms of air kerma and absorbed dose in water for external radiotherapy and brachytherapy (new ionisation chambers, new water and graphite calorimeters, etc.);
- To develop, if necessary, new standards for dosimetric quantities, innovative radiation detection methods and devices for new external radiotherapy methods (IMRT, stereotactic radiotherapy, MRI-guided radiotherapy, etc.).

A few examples of its R&D projects are given below:

- Development of quality control in stereotactic external radiotherapy based on 3D Fricke gel dosimeters: the aim is to develop an end-to-end 3D quality control to test the entire process by comparing planned 3D dose distributions with those measured using the gel
- Development of the first primary small-field references to restore metrological traceability (< 2x2 cm^2): as the miniaturisation of primary dosimeters has reached its limit for small beams, a new approach has been introduced, which consists of using dosimeters larger than the radiation beam. This method has required the introduction of a new dosimetric parameter, called the dose-area product.
- In brachytherapy, development of a method for establishing and transferring dosimetry references for electronic x-ray emitting brachytherapy machines
- In terms of radioactivity metrology, the triple-to-double coincidence ratio (TDCR) measurement method has been developed for the primary measurement of beta-emitting elements by liquid scintillation counters. New technologies, such as 3D printing and miniaturisation of electronics, have produced portable TDCR-based detection system for on-site calibration of radio pharmaceuticals. Work is ongoing to combine the measurement of radioactivity with the accurate measurement of radioactive volume to produce a device to measure volumes of very short-lived radionuclides used in positron tomography imaging (e.g. ^{18}F, ^{11}C, ^{15}O).

Modeling, simulation and artificial intelligence

One of the areas of expertise of the List Institute concerns the development and use of Monte Carlo-based simulation tools dedicated to the simulation of radiation-matter interactions. This includes research and development into the simulation of complex physical systems when using ionising radiation in health, along with the experimental validation of models. Teams working for the institute are experts in the development and optimisation of PENELOPE, a Monte Carlo coding system. Various research projects have resulted in the development of modules allowing accurate and rapid calculations, thanks in particular to the implementation of various strategies for accelerating MC codes. Teams now have a simulation platform (Phoebe platform) at their disposal, which allows the simulation of all radiotherapy treatments based on the Dicom-RT record of the patient.

Simulation is an essential tool; however, its cost means that it is often prohibitive for real-time use. Activities carried out at List include research into developing methods, algorithms and tools to use data from sensors and human expertise. The mission of the teams in this area focuses on the development of new technological building blocks for artificial intelligence (AI). AI capabilities for modelling complex functions appear to be a major avenue for accelerating these simulations. At the List Institute, hybrid techniques combining AI and simulation are being developed to design analytical and digital models.

In the field of statistical analysis, teams are also working on the development of an analysis software platform for the calculation of complexity indices for treatment plans, both for conventional IMRT (Intensity-Modulated Radiotherapy) and dynamic arc-therapy plans. The software includes tools for statistical analysis to determine any correlation between complexity indices and patient quality control (QC).

A few examples of current R&D projects include:

- Simulation for quality control of treatment plans or control of patient dosimetry by portal imaging
- Development of simulation modules to estimate out-of-field delivered doses in radiotherapy
- Development of software for the calculation of doses for positioning imaging

Instrumentation

At the List Institute, teams are engaged in technological research and development of ionising radiation detection devices. In terms of instrumentation, they design high-performance, accurate and robust detectors, sensors and dosimeters for medicine, radiation protection and the industry.

The four major areas of development in the detection of ionising radiation include:

- Synthetic diamond sensor and detector technologies for radiation detection to be used for radiotherapy, beam positioning or micro-dosimetry applications.
- The Optically Stimulated Luminescence - Fibre Optics (OSL-FO) technique has been the subject of various projects in external radiotherapy and brachytherapy. In external radiotherapy, it allows in vivo dosimetry at the end of each session, at several points distributed over the patient's body, as well as monitoring the progress of the treatment to detect any anomalies. In terms of brachytherapy, the List Institute has used its OSL-FO expertise to design, produce and validate fibre-optic dosimetric catheters connected to multi-channel instruments. These catheters have already been metrologically validated at the LNHB and pre-clinically tested.
- Research into organic materials for radiation detection with the development of special organic materials for specific detection applications, such as radiotherapy, or radiation protection. This includes the development of plastic and liquid scintillators and radiosensitive polymers (gels, elastomers, thermosets, etc.) for ionising radiation detection applications.

- The development of ultra-fast plastic scintillators coupled to a silicon photomultiplier (SiPM) sensor. These dosimeters could be applied to the measurement and control of FLASH beams.

Experimental DOSEO platform for radiotherapy and radioprotection

The DOSEO experimental platform is available to all operators in radiotherapy and radioprotection. Accessible by day, its technical platform allows manufacturers, researchers and hospital practitioners to benefit from the technological equipment and expertise of its teams.

The following equipment is available on the DOSEO platform:

- Two medical accelerators (ELEKTA and VARIAN) representative of French equipment:
    - A TrueBeam accelerator (VARIAN) that delivers radiotherapy beams in all new conditions in both photon and electron modes. It is fitted with a 120-slide multi-leaf collimator and an on-board 3D imaging system kV-CBCT. It has a 30x40 cm^2 amorphous Si MV imaging system. It also delivers high-speed beams at 6 and 10 MV. The accelerator also comes with a radio transparent carbon table.
    - A VERSA HD accelerator (ELEKTA) that delivers radiotherapy beams in all new conditions in both photon and electron modes. It is fitted with a 160-slide multi-leaf collimator and an on-board 3D imaging system kV-CBCT. It has a 41x41 cm^2 amorphous Si MV imaging system. It also delivers high-speed beams at 6 and 10 MV. The accelerator also comes with a radio transparent carbon table.
- A DISCOVERY CT750 HD scanner (GeHealthcare) for spectral and 4D imaging. It offers ASIR reconstruction software and AW SIM MD virtual simulation software
- Brachytherapy sources of ^{192}Ir and ^{60}Co, whose projection is remotely controlled using a projector, in HDR or PDR mode.
- A ^{60}Co irradiator (Best Theratronics).
- A multi-source ^{137}Cs and ^{60}Co radiation protection irradiator
- Beta reference sources
- 2 medical imaging devices (mammography and radiodiagnosis)
- Continuous low and medium energy x-ray generators for radiotherapy and radioprotection
    - GULMAY 160 kV X-ray generator, operating in the voltage range from 10 kV to 160 kV, with an electrical power of 3000 W
    - COMET 350 kV X-ray generator, operating in the voltage range from 20 kV to 350 kV, with a maximum electrical power of 4200 W
- Laboratory for the preparation of gel dosimetry and optical reader
- Laboratory for EPR reading of alanine dosimeters

DOSEO also has a conference room for 100 people, which can be divided into two rooms for 50 people for training, seminars, etc.

Annex 2: Unitrad Working Group

Groupe UNICANCER de Recherche Translationnelle et de développement en Radiothérapie Oncologique

UNICANCER group of Translational research and development in RADiation oncology (UNITRAD)

Dr Sofia RIVERA : présidente du groupe UNITRAD – Gustave Roussy
Assia LAMRANI-GHAOUTI : Responsable de programme UNITRAD –Unicancer R&D

Groupe UNITRAD

Le Groupe de Recherche Translationnelle et de développement en Radiothérapie oncologique d'UNCANCER (UNITRAD) a été créé en 2014. Le bureau actuel de ce groupe est constitué de :

- Présidente : Dr Sofia RIVERA - Oncologue radiothérapeute (Gustave Roussy - Villejuif).
- Vice-présidente: Catherine DEJEAN - Physicienne médicale (Centre Antoine Lacassagne – Nice).
- Secrétaire général: Pr Stéphane SUPIOT- Oncologue radiothérapeute (Institut de Cancérologie de L'Ouest – Nantes).

UNITRAD regroupe des experts de diverses disciplines tels que des oncologues radiothérapeutes, des physiciens médicaux, des dosimétristes, des qualiticiens, des radiobiologistes et des statisticiens.

La vision globale d'UNITRAD est que l'optimisation de la radiothérapie et des traitements combinés à la radiothérapie améliorera le pronostic et la qualité de vie des patients atteints de cancer.

Son objectif étant de faciliter la recherche clinique en oncologie radiothérapie, et d'accélérer ainsi le progrès dans ce domaine pour apporter un bénéfice au plus grand nombre de patients atteints de cancer.

Le programme de recherche en radiothérapie oncologique promu par UNITRAD inclut la radiobiologie dédiée à la clinique, la physique médicale appliquée, les technologies innovantes et les combinaisons de rayonnements ionisants avec des traitements systémiques, notamment les thérapies ciblées et l'immunothérapie.

UNITRAD en tant que Groupe transverse interagit étroitement avec les autres groupes d'experts d'UNICANCER, mettant en commun leurs réseaux respectifs ainsi que leurs expertises biologiques, méthodologiques et techniques, dans le but de mener des études cliniques innovantes et stratégiques à forte composante translationnelle de manière standardisée. Il met

également en place des réseaux collaboratifs pluridisciplinaires en France et à l'étranger pour le développement de programmes de recherche innovants en radiothérapie.

Working groups (WG) d'UNITRAD

La stratégie d'UNITRAD est centrée sur 5 axes de recherche et de développement qui passent par la mise en oeuvre d'essais thérapeutiques visant à changer les pratiques et par l'homogénéisation des pratiques visant à tirer les pratiques quotidiennes vers le haut pour l'ensemble des patients.

Cinq groupes de travail sont dédiés à développer ces 5 axes stratégiques d'UNITRAD :

H. WG1 : Intelligence Artificielle (IA) : Radiomique/Imagerie :

Coordonnateurs : Dr David PASQUIER (Oncologue radiothérapeute, Centre Oscar Lambret- Lille) - Charlotte ROBERT (Physicienne médicale, Gustave Roussy).

Les axes stratégiques de ce WG sont d'identifier des paramètres de radiomique prédictifs de la réponse à la radiothérapie et/ou pronostics en vue d'optimiser la prise en charge des patients, et de générer une base de données d'imagerie de qualité répondant aux critères nécessaires à leur utilisation en Radiomics/ IA.

I. WG2 : Radiobiologie: Immunoradiothérapie Radiosensibilité/ Radiopotentialisation:

Coordonnateur: Céline MIRJOLET (radiobiologiste, Centre Georges François Leclerc - Dijon).

Les axes stratégiques de ce WG sont d'optimiser le traitement par radiothérapie en combinaison avec l'immunothérapie et d'identifier les patients à risque de toxicités induites par la radiothérapie grâce à des tests biologiques. Pour ce faire, ce WG se focalise sur le développement des études prospectives interventionnelles évaluant la modification de la stratégie thérapeutique en fonction des résultats des tests prédictifs et promeut un programme de recherche translationnelle évaluant différents biomarqueurs potentiels et l'intérêt de les combiner.

J. WG3 : Nouvelles technologies et Développement physique :

Coordonnateurs : Pr Juliette THARIAT (Oncologue radiothérapeute, Caen) - Marie-Claude BISTON (Physicienne médicale, Centre Léon Bérard – Lyon).

Les axes stratégiques de ce WG sont de soutenir et promouvoir l'installation et l'évaluation des évolutions technologiques (IRM Linac, radiothérapie flash, protonthérapie,..) et mettre en réseau des centres pilotes pour promouvoir les essais cliniques évaluant ces technologies.

K. WG4 : Assurance Qualité de la Radiothérapie/ Sécurité :

Coordonnateur : Albert Lisbona (Physicien médical, Institut de Cancérologie de L'Ouest - Nantes).

Les axes stratégiques de ce WG sont de standardiser le contrôle qualité des données de radiothérapie des essais cliniques, de transférer la démarche qualité des essais vers la pratique courante et d'optimiser la qualité et la sécurité des traitements de radiothérapie en pratique courante

L. WG5 : PROMs/ Données de vie réelles :

Coordonnateur : Dr Sébastien Guihard (Oncologue radiothérapeute, ICANS - Strasbourg)

Les axes stratégiques de ce WG sont de renforcer le rôle du patient dans sa prise en

charge et d'optimiser l'utilisation et l'analyse des données rapportées par les patients et des données saisies au quotidien pour mieux orienter l'offre de soins et optimiser la prise en charge des patients.

Collaboration UNITRAD - RadioTransNet

L'ambition du groupe UNITRAD et du réseau RadioTransnet est de collaborer ensemble dans le développement notamment des projets de recherche préclinique en radiothérapie et mettre en commun leurs expertises dans les domaines suivants :

- Radiobiologie (expertise du WG2)
- Intelligence artificielle (expertise du WG1)
- Données de vie réelles (expertise du WG 5).

Les interactions scientifiques et cliniques entre ces deux groupes et la mutualisation de leurs compétences/expertises permettront de mettre en place des projets innovants et stratégiques dédiés à la radiothérapie.

Annex 3: SFRO Ethics charter

Charte commission éthique - SFRO

I Liminaire

L'oncologie radiothérapie est une activité médicale qui concourt au traitement des personnes atteintes de cancer. Il s'agit d'une spécialité médicale complexe avec de multiples aspects qui combine des connaissances humaines, scientifiques, pharmacologiques, biologiques et techniques. La technique prend une part de plus en plus importante et l'oncologue radiothérapeute est confronté à de nombreuses situations complexes qui peuvent générer des difficultés d'appréhension. Cette spécialité s'inscrit dans une prise en charge globale du patient, lui-même inscrit dans un système médical entier.
La pratique quotidienne met en évidence des tensions éthiques. Il y a aussi des problématiques individuelles d'aide à la décision médicale qui émergent. Toutefois cette commission n'a pas pour objectif de répondre à des conflits entre personnes ou structures car il existe des organisations propres pour y remédier.
Par ailleurs, la réflexion éthique s'inscrit actuellement comme l'une des bases du soin.
La réflexion conduite par la commission s'orientera vers une éthique de la pratique de soins en oncologie radiothérapie ainsi qu'une réflexion concernant l'éthique de la technique et de sa mise en œuvre.
En outre, de nombreuses organisations nationales ou internationales impliquées dans la recherche et les soins ont constitué de façon statutaire des structures ayant une dimension éthique. La SFRO a donc décidé de constituer une commission éthique afin de répondre à ces exigences.

II Les objectifs

La commission participe aux travaux de recherche en éthique portant sur le domaine spécifique de l'oncologie radiothérapie. Elle fournit un travail réflexif avec une thématique annuelle dont la présentation peut être assurée lors de congrès, ou d'articles scientifiques. La Commission a un rôle dans l'initiation de thématiques de recherche et dans la mise en lien de personnes ou d'institutions dans le cadre ses travaux de recherche dans le domaine spécifique de l'oncologie radiothérapie.

Ainsi, la commission éthique répond aux questions et problématiques, ancrées sur le terrain et posées par l'activité d'oncologie radiothérapie. Cela concerne des questions posées par les patients mais aussi celles posées par les médecins, tous les professionnels de santé ou la société. L'étendue des questions que la commission cherche à explorer n'est pas limitée à une dimension. Elle peut être saisie par le président ou le CA de la SFRO.
Elle cherchera également à répondre aux questions posées par les interactions entre les différents acteurs du soin.
Ses travaux pourront donner lieu à des communications écrites ou affichées.

La commission éthique développera la formation éthique au travers des structures ad hoc (SFRO et AFCOR)
La recherche ayant une part importante dans l'amélioration et l'évaluation des soins, la recherche en éthique en oncologie radiothérapie est l'une de ses préoccupations et elle pourra aider au développement et à la réponse à des projets en SHS.
Elle propose, en particulier, des thèmes de réflexion annuelle en éthique pour le congrès de la SFRO.
Sont exclues des missions de la Commission :

- Les missions de conciliation ou de médiation en lien avec des situations de conflit entre professionnels de santé ;
- Les missions relevant de Comités d'Ethique de la Recherche (notamment la délivrance d'avis éthiques pour les travaux de recherche ne relevant pas du champ des Recherches Impliquant la Personne Humaine tels que définis par les des articles L. 1121-1 et R. 1121-1 du Code de la Santé Publique).

III Organisation

III-a Constitution et Définition des membres.

La commission éthique a été mise en place par le CA de la SFRO. Elle en est constitutive comme les autres commissions (communication, pédagogie, internationale…). Elle est sous sa responsabilité et notamment sous la responsabilité *in fine* de son président. Son bureau peut à tout moment questionner, modifier ou dissoudre le comité éthique selon les règles démocratiques établies dans le règlement intérieur.
L'assemblée de la commission éthique est constituée de toutes les personnes intéressées ou impliquées dans le domaine de l'éthique et qui s'engagent à participer activement aux travaux.
Pour répondre aux exigences actuelles de démocratie sanitaire, cette commission comprendra des médecins mais aussi des représentants de toutes les parties prenantes dont un représentant des patients. Afin d'éclairer la réflexion seront adjoints des représentants des sciences sociales et humaines.
Elle s'appuiera sur des personnalités ayant une compétence reconnue.
Peuvent être membres :
- Membres de droit : les membres de la SFRO à jour de leur cotisation peuvent faire acte de candidature. Le bureau de la SFRO sera représenté par le président de la SFRO ou son représentant ainsi que par le secrétaire général ou son représentant. Afin que toutes les modes d'activité soient présents, l'un des membres sera représentant du Syndicat National des Oncologues Radiothérapeutes (SNRO).
- Oncologues radiothérapeutes en formation : ils sont choisis parmi les membres de la Société Française des Jeunes Radiothérapeutes Oncologues (SFJRO) et proposé par leur CA.
- Physiciens médicaux : ils sont représentés par un membre désigné par la Société Française des Physiciens Médicaux (SFPM).
- Les manipulateurs sont représentés par un membre désigné par l'Association Française du Personnel Paramédical d'Electroradiologie (AFPPE).

- Les membres des autres professions paramédicales.
- Personnalités des SHS
    - Un philosophe
    - Un psychologue impliqué dans les traitements en oncologie radiothérapie
    - Un sociologue/anthropologue
- Représentant des patients : un représentant des patients appartenant à une association de patients traités pour cancer ou représentant de patients dans un établissement dont l'activité principale est le traitement des cancers
- Autre personnalité : en cas de nécessité, si la question traitée demande des compétences particulières il peut être fait appel à une personnalité ayant les compétences ad hoc.

Un appel à candidatures sera réalisé annuellement lors du congrès de la SFRO.
La composition du comité d'éthique est validée par le CA de la SFRO.

III-b Gouvernance

La commission désigne en son sein un coordinateur ou une coordinatrice qui organise les réunions et les débats. Il est accompagné d'un co-coordinateur ou d'une co-coordinatrice
Les responsabilités sont réparties entre les différentes structures participant à cette commission. Toutefois le coordinateur, membre de la SFRO, participe statutairement au CA de la SFRO à qui il rend compte régulièrement de ses travaux.
Un coordinateur de la recherche en éthique est désigné. Une compétence reconnue en éthique est un prérequis. La commission s'appuie sur le secrétariat de la SFRO pour l'organisation de ses réunions.
Un ordre du jour est préparé par le coordinateur en accord avec le coordinateur de la recherche.
Un compte-rendu est préparé au décours de chaque réunion par la personne désignée par le coordinateur. Ils sont adressés aux différents membres ainsi qu'au président de la SFRO. Ils tiennent lieu de bilan d'activité.
La commission s'assurera de l'absence de conflit d'intérêt dans son fonctionnement ainsi que de son indépendance particulièrement vis-à-vis de l'industrie ou tout autre organisme pouvant mettre en cause son indépendance

III-c Durée des mandats des membres de la commission.

La durée des mandats est de 2 ans renouvelable. Toutefois, les coordinateur(trice)s, co-coordinateur(trice)s sont renouvelés(es) avec un décalage d'un an afin d'avoir un tuilage dans le fonctionnement. Ils(elles) ne peuvent avoir plus de 2 mandats consécutifs. A la fin de son mandat, le coordinateur assure la continuité avec une année de past-coordinateur.

IV Fréquence des réunions

Quatre à six réunions statutaires sont prévues par an. Les réunions présentielles sont privilégiées mais peuvent aussi être organisées en distanciel ou en distanciel et présentiel. Des réunions ponctuelles peuvent, en tant que de besoin, être organisées, en particulier lorsque l'actualité le nécessite.
Les communications pour l'adressage des documents se font par mail préférentiellement.

V Interactions avec d'autres commissions éthiques.

Les réflexions et le recherche en éthique pouvant avoir une dimension nationale ou internationale, la commission vise à établir des liens voire des collaborations avec des instances identiques au sein d'autres sociétés savantes en oncologie radiothérapie afin de mener si possible des travaux en commun et être force de proposition.

Annex 4: Partnerships table

Nbr-(City) Teams: name, identification, team leader, laboratory, administrative institutions	**Axe** in the project	**Domains of expertise and research**	**Constitution:** number of equivalent full time senior researchers of the team, Doc and Post-doc. **Specific equipment**	**Collaborations:** running collaboration, national, international	**Funding:** recurrent resources, research contract, etc.
Alphabetic classification with some regional grouping when appropriate, networks are at the end					
1-(Angers) **team- GLIAD Design and Application of Innovative Local treatments in Glioblastoma** Emmanuel Garcion **CRCINA** **INSERM U1232** INSERM - Université d'Angers, IBS - CHU, 4 Rue Larrey, F-49933 Angers	**1,3**	• Glioblastoma • Nuclear medicine • Vectorized radiation therapy • Preclinical models • miRNA targeting and delivery • Micro and Nanomedicine • Drug delivery • Imaging Theranostics	8 Principal investigators 5 ITA 3 postdocs 12 PhD students **Specific equipment**: Shielded enclosure Synthesis robotic platform Hypoxic chamber L2 cell culture rooms Stereotaxic injection platform Analytic apparatus (microplate reader, cytometric station, HPLC, etc…)	• National CBM Orléans GIN Grenoble **ONIRIS Nantes** Univ. Lille 2 CRCINA Team 4, 13, 14 • International University of Liège (Be) University of Nottingham (UK) University of Santiago de Compostela (Spain) University of Modena (Italy) Technion (Israël) University of La Plata (Argentina) University of Western Cape (South Africa) Unicamp (Brazil)	INSERM University of Angers European Commission NANOFAR ANR – LABEX IRON Inca PL_BIO MARENGO Ligue Nationale contre le Cancer Région PDL MECASTEM NANOFAR+ Cancéropole GO
2-(Avignon) **Léa Vazquez,** **DVM, MsC**	**1,2,3**	• Preclinical research • Radiation therapy • Comparative oncology	Funding to support the development of a platform dedicated to preclinical studies through irradiation of cats and dogs is currently under research		
3-(Bordeaux) **INSERM U1035, BMGIC** (Biotherapie des maladies génétiques inflammatoire et du cancer) **Team leader : Pr François Moreau-Gaudry** **University of Bordeaux (**will become part of BRIC on January 2022) **CHU Bordeaux**	**Combined therapies**	**Radiobiology** **Vectorology** **Pre-clinical irradiation** **Radiosensitization** of pancreatic cancer and rectal cancer using BFCs **CRISPR-cas9** **Extracellular vesicles** (rectal cancer response evaluation after chemoradiotherapy) • **X-PDT (**Glioblastoma radiosensitization by 5-ALA)	Senior researchers :3ETP Doc: 2ETP Specific equipment: Vectorology platform XENX Pre-clinical irradiator	**CELIA** **IBGC-UMR 5095** **ISVV (institute de la vigne et du vin)** **INSERM 1029**	GSO Siric brio Ligue Inserm university
4-(Bordeaux) **POPRA : Programme Optique, Physique Radiothérapie en Aquitaine)** Pr Guy Kantor Consortium: • **Institut Bergonié,** • **CHU Bordeaux** • **CELIA** (University, CNRS, CEA) • **CENBG**(CNRS IN2P3, University)	**2,3,4**	• **Algorithms of dose calculation** (CELIA), for external- internal- and brachy radiotherapy, MRI and LINAC • **Energetic Sources created by ultra-intense laser** (CELIA) protontherapy • **Comparative dosimetry** • **Nano medicine**	• **Institut Bergonié** 0,2 ETP admin. 0,4 ETP med. 0,75 ETP med. phys. • **CHU** : 0,25 ETP med. phys. • **CELIA:** 2x 0,5 phys.; 4 PhD (1 past) **CENBG** : iRiBio : 4 x 0,5 ETP, 2 Doc (1Past), 2 Post-doc (2 Past) • **LaBRI** : 0,5 ETP; 1 doc	• National : – Pôle de compétitivité laser (RLH) – Canceropôle GSO (axe technologie et santé) – Oncopôle Toulouse, – Centre Antoine Lacassagne de Nice – CEA – ICMCB (nano chemistry) – Aquitaine sciences transfert (AST/SATT) – Industrial partnership	Conseil Regional Nouvelle-Aquitaine (co-funding) and European FEDER funds University of Bordeaux ; CNRS ; CEA ; IDEX; ANR; Canceropôle GSO European PM Curie program

• **INRIA** (équipe Monc, IMB) **LaBRI**		**CENBG** radio enhancement measurements • **Spectral Measurements** beams (CHU, CENBG) • **Adaptative radiotherapy, Evaluation** (MONC/INRIA) **X rays produced by laser** for imaging (Alphanov)X-pulse project	• **Inria** : 2 doc (past)	International: Univ of Dresden (Germany)	
5-(Brest) **LaTIM,** **Team ACTION,** Dimitris Visvikis **INSERM UMR1101,** UBO, IMT Atlantique, CHRU Morvan, Bat 1, 2 Av. Foch, 29609 Brest cedex	**1,4**	• Image guided radiotherapy • Multimodality quantitative imaging • Intra-operative radiotherapy • Image processing Tumor modeling	11,5 FTE senior researchers Postdocs : 6 PhD students : 10 **Equipment:** • TheraFonc Platform: • Varian TrueBeam Novalis (50% temps R&D) • Aixplorer US imaging platform (100% R&D) • Dual energy CT scan (dedicated to R&D in radiotherapy) Intensive computing and modelling platform (1000 CPUs, 40 Tflops; 100 GPUs, 380 Tflops)	• Regional: Director: CGO network on "Targeting and Radiotherapies" 25 labs and 17 clinical teams INSERM Tours, CRCINA, LTSI, CRCINA, LabEx CominLabs: image processing; multi-scale modeling for radiotherapy treatment • National TIMC, ICUBE, CHU Grenoble, LabEx CAMI • International MAASTRO, CHU Liege, Torino, DKFG Heidelberg, Dresden,SIEMENS, Montreal; Univ Patras, BET solutions (Grece); Libra (UK), St Thomas.	INSERM lab recurring funding Industrial contract: VARIAN, SIEMENS Research contracts: MC ITN PREDICT; ANR: tGATE, FOCUS; CGO: Mumofrat, MATURE; INCA : PRINCE; LaBEX CAMI: project CAPRI; CE: project ERROR
6-(Brest) **Radiotherapy department, CHRU Brest** Pr Olivier Pradier **CHRU Morvan**, 2 av. Foch, 29200 Brest	**1,3**	• Radiomics in radiotherapy • Adaptive radiotherapy Image guided radiotherapy • Combination treatment: Chemotherapy/US mediated radiobiology effects	3.5 FTE senior researchers; 4 Doc., 1 Post-doc **Equipment:** Cellular Analysis laboratories Varian TrueBeam Novalis (50% R&D) INTRABEAM platform (50% R&D)	• Regional: INSERM Tours, LTSI, CRCINA, LaBEX CominLabs: image processing; multi-scale modeling for radiotherapy treatment • National TIMC Grenoble: intra-operative radiotherapy	Research contracts: MC ITN PREDICT ANR : FOCUS Cancéropole GO: Mumofrat Industrial contract: VARIAN
7-(Caen) **Medical Applications Group**, Jean-Marc Fontbonne, **LPC-CAEN UMR6534, Normandie Univ**, ENSICAEN, UNICAEN, CNRS/IN2P3, LPC Caen	**4**	• Nuclear physics : **fragmentation** and beta+ emitters in hadrontherapy • **Instrumentation** : beam diagnostics, monitors units and dosimetry devices. • Computing : multiscale **modeling** of clinical outcomes in radiotherapy and	6 Senior researchers (4.7 FTE) 5 doc and post-doc A large vacuum chamber for detectors Proximity of GANIL and CYCLHAD	• IPHC (Strasbourg) • ICPO (Orsay) • Centre François Baclesse (CFB, Caen) • Centre Paul Strauss (CPS, Strasbourg) • CIMAP, GANIL, ARCHADE (Caen) • IMPT (Nice)	• CNRS/IN2P3 • ANR (EquipEx) • Possible Regional funding

		protontherapy.			
8-(Caen) **CERVOxy group** Myriam Bernaudin & S Valable **ISTCT laboratory** GIP CYCERON, CNRS-CEA-UNICAEN	**1,2,3**	Translational research in **hypoxia and brain tumors**, with multidisciplinary approaches (from molecular biology to imaging).	27 FTE: 3 CNRS researchers, 10 prof/lecturers, 6 engineers/tech, 10 Doc.; 3 Post-docs Specific equipment for cell and mol. biology (hypoxic chambers, time-lapse), animal surgery. Own non-human primate breeding (marmosets) Access to animal care facility (ONCOModels/CURB) and imaging platform (CYCERON)	• National – UGA 7442 RSRM, Grenoble – CRCINA Inserm U1232, Nantes – CLCC Becquerel, Rouen – CLCC Baclesse, Caen – LCS UMR6506, Caen – LARIA UMR6252, Caen – LPC UMR6534, Caen • International CRUK/MRC Oxford Institute for Radiation Oncology	- CNRS, UNICAEN - ANR: Maestro, Labex IRON, EquipEx Rec-Hadron, France HADRON - INCa PLBIO Zeoxy - Région Normandie MET-Oxy (RJC) - Cancéropôle Nord-Ouest (Emergence) - Ligue Contre la Cancer
9-(Caen) **LDM TEP group**, Pr Louisa Barré & C Perrio **ISTCT laboratory** GIP CYCERON, CNRS-CEA-UNICAEN	**1**	LDM TEP team develops and evaluates **novel PET probes** using radionuclides as ^{11}C , ^{18}F, ^{68}Ga..	3 researchers (2CEA, 1CNRS), 6 engineers / tech., 4 Doc, 2 Post-docs **Specific equipment** Labs for radiochemistry and quality control of radionuclides and radiopharmaceutics	• National – CLCC Baclesse, Caen – CERMN, Caen – COBRA, Rouen – Subatech , Nantes – CRCINA, Nantes – IMIV, Orsay – CHRU, Caen • International – Rotterdam /Erasmus center – Barcelona/ IMIM Hospital del Mar research center – Louvain/ UCL – Texas University /A&M	-CEA -CNRS -ANR IRON -SANOFI -Cancéropôle Nord-Ouest -Région Normandie -Fédération INC3M
10-(Caen) **LARIA** **Laboratoire d'Accueil pour la Recherche sur les ions Accélérés** Yannick Saintigny **IRCM /CEA/GANIL**	**Cf (Fontenay-aux-roses, CEA) IRCM**				
11-(Caen et Rouen) **ABTE EA4651** Pr François Sichel **Université de Normandie (Caen et Rouen)**	**2,4**	Radiobiology, toxicology, genotoxicology, analytical chemistry, mitochondrial biology, oxidative stress **Research in radiobiology:** Toxicity of radiotherapy on normal tissues (skin, lung, heart and vessels).	SR : 2 FTE Doc : 1 FTE Post-doc : 1 FTE HPLC-MS/MS, HPLC-UV array, fluorescence microscope, image analysis software, echograph.	• National : CRLCC F Baclesse, Caen Curie Institute, Orsay	• Etat • Europe, • Région Normandie • Cancéropôle Nord-Ouest
12-(Clermont-Ferrand) (hors LabEx PRIMES, cf plus loin) **UMR 1240 INSERM** **IMoST : Imagerie Moléculaire et Stratégies**	**1,2,3,4**	• Targeted Radionuclide Therapy, • External radiation therapy, • Radiobiology, Dosimetry,	**20 FTE:** Senior researchers : 12 Doc : 7 Post-Doc : 1 **Specific Equipment** Plateforme d'imagerie préclinique : IVIA : PET,	• National : IRCM - Montpellier UPS- Strasbourg ISA - Lyon LPC – Clermont Fd Cyclopharma-Clermont Fd Caminnov, Alès	UCA INSERM CRLCC Centre Jean Perrin Ligue Contre le Cancer INCA/PRTK

Théranostiques **<u>Directrice :</u>** Dr E Miot-Noirault **<u>Directrice adjointe :</u>** Pr Frédérique Penault-Llorca **<u>Equipe 1 :</u>** *Cibles et outils pour l'imagerie et la thérapie* Dr F Degoul **<u>Equipe 2 :</u>** *Recherche translationnelle en imagerie fonctionnelle, radiopharmaceutiques et biomarqueurs théranostiques* Pr F Cachin **UCA : Université Clermont Auvergne ; CRLCC Jean Perrin ; INSERM ; CHU Clermont Fd**		• Metrology, • Chemistry, Radiochemistry.	SPECT CT, imagerie de fluorescence et de bioluminescence, scanner X haute résolution, imagerie ex vivo,radiochimie, enceinte et automates de radiomarquage pour les isotopes gamma et beta+, Autoradiographie quantitative corps entier rongeurs, <u>Plateforme d'imagerie clinique :</u> **CIRMEN** : Centre d'Innovation et de recherche en Médecine Nucléaire : Radiopharmacie expérimentale dédiée au « first into humans » de radiopharmaceutiques PET-CT, SPECT-CT. Automates de synthèse et de radiomarquage, chambres radioprotégées	CLB – Lyon ILM – Lyon ISPB/UCBL – Lyon IPHC – Strasbourg UCBL – Lyon - EA3738 Institut de Cancérologie de L'Ouest, Nantes	CPER FEDER ANR
13-(Dijon) **Radiobiology/Radiotherapy research team** **Céline Mirjolet** **Radiation Therapy Department, CRLCC** **G-F Leclerc**	**3**	- Preclinical Development of 3D image guided radiotherapy -Nanoparticles for RT -RT schedule to improve Immunotherapy - Radiosensitivity predictive parameters	**Constitution:** 2,1 FTE 1 radiobiologist 1technician; 0,1 radio-physicists, + master student **Specific equipment** : SARRP 3D (X-Strahl) with variable collimator	• <u>National</u> – netwo. RESPLANDIR – UMR 6303 CNRS, Equipe MaNaPi, Dijon – Le2i UMR CNRS 6306, Dijon – Lipide, nutrition, cancers UMR INSERM 866, Dijon – Lab Radiobiologie – EA3430, CRLCC P Strauss, Strasbourg – ICMUB UMR CNRS 6302, Dijon – EPHE, Immuno et Immunothér cancers, Dijon – UTINAM UMR CNRS 6213, Besançon – Biotechs: Oncodesign	Ligue contre le cancer Cancéropôle Grand est Conseil régional Bourgogne Franche Comté BPI Service Contract
14-(Lille) **Radiotherapy & Medical physics Departments, CRLCC O. Lambret** Dr X Mirabel, T Lacornerie, Pr E Lartigau **(Lille)** **IEMN, UMR CNRS 8520**	**4**	MRI dosimetry	4 researchers MRI 3T, 1.5 T Dosimetry	• Institut J. Bordet, • Bruxelles,	• Physicancer • Siric ONCOLille
	1	<u>NAMASTE</u> (Nanomaterials and Soft Matter Theory and Modeling)	3 researchers 1 doctorant Molecular and multi-cellular modeling	• Small Systems Laboratory, U. Barcelona • Catholic Univ. Leuven	• CNRS • INSERM • Siric ONCOLille
	3	<u>NanoBioInterfaces</u>, nanoparticles, nano compounds, graphene	4 FTE SPR Spectroscopy Surface chemistry Nanoparticle synthesis		• ANR Générique "SINCOLISTIN" • ANR PRCI "2DPS"

					• H2020-MSCA-RISE-2015 • FLAG-ERA JTC 2015 • INCa • CPER « Photonics for Society »
	1,3	AIMAN/LIA LICS, « théranostique », imagerie médicale multimodale	6 researchers	• Univ. of Illinois at Urbana-Champaign • Catholic Univ. Leuven Campus Kortrijk	• CNRS • Ecole Centrale Lille
15-(Lille) **SMMiL-E** D. Collard **UMI CNRS 2820**	**3**	BioMEMS, microfluidiques and *Silicon nano tweezers (SNT) pour la biomécanique sous faisceau*	6 researchers	Institut des sciences Industrielles, Tokyo	• CNRS • CPER IRICL • Centre Oscar Lambret
16-(Lille) **Plasticity and Cancer »** X Le Bourhis **INSERM U908 « Cell**	**2**	Stem cells Preclinical models (Zebra, transgenic mice)	2 researchers		• INSERM • Centre Oscar Lambret
147-(Lille) **« Approches Génétiques »** **Fonctionnelles et Structurales des Cancers »** C Abbadie **CNRS UMR 8161**	**2**	Cellular senescence, Oxidative stress, DNA damage,	3.5 FTE researchers	• Univ Ghent • Univ Libre de Bruxelles	• CNRS • Univ Lille • Institut Pasteur de Lille • Ligue contre le cancer • Siric ONCOlille • SFR Cancer • Cancéropôle Nord-Ouest
18-(Lille) **Plateforme PRECI** www.oncovet-clinical-research.com www.plateforme-preci.fr Dr Dominique TIERNY, DVM, CEO **OCR (Oncovet Clinical Research)** OCR Parc Eurasanté Lille Métropole 80 Rue du Docteur Yersin 59120 Loos - France	**2,3**	• **Comparative Oncology** : Clinical studies in dogs with spontaneous tumors for accelerating therapeutic development in human health (in particular combination treatments with radiation) • **Radiotherapy Platform for research use.** Dedicated housing facilities for rodents and large mammels with DDPP accreditation.	**Team research radiotherapy : 8 FTE** 4 DVM, 1 ingeneer,2 technicians, 1 supervisor **Specific Equipment** (accreditation ASN & DDPP) - Dual energy accelerator (Precise, Elekta, 6MV photons and electrons) - 3D treatment planning software, Oncentra and Mosaiq, Elekta - HDR Brachytherapy (microselectron-HDR) - Low-energy photon unit - Nuclear medicine service with gamma-camera - CT scanner - Fully equiped surgical theaters - Housing facilities	**National collaborations** with : Lille University, Oscar Lambret anticancer center COL, Pasteur Institute, CNRS and INSERM teams : Mixed team O'Dreams : OCR- PRISM (Inserm U1192) **International collaborations :** Project CoBra approved (Nov 2017) : Interreg 2seas European Program (Lille University; COL, Oncovet-OCR, Delft University –Nl,Portsmouth Hospitals NHS –UK,…) *Aims to develop a new medical robot prototype for treatment of localized cancers by brachytherapy under guidance of MRI.*	- Research contracts for biotechs and pharmaceuticals laboratories. - Innovative research program Immunodog (combination therapy : PRI BPI) - Application for collaborative research projects with academic teams : regional (Haut de France Region), national (FUI, ANR, INCa) and Europeen funds (Interreg2 Seas)
19-(Lyon and Auvergne-Rhône-Alpes) **LabEx PRIMES** Françoise Peyrin		**Physique, Radiobiologie, Imagerie Médicale et Simulations**	Federates 16 teams including 8 teams directly involved in preclinical research in		Each team has its own funding and the LabEx has specific ANR

8 teams			radiotherapy		funding
20-(PRIMES Lyon) PRISME-LRCM Development of fondamental and translational research in radiobiology for innovative radiotherapies Pr Claire Rodriguez-Lafrasse **IPNL UMR5822 (CNRS/IN2P3, Univ Lyon1)** Fac. de Médecine Lyon-Sud	**1,3**	• Radiobiology for innovative radiotherapies (cell response to carbon ions, protons and radiosensitizing nanoparticles) • Predictive biomarkers of response to radiotherapy in tumors and liquid biopsies (CTCs)	11 FTE: 3 PU-PH, 1 Pr, 1 MCU-PH, 1 Engineer, 1 AHU, 3 Techs, 1 post-doc, 5 Doc. Equipement Xray Irradiator (XRad320), cell. and mol. biology (hypoxic chambers, video microscopy, Nanostring, NGS...), animal facilities	• National : LabEx PRIMES, France Hadron. • International : ENLIGHT, NIRS (Chiba, Japon), GSI (Germany) University of Montreal.	IN2P3, Labex PRIMES, INCa, ANR, UCBL, CLARA, Ligue contre le cancer, EDF
21-(PRIMES Lyon) PRISME-PHABIO Modelling and instrumentation for control and optimisation of innovative radiotherapies Pr Michaël Beuve **IPNL-UMR5822 (CNRS/IN2P3, Univ Lyon 1)** Faculté des Sciences	**2,3,4**	• Radiobiology (experiments and multiscale modelling from atoms to tumor control), • Instrumentation - for cell irradiation dosimetry - for on-line control of treatments	7 FTE: 1 Pr, 2 MCU, 1 CR, 1 Engineer, 1 Post-doc, 5 Doc. Equipment - Proton beam line; - cell biology laboratory; - instrumentation laboratory.	• National : LabEx PRIMES, France Hadron, CIMAP • International : ENLIGHT (UE) ; IFIR (Argentine) ; Univ. St Petersbourg (Ru); Univ. Duisburg-Essen (D);	IN2P3, Labex PRIMES, INCa, UCBL, FRM, Bourse P&M Curie
22-(PRIMES Lyon) Tomoradio Françoise Peyrin & David Sarrut **CREATIS team 4, UMR 5220 INSERM 1206** (CNRS, INSERM, Univ. Lyon 1, INSA-Lyon)	**1,4**	**Image processing,** tomographic reconstruction, registration and simulations in radiation therapy and nuclear medicine	2.5 FTE; 3 Doc; 4 Post-doc Access to micro SPECT imaging and to the technical platform of the Lyon CRLCC	• National Nantes Cancer center on XRad small animal irradiators France HADRON • International D. Sarrut is member of the ESTRO ACROP (Advisory Committee on Radiation Oncology Practice) ENLIGHT	Univ.Lyon1, Labex PRIMES, INCa Physicancer SPEDIV, ANR tGATE, Lyric project (SIRIC INCa funds), FRM
23-(PRIMES Lyon) SAARA Behzad Shariat **LIRIS, Univ. Lyon 1**	**1,4**	**Moving organs** modeling (biomechanics)	2 pers, 1 FTE	• National : LabEx PRIMES, France HADRON • International : ENLIGHT	Labex PRIMES, Univ. Lyon 1, INSA, ANR
24-(PRIMES Clermont-Ferrand) Department of Physics for Health, Environment and Energy Gérard Montarou **LPC Clermont** CNRS/IN2P3 Univ. Clermont Auvergne (UCA)	**2,4**	• Particle Therapy: instrumentation and simulation • Radiobiology : experimental and modeling • Multiscale Dosimetry • Multiscale simulation of the radiation in cells and tissues • Biomaterials: elaboration and characterization	12,5 FTE 8,5 Senior researchers; 3 Doc 1 Post-Doc Specific equipment: • X ray Irradiation facility (PXI XRAD320) • 2.4 MeV Neutron Tube (G16 SODERN) • TIRF Microscope (Eclipse Ti-E NIKON)	• National LabEx PRIMES, France HADRON • International H2020- European Nuclear Science and Application Research2 : MediNet OpenGATE coll. Geant4-DNA ENLIGHT	Recurrent resources: – CNRS/IN2P3, – Univ. CA – Labex PRIMES Research contract – ANR, – INCa – CLARA Regional fundings on specific contract
25-(PRIMES Grenoble) Rayonnement Synchrotron et Recherche Médicale	**1,2,3**	• In-vitro and in-vivo micro imaging, • Experimental synchrotron	9 pers, 5,5 FTE, team located at ESRF/ID17	• National : LabEx PRIMES, CEA • International : European MRT coll.,	Labex PRIMES, INCa/DGOS, UGA, FRM, Région AuRA

(RSRM) EA 7442 Pr Sam Bayat **Univ. Grenoble-Alpes**		radiation therapy (SSRT, MRT), • Nanoparticle preclinical studies.		Australian Synchro., Daegu Synchro. (Korea)	
26-(PRIMES Grenoble) SyMMES UMR5819 Jean-Luc Ravanat **CEA, CNRS, UGA**	**2**	Approches thérapeutiques ou diagnostiques innovantes par de nouvelles molécules ou biomolécules ou agents génotoxiques	8 pers.; 2,2 FTE	LabEx PRIMES	Labex PRIMES, CEA segment radiobiology, INCA, UGA,ANSES, ANR
27-(PRIMES Grenoble) ProMD Serge Candéias **LCBM, UMR5249 CEA/CNRS/UGA**	**1**	• Radiobiology; • Immunology; • Low dose effects	4 pers., 2,8 FTE	• National : LabEx PRIMES, CEA • International : PHE (UK), UKER (D), SUT (Pol)	Labex PRIMES, CEA segment radiobiology, EDF
28-(PRIMES Grenoble) Physique pour les Applications Médicales Denis Dauvergne **LPSC, UMR 5821**, CNRS/IN2P3 UGA	**2,3,4**	Detectors for online control of radiotherapy	14 pers., 5,8 FTE	• National : LabEx PRIMES, France HADRON • International : ENLIGHT	LabEx PRIMES, IN2P3, INCa Physicancer CLARYS-UFT, UGA, CLARA
29-(PRIMES Lyon) FENNEC Olivier Tillement **ILM**, UMR 5306	**1,3**	Nanoparticles for radiosensitisation (from synthesis to clinical development)	7 pers., 3,5 FTE	• National : LabEx PRIMES, CHU de Grenoble, IGR, Institut Curie, LCAM Orsay • International : European network ITN Argent ; Mecanistic modelization, Queen's university Belfast; Harvard medical school; Stanford.	ILM Lyon, LabEx PRIMES, Research contracts
30-(Grenoble) Team COLL Institute for Advanced Biosciences Jen Luc Coll **INSERM U1209 CNRS UMR5309 Univ Grenoble-Alpes** Collaborators : L Sancey, X Le Guevel, B Busser	**1,3**	• High-Z/Gold nanoparticles • PDT activated by x-rays • Biodistribution's optimization and elimination process' elucidation Delivery of Boron for AB-NCT	3,5 Senior researchers; Doc : 1 Post-doc : 2 Small X irradiator (120kV)	• National : Grenoble RSRM/ILL/ESRF/CHU/ CERMAV ; Dijon C Goze • International : K Butterworth, Queen's Univ. Irlande ; I Porras, Univ de Granada Spain	• Institutional fundings (INSERM, CNRS) • Regional funding (NEPTUNE project)
31-(Lyon) Group of P Pittet **INL: Institut de nanotechnologie de Lyon, UMR5270** Univ. Lyon 1 - INSA de Lyon - ECL - CPE - CNRS	**4**	• **Instrumentation** for dosimetry and medical physics applications	4 FTE (2 professors, 1 assistant professor and 1 research engineer) Highly resolved point dosimeter (patented technology), Tomographic dosimetry (patent pending).	• National : Medical physics department of HCL, CREATIS, TIMC-IMAG, IPNL • International : Dosilab AG (Swiss) Univ. Uppsala (Sweden)	• Ppartnership with Dosilab AG, • ANR TECSAN DoRGaN (finished in 2016) • ANR NEWLOC (generic call 2018) • QASys project (physic cancer call 2018)
32-(Montpellier) Radiation Oncology Department - Montpellier Cancer Institute Pr David Azria	**2,3,4**	• Large-scale clinical translational studies on radiotoxicity biomarkers • Preclinical/clinical studies on new drug	6 linear accelerators 1 MRI accelerator *(ViewRay's MRIdian Linac system, ongoing implementation)*	• National : - UNICANCER group for translational research and development in radiation oncology (UNITRAD, Head D. Azria)	• Institutional funding: INCa, DGOS • Charities: League against cancer, ARC

		and radiotherapy combinations • Preclinical and clinical dosimetry		- Other national thematic networks (SFRO, GETUG, SFPM, …) - Regional Univ. Federation of Radiation Oncology (ICM and CHU of Nîmes) • <u>International :</u> - European FP-7 Requite consortium - International RadioGenomics consortium (RGC) - Univ. of Arizona, Mount Sinaï Hospital of New-York (US) - CHUV, Lausanne (Switzerland)	Foundation, FRM • Industry contracts (Roche, Genentech, Novartis, Varian) • Territorial authorities: Montpellier Metropole "Health Capital", Occitanie Region
33-(Montpellier) Experimental radiotherapy platform – Montpellier Cancer Research Institute Dr Muriel Brengues	**2,3**	• Radiobiology studies on cells and animal models (whole body mice and subcutaneous grafted tumours)	<u>4 FTE:</u> 1 senior researcher 2 engineers 1 physicist **X-ray irradiator** (SARRP Lite Xenx - XStrahl)	• <u>National :</u> - ITMO-Cancer PROUST network • <u>International :</u> - European FP-7 Requite consortium • <u>Industrial collaborations:</u> NovaGray, Varian	• SIRIC Montpellier Cancer • European Fund for regional development (FEDER) • ITMO Cancer • Others: GEFLUC, League against Cancer • Services provision to academics and private companies
34-(Montpellier) Micro-PET-CT imaging platform - Montpellier Cancer Research Institute Dr Jean-Pierre Pouget *(Emerging platform to be delivered by Q2 2018)*	**1**	• Imaging of small animals and plants	1 senior researcher 1 nuclear medicine physician 2 engineers 1 physicist **Micro-PET-CT imaging system**	• SIRIC Montpellier Cancer • BionanoMRI consortium (Montpellier University) • Others to come	• European Fund for regional development (FEDER) • ITMO Cancer • SIRIC Montpellier Cancer
35-Montpellier) Immunotargeting and radiobiology in oncology Dr André Pèlegrin	**2,3**	• Correlation studies between lymphocyte apoptosis and radio-induced late toxicities • Radiotherapy Biologics associations	3 senior researchers 1 PU-PH 1 MCU-PH 2 engineers 1 PhD student	• <u>National</u> SIRIC Montpellier Cancer CEA (Fontenay-aux-roses) • <u>International</u> University of Leicester	• SIRIC Montpellier Cancer • Labex MabImprove • Plan Cancer (Proust) • GEFLUC
36-(Montpellier)	**1,3**	• Radiobiology of	2 senior researchers	• <u>National</u> collaborations	• Nordic

Radiobiology and targeted radiotherapy Dr Jean-Pierre Pouget		targeted radiotherapy (ovarian and colorectal cancers) • Development of radiopharmaceuticals for theranostic approaches of ovarian cancer	1 MCU 2 MCU-PH 1 PH 1.5 post-doc 2 PhD student • Specific equipment SPECT-CT/PET-CT	ONIRIS Nantes CRCT Toulouse IBMM Montpellier INSERM Clermont Ferrand • <u>International</u> Queen Mary University London NRG Petten Netherlands NECSA South Africa ITU Karslruhe Germany	Nanovector, Oslo Norway • Physicancer • SIRIC Montpellier • Labex MabImprove/ Labex Chemisyst • Others: Bionov, EDF, LNCC, Canceropole (CGSO), GEFLUC
37-(Montpellier) Cancer bioinformatics and systems biology Pr Jacques Colinge	**1,4**	• Methods of large-scale dataset analysis and systems biology applied to cancer research • Computational modeling program for personalized cancer radiotherapy	1 senior researcher 1 post-doc	• SIRIC Montpellier Cancer	• ANR, INCa, ARC Foundation, SIRIC Montpellier Cancer
38-(Montpellier) Immunity and cancer Dr Nathalie Bonnefoy	**2,3**	• Relationships between cancer and immune cells within the microenvironment • Immune-based combined therapies (chemo-and radiotherapy) • In vitro and in vivo preclinical syngenic tumour models (melanoma, fibrosarcoma, colon, breast, pancreatic, cervix cancer)	2 senior researchers 1 PhD student 1 engineers • Mass Cytometry and Imaging Mass Cytometry	• <u>National</u> : - CRCT Toulouse - Labex IGO Nantes - CHU Montpellier • <u>Industrial collaborations:</u> - OREGABioteck - InnatePharma - Varian - Roche	• INCa, ITMO Cancer, ANR • Labex MabImprove, SIRIC Montpellier, Canceropole GSO • League against Cancer, GEFLUC, interregional clinical research program (API-K) • Industry contracts (Roche, Varian Medical systems)
39-(Nancy ICL) IMOPA, Team 1, Group radiobiology Leaders: Guillaume Vogin & Isabelle Behm-Ansmant Head: Bruno Charpentier **UMR 7365 CNRS-UL**	**1,2**	• RNA maturation and splicing • RNP biogenesis and functions • Epitranscriptomics • Molecular radiation response (healthy tissues and tumors) • Radiomics	<u>Team 1</u>: 3PU, 3MCF, 1 MCU-PH, 4 senior researchers, 7 technicians, 5 Doc. <u>Group RB</u>: 1 MCU-PH, 1 senior researcher, 1 PhD st, 1 M2 st <u>Platforms:</u> next generation high-throughput DNA-sequencing platform, Imaging Platform for Cell and Tissue analysis (IbiSA), Quality of Life and Cancer Platform, CIC-IT, Clinical Molecular PET Imaging Platform	• <u>National</u> Institut de Cancérologie de Lorraine CHRU Nancy IMOPA team 2, Nancy CRAN-UL, Nancy LORIA, UMR 7503 (*CNRS – INRIA – UL*) IGBMC Strasbourg U866 Inserm, Dijon • <u>International</u> Maastricht Univ. (NL) Liege Univ. (BE) Luxembourg (LU) Saarlandes Univ. (DE) Mainz Univ. (DE)	Ligue CCIR-GE Institut de Cancérologie de Lorraine PHRCi SFCE AFRETh EU (INTERREG)

			(NANCYCLOTEP)		
40-(Nantes) **Nuclear oncology & innovative radiopharmaceuticals** Michel Chérel **CRCINA: Nantes-Angers Cancer & Immunology Research Center, UMR INSERM 1232** ERL 6001 Nantes University. IRS UN 8 quai Moncousu F-44000 Nantes	**1,2,4**	Fundamental and translational research in: • Metabolic imaging (PET) • Tumor targeting with innovative α, β- et β+ radionuclides. • Radiobiology (relationship between ionizing radiation and immune response) • Quantitative imaging • Dosimetry • Radiophysic	16 FTE + 10 Doc. and 2 post-docs **Specific equipment**: Preclinical imaging platform : macroPET, macroSPECT, Mice and Rats : µTEP/Scan and µTEM/MR, Optical Animal facilities (in radioactive area) **Arronax** facilities :Time lapse microscopy, radiobiological platform	• **Regional: ICO-CHU**, CRCINA, CNRS (Subatech, Ceisam), Oniris and Tumor targeting & radiotherapies network of the CGO. • **National** : GDR CNRS ACCITH, Labex IRON & IGO • **International**: ITU, Germany ; Immunomedics, USA,	**recurrent resources** INSERM, CNRS, University of Nantes **research contract** INCa, ANR, Region Pays de La Loire, Ligue, CGO, **industrial grants** Atlab/Telix Pharma, Immunomedics, Roche, Amgen, Siemens and Kéosys
41-(Nice) **TIRO laboratory** Thierry Pourcher & Béatrice Cambien **UMRE-4320, Nice** cambien@unice.fr	**3**	**Translational research:** • radio-sensitization • radioprotection, with multidisciplinary approaches (preclinical expertise from in vitro to in vivo, nuclear imaging and spectrometric platform).	14 FTE: 4 senior researchers (INSERM, CNRS, CEA) 1 faculty researcher, 2 MD, 4 engineers /tech., 4 Doc., 1 Post-doc. Specific equipment micro SPECT/CT imaging, nuclear imaging and radioisisotope handling, animal care facility, animal models, cellular biology, spectrometric platform. Access to medical irradiators: EBRT (Cyberknife, protontherapy: Medicyc 65 Mev, ProteusOne 235 MeV) in the Centre Antoine Lacassagne.	• National IRSN; IRBA; CEA Saclay & Cadarache ; CLCC Baclesse, Caen ; INRIA & IPMC at Sophia Antipolis, Inserm (Nice). • International Colombia, Madrid, USA. • Industrial : Theraguix, Lyon.	- CEA/PTTox, DRF impulsion - ANR PRIODAC - Cancéropôle Sud-Est - Plan Cancer ….
(Paris, Ile de France)					
Institut Curie					
42-Institut Curie Department of medical physics; Ludovic De Marzi **Institut Curie** Paris – St. Cloud – Orsay	**1,4**	• Medical Physics and Engineering: measurements, models, calculations, procedures	In total 2 FTE shared among all medical physicists and engineers + in general 1-2 docs and/or post docs	• National : CNRS, CEA, • International : IAEA • Industrial : Varian, IBA, Siemens, …	Institut Curie foundation, Migac, PhysiCancer, industrial contracts, European grants
43-Institut Curie Department of radiation oncology; Pr Gilles Créhange **Institut Curie** Paris – St. Cloud – Orsay	**1,4**	• Modulation of radiation therapy parameters; • Combination therapy with systemic agents.	In total 2.45 FTE shared among all senior radiation oncologists: 3 as major occupation; 4 as minor occupation.	• National : UNICANCER; GORTEC; GETUG • International : EORTC	Institut Curie foundation
44-Institut Curie Marie Dutreix	**1,2,3**	• Preclinical models, normal and tumor	5 teams	• National. F. Lemoine, CHU	Institut Curie foundation,

Centre de Recherche, Orsay		tissue differential index • FLASH irradiation (high dose rate irradiation) • Protons • Development of new radiosensitising molecules • Preclinical studies on combined treatments • Biomarkers	7 senior researchers, 3 post-doc, 4 doc, 8 engineers, technicians	Salpétrière, Paris ; E. Charafe, IPC,Marseille NANOTHERAD network • <u>European:</u> ITN-RADIATE R. Michel, University, Oxford, UK; P. Lambin et al., Maastricht, NL ; Cordes, Dresden, D; V. Gregoire, P. Sonveaux, Brussel ; V. Jendrossek, Essen, D. • <u>USA</u>: S. Bhaskara, Huntsman Cancer Center,Utah,USA	INSERM, CNRS, Institut Curie centre de recherche, Univ. Paris-Saclay, INCA, Onxeo, EU
DNA Repair, radiations and innovative cancer therapies, **Marie Dutreix,** **UMR3347/U1021**	**2,3**	• FLASH radiotherapy • DNA repair inhibitors	3 researchers 1 post-doc 2 doc 3 technician Electron-FLASH Linac SIT Proton IBA SARPP Xrad500	International **EMPIR** **INSPIR** **ITN-Radiate** **ANR-Astrolabe** Industrial **VARiAN** **SIT** **ONXEO**	INSERM CNRS University Paris-Saclay Institut Curie
New Approaches in Radiotherapy, Yolanda Prezado, **UMR3347/U1021** **IMNC : Imagerie et Modélisation pour la Neurobiologie et la Cancérologie** CNRS, Univ. Paris VII et Paris XI	**2, 3**	• Medical Physics (Experimental dosimetry, Monte Carlo simulations) • Radiobiology (in vivo studies) Development of new strategies in RT using the **spatial fractionation of the dose**	2 seniors, 2 post-doc fellows, 1 PhD student.	• <u>National</u> : – ICPO (Institut Curie) – RadExp (Institut Curie) – IR4M (Paris Sud) – Human path and animal models (Instit. Pasteur) – Institut Neurosciences Paris Saclay – LOA • <u>International</u> : – ALBA synchrotron – Centro nacional de Microelectronica – Univ. de Santiago de Compostela – Hospital Clinico de Santiago (Spain) – HIMAC (Japan) • Univ. medizin Berlin	Contracts (see collaborations) • CNRS ERC
45-Institut Curie RadeXp (Experimental Radiotherapy Platform), Translationnal Research Department Frédéric Pouzoulet **Centre de Recherche, Orsay**	**1,2,3,4**	Translationnal research Medical physics Radiotherapy Preclinical models	<u>Staff permanent position:</u> 1 radiation biologist 1 Medical physicist 3 engineers <u>Specific equipment</u>: - XRAD320(X-rays) - SARRP (Xrays + imaging + TPS) - CIXD (double x-rays) - GSRD1 (^{137}Cs) - KINETRON (HDR Linac) - Medical proton beamline (ICPO)	• <u>National:</u> RESPLANDIR network Y Prezado (IMNC/IN2P3) C Laurent (ToxEMAC ABTE, univ. Caen) Khe Hoang-Xuan (ICM/APHP) • <u>International :</u> F Lebrin (Leiden univ. medical center, NL) Han Tun (Mayo Clinic, Jacksonville, FL, USA)	<u>Recurrent resources</u> – Invoicing – institutional <u>Research contract</u> – INCA (PRT-K, canceropole IDF2016) – ITMO Cancer – Equipement (2015regional funding) <u>And 4 Industrial contracts</u>
AP-HP					
46-GRRAP Member: Recombinaison DNA repair and cancer: "de la	**3**	• DNA repair • Anticancer drugs combination	<u>6,5 FTE:</u> 3 Seniors researchers 1 Professor	Pharma Industry Paris VI university	Institut Curie CNRS INCa

molécule au patient" Marie Dutreix **Inserm U1021 / CNRS UMR3347**, Orsay Assoc. GRRAP member: Laurent Quéro		• Translational research	2 Doc 1 Post Doc		
47-GRRAP Member: **Recherches en Hémato-Immunologie** Edgardo Carosella, **CEA/SRHI**, Assoc. GRRAP member: Pr Ch. Hennequin Univ. & AP-HP St Louis	**2,3**	• Tumors immunology • HLA-G and immune checkpoints	6,5 FTE: 5 Seniors researchers 3 Prof. and Assoc. Prof.	IUH Paris VII HLA-G working group (international)	CEA Univ. Paris 7 Pharma Industry
48-GRRAP Member: **IMRB** Alexandre de La Taille **INSERM 955 EQ 07** Univ. Paris Est Créteil Assoc. GRRAP member: Pr Yazid Belkacemi Department of radiation oncology and Breast Center CHU AP-HP H. Mondor	**2,3**	**Microenvironment and biopathologic markers:** - Predictive factors for efficacy of chemo-radiotherapy in triple negative breast cancers; - Biological markers of severe RT toxicity. Proust project	6 FTE: 4 Seniors researchers 3 Professors 1 Assistant Professor	• National : Pathology lab of CRLCC Clermont-Fd INSERM Montpellier INSERM Lyon Univ. Paris Est Créteil	INSERM, INCa grant (Proust project)
49-GRRAP Member: **Cancer biology and therapeutics** Annette Larsen **Centre de Recherche Saint-Antoine** **UMR_S 938 – INSERM** Univ. P et Marie Curie Assoc. GRRAP member: Pr Florence Huguet Depart. Radiation Oncol, CHU AP-HP Tenon	**2,3**	Mechanisms driving of tumor progression and plasticity to identify novel targets and biomarkers of response to novel agents and combinations	15 FTE: 3 Seniors researchers 1 Professors 10 University-associated clinicians 6 Doc. 3 Post-doc	• National : UPMC • International : - EU network of excellence - EORTC-PAMM - National University of Singapore - French-Brazilian univ. research network (CAPES-COFECUB) • Industrial pharma: - Europe, USA, China	Univ. Paris VI INSERM Grants
50-GRRAP Member: **Personalized medicine, pharmacogenomics, therapeutic optimisation** Pr Pierre Laurent-Puig **INSERM UMR-S 1147** : Univ. Paris Descartes Assoc. GRRAP member: Pr Florence Huguet Depart. Radiation Oncol, CHU AP-HP Tenon	**3**	• **Pharmacogenetic** -metabolism and drugs transporters -intra-tumoral metabolism of pro-drugs - nucl. gene transfer • **Molecular mechanisms of cytotoxicity** • **Tu. pharmacogenomics** prediction / monitoring of response and prognosis	14 FTE: 2 Seniors researchers 1 Professors 10 University-associated clinicians 5 Doc. 4 Post-doc	• National : CICB Paris CARPEM Paris V Paris VI UPMC	Univ. Paris V INSERM Grants Emergence grant (RADON project)
51-GRRAP Member **Department of radiation oncology and Breast Center** Pr Yazid Belkacemi	**1**	Target volumes imaging by PET-MRI	2.5 FTE: 1 Assistant professor 2 Senior researchers	• Local: - Dept. Nuclear Medicine E Itti - Dept. Medical Imaging A Luciani	Univ. Paris Est Créteil INSERM

CHU AP-HP H. Mondor **INSERM 955 EQ 07** Univ. Paris Est Créteil					
52-GRRAP Member **Radiotherapy Department** Pr Philippe Maingon **CHU AP-HP Pitié-Salpêtrière**	**1,4**	• PET-MRI in whole-body oncology imaging • MRI evaluation in the Linac-MR concept.	2.5 FTE senior researchers	• Local: Lab. of parametric imaging (LIP) UMR 7623 CNRS/Univ Paris VI	CNRS
53-TEAM 02 "In Vivo Imaging Research" Bertrand Tavitian Laure Fournier Charles-André Cuenod Olivier Clemend Philippe Halimi Philippe Giraud **Inserm UMR-970 Paris Cardiovascular Research Center**	**1**	Target volume definition, MRI, PET-CT	Team: 16 FTE 5 PU-PH 1 PH 1 Post-Doc 8 Doc 4 engineers Equipment: Small animal PET-CT Small animal 4.7T MRI	• National : Inst. Langevin, Inst. Cochin, Odontology school, Biomedical Faculty, INRA Toulouse, INSERM 1146, MSC lab (lab. matières et systèmes complexes, UMR 7057 CNRS, Univ. Paris-Diderot.); lab. biosurgical sciences (INSERM U633) • International : TRANSACT consortium (EU); Argentina (D Craeim, Favarolo Univ., ECOS grant). Univ. Federal do Rio Grande do Norte in Natal, Brazil (Pr. I. Araujo Filho).	National: BIMUPET, Plan Cancer; HECAM; CARPEM; SIRIC InCA; PETRUS; France Life Imaging; RIHDO; FUI; RADIOMICS (FRM) European: ENCITE, UE FP7; Industrial contracts.
54- Service de radiothérapie HEGP Dr Jean-Emmanuel Bibault Pr Philippe Giraud Pr Catherine Durdux Pr Anita Burgun **Hôpital Européen Georges Pompidou – AP-HP**	**1,4**	• Intensity Modulated Radiation Therapy, • Stereotactical Body Radiation Therapy, • Gating	9 physicians including three full time Professors	INSERM UMRS 1138 Team 22 – Centre de recherche des Cordeliers – Anita Burgun Radiomics, Machine Learning, Big Data	BPI : Invest Public Bank
55-(Paris AP-HP) Laboratory of Integrative Cancer Immunology, Jérôme Galon **INSERM UMRS1138**, (INSERM, HEGP, AP-HP) Paris,	**3**	• Immunology, tumor-immunology, immune response to cancer, immunotherapy, • impact of radiotherapy on immune microenvironment, defined the concept of immune contexture, and the Immunoscore.	2.5 FTE senior researchers ; 2 Doc; 6 Post-Doc	• Local: Radiotherapy department, IGR, Villejuif, immune response after radiotherapy ± immunotherapy. • Multiple International collaborations PI of the Worldwide Immunoscore consortium	Recurrent resources (INSERM laboratory, LabEx immuno-oncology) Co-funding from EU (ERAnet Transcan and APERIM);
56-(Paris) **LIMP Laboratoire d'Imagerie Moléculaire Positonique (**UMS28 phénotypage du petit animal) Aurélie Prignon Sorbonne Université, Paris	**1,4**	• Preclinical tumor models • Evaluation of novel PET probes using radionuclides as 18F, 68Ga, (177Lu in preparation) • In vivo and ex vivo dosimetry	1 engineer 1 doc Equipment: Small animal PET/CT and Animal facilities (in radioactive area) Specific equipment for radiochemistry (Fluor-18 and gallium-68) and quality control Gamma counters	SIRIC CURAMUS (Sorbonne Université) APHP Nuclear medicine Tenon hospital France Life Imaging ICMUB UMR CNRS 6302, Dijon •	Inserm and Sorbonne University, research contract: Edinburg Molecular Imaging,
57-(Villejuif) **Molecular radiotherapy**	**1,2,3**	• Preclinical models, normal and tumor	2 senior researchers, 6 doc., 4 post-docs	• Nationale: - Ecole central Paris,	INSERM, FRM, Ligue

Pr Eric Deutsch **INSERM 1030** Gustave Roussy (IGR)		tissue differential index, Lung and head and neck models • Radiomics and functional imaging • Biomarkers • Immunotherapies combined to radiotherapy		- LOA école polytech., - Dosisoft, IRSN, CEA, - A Boissonnas UPMC-INSERM, - P Sansonetti Institut Pasteur, - I Buvat, SHFJ CEA Orsay. - J Galon U1138 (immunology)	contre le cancer, ARC, EDF, INCA. NanoH, Nanobiotix, + pharma
58-(Villejuif) **Cell death and aging** Jean Luc Perfettini **INSERM 1030**, IGR	**2,3**	Cell death, immune response	2 senior researchers, 6 doc., 3 post-docs	CEA, IRSN	INSERM, Labex Lermit, INCA, ARC,EDF
59-(Villejuif) **Espèces Réactives de l'Oxygène et Radio carcinogenèse** Corinne Dupuy, **UMR 8200**, IGR	**2**	• Radiation induced fibrosis, Free radicals, • Carcinogenesis and X-ray induced mutagenesis	1 senior researchers, 2 doc., 2 post-docs	INSERM U1030	CNRS, INCA, EDF
60-(Villejuif) **Epidémiologie des radiations,** Florent de Vathaire, **U1018**, IGR	**2,4**	Dose modelling and cancer risk	2 senior researchers, 2 doc., 3 post-docs		INSERM, INCA, H2020,
61-(Villejuif) **Dosimetry Platform**, Ibrahima Diallo, **U1018-CESP**, IGR	**4**	• Dosimetry for late effects studies • Out-of-field dose measurements and modelling • Organ modelling • RT patient phantom development • QA of late effects dosimetric studies	**Constitution** • 2 Principal investigators. • 1 ETP postdoc • 1 ETP MD • 1 Master II student • 1 Master I student **Specific equipment** • Library of whole body of phantoms for paediatric and adult RT patients. • Software for whole body dose calculations. • Radiophotolumines cence (RPL) dosimetry system. • Specially dedicated water tank for out-of-field dosimetry.	**National** Gustave Roussy, Villejuif Curie Institute, Paris Dosisoft, Cachan Equal-Estro, Villejuif Centre G.F. Leclerc, Dijon Centre L. Bérard, Lyon ICL, Nancy **International** Univ. of Birmingham, UK NKI, The Netherlands ISGLOBAL, Spain MD Anderson Cancer Center, USA	INSERM Plan Cancer Inca Dutch Cancer Society European Commission
62-(Villejuif) **Medical Physics Department,** IGR Dimitrios Lefkopoulos	**4**	Medical Physics and Engineering : Radiation metrology, Adaptive planning and dosimetry, target deformation Dose modelling, Quality assurance, transit dosimetry. Quantification and patient dosimetry in	**Constitution** • 1.5 FTE Medical Physicists • 1 ETP QA technologists • 2 Master/year • 1-2 docs and/or post docs **Specific equipment** • High level technological	**National** INSERM, Villejuif Curie Institute, Paris Dosisoft, Cachan Equal-Estro, Villejuif Raysearch ELEKTA **International** IAEA	INSERM Plan Cancer Inca European Commission

		medical imaging.	platform • TPS VOLO Tomotherapy • TPS PRECISION CyBerknife • TPS Raystation (VMAT) • 10 Linacs • Brachy dedicated TPS. • PLANETDose (Targeted Radionuclide Therapy)		
63-(Fontenay-aux-roses, CEA) **Institut de radiobiologie cellulaire et moléculaire iRCM**, Paul-Henri Romeo 14 teams: **LRIG**: Pablo Radicella **LION**: Karine Dubrana **LTR**: Stéphane Marcand **LRGM**: Eric Coïc **LRP**: François Boussin **LREV**: Pascale Bertrand **LGAG**: Isabelle Allemand **LDG**: Gabriel Livera **LSHL**: Françoise Pflumio **LRTS**: Paul-Henri Romeo **LGRK (Evry)**: Michèle Martin **LCE**: Sylvie Chevillard **LRT**: Jaime Angulo **LARIA (Caen)**: Yannick Saintigny **CEA**, Direction de la Recherche Fondamentale	**1,2,3**	**Radiobiology** **Radiotherapy** **Individual sensitivity to irradiation**	86 Full time researchers 35Technicians 29 Doc 20 Post Doc **Specific Equipment** : iRCM Platform equipments • SARRP (small animals radiation research platform) XRray generator with CBTC (cone beam computed tomography) • GSRD 1: source of Cesium 137 • Irradiateur X Rec-Hadron et plateforme d'irradiation par ions accélérés du GANIL (CIRIL)	• National collaborations through several ANR and Inca programs • International collaborations Japan, EU, USA • Industrial collaborations AREVA, EDF	2017 Recurrent : Logistic : 1,8 M€ Contracts : 3 M€ Plateforms : 0,75 M€
64-(Fontenay-aux-roses, CEA, suite) **PROCyTox,** Michelle Ricoul **Scientific director :** Laure Sabatier **CEA/Paris-Saclay** **Fontenay-aux-Roses**	**2**	• New approaches in molecular cytogenetics including telomere length measurements. • Biological dosimetry with cytogenetics biomarkers. • International intercomparison exercices for dose estimate.	4,2 FTE: 1,2 researchers, 2 technicians, 1 Post-doc Specific equipment cellular and molecular cytogenetics, image analysis with Metasystems set-up. PROCyTox acts as a platform for characterization of genotoxic damages.	• National -Neurospin, Saclay Joliot/SPI/ LERI Saclay -CEA/BIG/Grenoble -IGR Radiotherapy -INSERM Nantes • International - RENEB Network (17 labs all around Europe) - SUBI (South Ural)	-CEA (3,2 FTE) -EC-Eurotalents (1 Post-doc) - NRBC-E -EC- EJP-CONCERT (Radiation Protection) -External resources coming from platform activities.
(Fontenay-aux-rose) IRSN					
65-Laboratoire de Dosimétrie des Rayonnements Ionisants (LDRI) Carmen Villagrassa, PhD, **IRSN, Fontenay**	**2,3,4**	**External dosimetry:** micro/nano-dosimetry, dosimetry for medical applications	5.5 FTE researchers + 3 doc. students. Equipment: Medical Linear accelerator, Metrological photon and beta calibration laboratory, ESR spectrometers. OSL/TLD	EURADOS members, Geant4-DNA/Geant4 collaboration, European project MEDIRAD, EURAMED, EURAMET	IRSN recurrent resources; EU

			dosimetry capabilities; Calculation cluster		
66-Laboratoire of Radiobiologie des expositions médicales (LRMed) Fabien Milliat, PhD **IRSN, Fontenay**	**1,2,3**	**Normal tissue response** to cancer treatment, therapeutic approaches to treat severe radiation injury	8 FTE researchers + 4 FTE technical support+ 4 Doc. students Equipment: Small Animal radiation Research Platform (SARRP, X-Strahl)	INSERM U1030 Gustave Roussy, Centre de Recherche sur l'inflammation Bichat, CDR Saint Antoine, INSERM UMR 1229 Nantes, INSERM U1180 Faculté de Pharmacie	IRSN recurrent resources; INCa, ANR
67-Laboratoire d'évaluation de la dose interne (LEDI) David Broggio, PhD **IRSN, Fontenay**	**3**	**Internal dosimetry**, medical physics, computational human phantoms development	2.5 FTE researchers + 2 Doc. students Equipment: TPS for external and internal dosimetry, calculation clusters	OpenDose, Claudius Regaud Hospital (Toulouse), EURADDOS members, EU-CONCERT.	IRSN recurrent resources; EU
68-Unité d'expertise medicale Cécile Etard **IRSN, Fontenay**	**4**	Medical Physics, Radiation protection in medical field, lessons learned for incidents / accidents in radiotherapy	5 equivalent full time medical physicists + 1 equivalent full time radiation protection engineer	National collaboration with UNICANCER (training) International Member of advisory board of EUCLID EU Project	IRSN recurrent resources; EU
69-Laboratoire de micro-irradiation, de métrologie et de dosimétrie neutrons (LMDN) Jean Marc Such, PhD **IRSN, Cadarache**	**2,3,4**	**Micro-irradiation**	1.4 FTE researchers + 0.6 FTE technician Equipment: Micro-beam for heavy particles (MIRCOM)	CENBG (Bordeaux)	IRSN recurrent resources;
70-(Saclay / CEA) 3 teams and 1 experimental plateform: **LM2S** : modelling and simulation systems laboratory, Dephine Lazaro **LMD** : dose metrology laboratory, Valentin Blideanu **LSOC** : Oxydative Stress & Cancer laboratory Carl Mann **DOSEO Platform**, Bénédicte Poumarède http://www.plateformedoseo.com/en/ **CEA,** Direction de la recherche technologique	**2,4**	**Dose modelling** Monte Carlo simulations (PENELOPE, MCNP, EGSnrc, GATE) for radiotherapy, associated imaging (kV- and MV-imaging, radiology), out-of-field dose,QA using EPIDs, TPS quality control. **Statistical methods and nonparametric approaches** radiotherapy, PET, radiomics **Metrology for ionizing radiation** (LNHB primary laboratory "Laboratoire National Henri Becquerel") **Instrumentation :** diamond technology and OSL dosimeters primary and secondary metrology, expertise in commercial use of	22 FTE researchers 1 doc; 3 post doc **Specific Equipment** : DOSEO Platform equipments • 1 Elekta LINAC "Versa HD" • 1 Varian Linac "Truebeam" • 1 GE CTscan "DT 750 HD Discovery" • Brachytherapy projector with ^{60}Co and ^{192}Ir • 1 ^{60}Co irradiator	• National : several ANR and Physicancer projects (clinical centers (IGR, Curie Institute, CLCC, …), CEA/SHFJ, CEA/IRCM • International BIPM, European metrological centers • Industrial : AQUILAB, RTC, DOSISFOT, ELEKTA	CEA recurrent : 1,2 M€ Contracts : 1,4 M€

		dosimeters. **Experimental measurements**: dose, in vivo dosimetry.			
71-(Palaiseau, X) **Laboratoire d'Optique Appliquée (LOA), team SAPHIR,** Alessandro Flacco, **CNRS-7639, ENSTA-PARISTECH, Ecole Polytechnique**	**2,3,4**	• Protons acceleration by ultra-intense laser plasma technology, • Radiobiology of pulsed protons: **short pulse (ns)** & ultra-high dose rates (**10^8Gy/s**) *in vitro* (*in vivo* coming)	4 FTE: 2 senior researchers (1 physicist, 1 radiobiologist), 1 Doc 1 engineer SAHIR Laser facility: pulsed protons (electrons and X ray coming) Cell culture lab	• National : U1030-IGR (E.Deutsch), ISMO (S.Lacombe), ICPO, CEA (IRAMIS) IRS Nanotherad Network Amplitude Technologies • International : Helmholtz-Zentrum Dresden-Rossendorf (D) Weizmann Institute (Is) CHUV (CH)	CNRS, ENSTA, Ecole Polytechnique, IRS Nanotherad, EDF
72-(Orsay) **Nom : PRAZERES Rui** **Projet : ESCULAP** **Labo. : LCP/CLIO** **Bât.201P2** **Université Paris-Sud** **91405 Orsay cedex**	**2, 4**	• Production de pulses d'électrons de haute énergie (>200MeV) et durée femtoseconde	½ senior researcher	• CNRS & Université Paris Saclay : LAL, LPGP, LCP	• CNRS
73-(Brétigny s/ Orge) **IRBA** **Pôle NRBC - DEBR/RAD (Dépt. Effets biologiques des rayonnements, unité RADiologie)** Dr Michel DROUET **DAR/SCR (Division Appui à la Recherche-Sce Compétent radioprotec.)** Dr Patrick Martigne **IRBA (Institut de Recherche Biomédicale des Armées)**	**3**	• Diagnostic/Pronostic des irradiations (Dosi. bio. cytogénétique et biomarqueurs), • Prophylaxie des RI (radioprotecteurs et radiomitigateurs), • Thérapeutique: - irradiation globale (cytokine et facteurs de croissance) - localisée (R&D thérapie cellulaire et génique)	11,5 FTE: 8 chercheurs (dont 3 militaires), 1 radiothérapeute (IGR/IRBA) 3 techniciens. Equipement : irradiateur ^{60}Co (IRDI 4000); X auto-protégé (SARRP, Culture cellulaire, Microscopes motorisé, comptage automatisé (MetaSystems, Biodosimetry), Modèles animaux, Plateformes mutualisées de BM, histologie, RMN liquide/HRMAS, microscopie photon./électro. etc.	• National : Institut Curie (plateforme RadeXp), IGR, CEA, IRSN, Inserm Lyon (N. Foray) etc., • International : Bundeswehr, réseau OTAN dont l'AFRRI (USA)… • Industrial : (start-up Acubens, MEDESISPharma, …)	DGA (programme Biomedef spécifique au Service de Santé des Armées), DGCIS (projets RAPID ou ASTRID), EDF, voire projets ANR ou européens...
74-(Rennes) **Laboratory of Signal and Image Processing: LTSI**, **IMPACT team,** Pr Renaud De Crevoisier **UMR INSERM 1099, Rennes University.** Campus de Beaulieu, Université de Rennes 1 F-35042 Rennes	**1,4**	• Image processing • Predictive modeling • Adaptative radiotherapy • Functional imaging	7 FTE senior researchers 10 post-docs and PhD students	• National: LaMCoS CNRS UMR 5259 Lyon, CIS-ENSMSE Ecole des Mines Saint Etienne, TIMC-IMAG CNRS UMR 5525 Grenoble, LATIM Inserm U1101 - Institut Telecom Brest, LabTau INSERM U1032, Lyon, UTC CNRS UMR 7338 Compiègne). • International: LIST-CRIBs, SouthEast University, Nanjing, China; CSIRO, Australia; Ryerson University, Toronto, Canada; UNET, Tachira, Venezuela; UNC-Universidad Nacionale de Colombia, Bogota	recurrent resources: INSERM research contract: INCa ANR- Labex CominLabs & CAMI IResP CGO Industrial partners: ANSYS (Lyon), AQUILAB (Lille), EDAP (Vaulx-en-Velin), ELEKTA (Paris), KEOSYS (Nantes), THERENVA

					(Rennes), PHILIPS (Aachen, Best), SIEMENS (Forchheim, Paris), GE (Horten, Norway).
75-(Strasbourg) Département de Radiobiologie, Hadronthérapie et Imagerie Moléculaire: DRHIM Patrice Laquerière **IPHC: Institut Pluridisciplinaire Hubert Curien,** CNRS, Univ. de Strasbourg. **76-Groupe de radiobiologie,** Pr. Georges Noël **CRLCC Paul Strauss, Université de Strasbourg**	**2,3** **2,3**	• Chimio-radiothérapie, • Fortes doses • Radiobiologie des protons et ions	5 FTE: 3 senior researchers: (1PUPH-HDR,1MCU-HDR,1CR), 2 Doc; 1 Post-doc. Equipment • Plateforme de radiobiologie expérimentale in vitro et in vivo proton (25 MeV) • Biobeam 8000 (^{137}Cs), • LINAC, • dosimétrie associée.	• National : laboratoires CNRS-IN2P3, CRLCC Dijon, CRLCC Nancy, CHU Bordeaux. • International : Equipes radiobiologie Namur et Liège (Be)	CNRS, INCa, Région grand-Est, Eurométropole Strasbourg, CRLCC Paul Strauss, Ligue régionale contre le cancer, Alsace contre le cancer, Département du Bas-Rhin, EDF.
77-(Toulouse) Imagerie et balistique en radiothérapie Pr Anne Laprie **Part of the DEVIN TEAM** (Development and Evaluation of Imaging BIomarkers) **Unité INSERM UMR 1214 ToNIC** (Toulouse Neuro Imaging Center) Toulouse III University and IUCT-Oncopole	**1,4**	• Pediatric and adult brain tumors • Head and neck tumors • Metabolic and functional imaging, particularly MRI, MRspectroscopy. • Radiomics • Prospective translational clinical trials • In Silico photons and protons dosimetric studies	3 FTE senior researchers 1 Doc 1 post-doc	• Past International collaborations : FP7 Marie Curie SUMMER (Aquilab, Delft, Roma, Vienna, Friburg) • Running national collaborations : - PAIR pediatric - PEPPI Study -SPECTRO GLIO Trial • Running International collaboration: RETRACE Study (Maastricht, Dresden, Toulouse)	Ligue contre le Cancer SFCE INCa Fondation pour la Recherche Médicale Industrial contract : Accuray
78-(Toulouse) Team 11 "Glioblastoma radioresistance :from signalling to clinical trial" INSERM Team Pr Elizabeth Cohen-Jonathan Moyal **CRCT, UMR1037**	**1,3**	• Radioresistance mechanisms deciphering • Glioblastoma stem cells radioresistance mechanisms, radiation-induced plasticity • Invasion and hypoxia pathways • Study of glioblastoma heterogeneity • In vitro and in vivo	Senior researcher ETP : 4 ETP Tech and engineers : 2.5 ETP Post-doc : 1.5 ETP PhD students :3 Specific equipment : Currently Gamacell Nordion that will be replaced in march 2018 by an animal irradiator for precise irradiation as well as in vito irradiation	• Coordination of the of the national MOGLIMAGING project (National HTE program) • Coordination of the clinical trial and biologic project STEMRI (Radiomics and GBM stem cells) • Coordination of the study of the radioresistance signature of the patients included in the national POLA data	• Plan cancer/ITMO/ Aviesan (HTE program) • INSERM (Gros équipement) • ARC • Ligue contre le Cancer • RITC / Region • PHUC

		target validation (orthotopioc xenografts) • Study of the radionsensitizing effect of targeted drugs against the previously studied targets and radiotherapy in vitro and in vivo. • Clinical trial design coming from the lab results • Validation of the targets on national data base		base • WP radioresistance of the RAD 18 program (national program granted by ARC) • WP1 of the CAPTOR PHUC program (FGFR and radioresistance) • Proteomic study of the clinical trial (coordination E Moyal) associating cilengitide and radiochemothera in stade III NSCLC (with Meck KGa)	
79-(Toulouse) **CRCT UMR 1037 INSERM** Université Paul Sabatier Centre de Recherches en Cancérologie de Toulouse **Équipe 15** **Responsable: M. Bardiès**	**1,2,3,4**	Modélisation Monte-Carlo : dosimétrie en radiothérapie interne et externe	Statutaires: 6 (3,2 ETP) Post Docs : 2 (2 ETP) Docs : 4 (4 ETP) ITA : 1 (1 ETP)	OpenGate (Steering Committee) opengatecollaboration.org Geant4-DNA (Core Development) OpenDose (opendose.org) EURADOS <u>Enseignement :</u> EANM (ESMIT WG3) EFOMP (ESMPE Board) SFPM (CE/CA)	EuraMET MEDIRAD CRP IAEA SCK-CEN Keosys
Networks					
Local Networks					
Région Normandie **ARCHADE :** **Advanced Resource Centre for HADrontherapy in Europe**		• Hadrontherapy research • Development of hadrontherapy technology • Facility for research	8 teams mainly included in this table	Federates about 8 teams from Caen University and associated institutions	Teams own funding plus Région Normandie (CPIER)
Research Network : Le GRRAP	**2,3,4**	• **G**roupe de **R**echerche en **R**adiothérapie de l'**A**ssistance **P**ublique - Hôpitaux de Paris (AP-HP)	**Domain of Translational Research:** <u>Prediction of efficacy of radiotherapy</u> and combined radiotherapy to new drugs <u>Prediction and prognostic of radiation-induced damage</u> in healthy tissues		
MED-OSIRIS **Pierre Saintigny, Christophe Ketterlé** **CLB, Institut Curie, Institut Bergonié, CHU de Bordeaux**	**5**	Oncology Data modeling (Interoperability) of health data in Oncology	9 EFT	Inter-SIRIC: AP-HP – HEGP (SIRIC CARPEM); IPC; IGR (SIRIC SOCRATE 2.0); CHU Nantes – CHU Angers - ICO (SIRIC ILIAD); AP-HP- Sorbonne Université (SIRIC CURAMUS) ; ICM (SIRIC Montpellier). UNITRAD RadioTransNet	INCa
National Networks					
RESPLANDIR :	**2,3,4**	• <u>Translational</u>	<u>Specific equipment (in</u>	**RESPLANDIR** is a National	Each team has

Réseau de plateformes de radiothérapie préclinique (GDR-Mi2B) (Mickael Beuve, David Brasse, Céline Mirjolet, Frédéric Pouzoulet, Marc Rousseau)		research • Medical Physics • Preclinical radiation therapy	evolution): - 3 Xrad320 - XRad 225Cx - 4 SARRP - 2 linac - XenX - neutrons generator, 2.5<E<14 MeV - neutrons generator, E<2.5 MeV - proton generator, E< 3.5 MeV - alpha generator 17MeV<E<70 MeV - deuton generator - proton generator E<25 MeV - 12C, Ions lourds, E< 95 MeV/n - 1 CIXD - micro-faisceau alpha/proton E< 3MeV Access to proton medical beam line Constitution : ≈ 36 ETP - Radiobiologists - Radio physicists - Technicians - Students	Network of -PAVIRMA (Clermont, In2P3, UCA) : G Montarou -Plateforme d'Imagerie et de Radiothérapie préclinique, Unité RT (Dijon, CGFL) : C Mirjolet - RadexP (Curie) : F Pouzoulet - Lyon University : G Alphonse - IRSN, Paris : M Dos Santos - CEA, Paris : V Ménard - IRBA, Paris : P Martigne - GENESIS (LPSC,Grenoble, IN2P3-Université) : Maud Baylac - AIFIRA (CENBG, Bordeaux, IN2P3-Université) : Philippe Barberet - ARRONAX (GIE ARRONAX, Subatech, IN2P3-Université): Vincent Metivier, Charbel Koumeir - PRECy (IPHC, Strasbourg, IN2P3-Université): Marc Rousseau - IRABAT/IRASME (LARIA, Caen, CEA) : Yannick Saintigny - Biobeam 8000 (Centre Paul Strauss, Strasbourg) : Hélène Burckel - IRCM, Strasbourg, Muriel Brengues	its own funding to perform their research activity but currently, RESPLANDIR has not specific funding
Ex-France HADRON		**4 WP** Hadrontherapy research: - Clinical research - Data for dose modelling - Radiobiology - Instrumentation	26 teams mainly included in this table	Federates 26 teams from all over France International collaborations: ENLIGHT	Teams own funding plus network funding by ANR (2013-2017)
Cancéropôles		- reinforce the mobilization of research teams - boost clinical research - enable the emergence of innovative research projects - anchor within the European collaborative dynamic - contribute to position France as an	7 Cancéropôles : - Nord Ouest - Ile de France - Grand Ouest - Est : RIBIOTHIM-Onco - Grand Sud Ouest - CLARA - PACA	Federate research institutions, university hospitals, cancer centers, pharmaceutical and biotech companies and are supported by French Cancer Institute (INCa) and many local governments	INCa Local & regional authorities Fundations & associations, pharmas, …etc.

		international reference in cancer research			
UNITRAD (Unicancer radiation oncology group) board: • Sofia RIVERA, MD PhD, radiation oncologist (Gustave Roussy - Villejuif) • Catherine DEJEAN, PhD, Medical physicist (CAL – Nice) • Stéphane SUPIOT, MD PhD, radiation oncologist (ICO – Nantes) A. LAMRANI-GHAOUTI, PhD, Clinical program Lead (Unicancer R&D)	**1,2,3,4, 5**	• Artificial Intelligence (AI) : Radiomic/Imaging • Radiobiology : Immunoradiotherapy /Radiosensitivity/ Radiopotentialisation • New technologies and physics • innovation • Radiotherapy Quality Assurance • Safety/ Security • PROMs/ Real-world data (Data Farming)	• Operational team (R&D Unicancer) : project lead/project managers/CRAs/ clinical trial coordinators/project assistant Steering Committee & General assembly radiation oncologists, physicists, dosimetrists, qualiticians radiobiologists and statisticians.	• **Industry collaborations:** ▪ Pharma: Pierre Fabre médicaments/MSD/Institut Roche ▪ Start-ups: TheraPanacea, Aquilab, Natera ▪ Radiotherapy vendors: Elekta • **Academic collaborations** EORTC/EADO/Sakgen group/Canadian cancer Trials Group/University of Leicester	Funding ressources : PHRC, Pharma
SFBR (French Society of Radiation Biology) Members from INSERM, CNRS, CEA, IRSN, CLCC, Curie Institute, Universities, Hospitals	**1, 2, 3**	"From fundamental radiation biology to (pre)clinical transfer": (internal and external radiotherapies (RT); innovative RT; radioprotection; effects on healthy tissues, tumors and tumor microenvironment; Biological prediction of response to RT; treatment of side effects; combinations of RT with other therapies	French learned society of radiobiology: 180 active members distributed throughout the territory. Access to numerous facilities (own material or shared platforms): irradiation, imaging, genomic, proteomic, metabolomic, microscopy, flow cytometry, animal experiments …		Annual membership contribution to SFBR All the members have their own funding for their research activity.
Industrials					
(Strasbourg) **Spin Up** Thomas Puiseux 7 allée de l'Europe, 67960 Strasbourg-Entzheim	**1**	- MRI geometric distortions for radiotherapy - quality control and phantom conception - Numerical simulation (fluid dynamics, electromagnetism, MRI physics) - 4D flow MRI	**Researchers :** Senior researchers: 4 Doc: 1 Part-time engineer: 1 **Specific equipment :** geometric distortion quality assurance phantoms, access to MRI facility, pulsatile flow test bench, access to HPC resources	- I2MC Inserm UMR1048, Toulouse - IMAG UMR5149, Montpellier - CHU Rangueil, Toulouse - Centre Henri Becquerel, Rouen	ANRT (CIFRE) ALARA group Own resources
(Strasbourg) **FIBERMETRIX** Mélodie MUNIER 7 allée de l'Europe, 67960 Strasbourg-Entzheim	**4**	- Dosimetry - Medical Physics - Conception of real-time (in-vivo) radiation detectors, development and manufacturing, - Connected Devices, - Optical fiber	**Researchers:** 1 (1/2 PhD physics, 1/2 PhD radiobiology) PhD Student: 1 CIFRE contract (medical physicist) Engineers: 3 **Specific equipment:**	- CHU Rangueil, Toulouse - CLB Lyon - CHU Saint Quentin - INSERM UA8 : Radiation, Défense, Santé et Environnement	ANRT (CIFRE) ALARA group Own resources

		technologies - IHM and software developments - Monte Carlo Simulation, - Low doses and doses repetition effect - Patient dose estimate	Radiation plateform X-Rays generator (15-160kV)		
(Strasbourg) **ALARA Expertise** Ramiro Moreno 7 allée de l'Europe, 67960 Strasbourg-Entzheim	**1,4**	- Medical Physics - Multimodality Medical Imaging Expertise (CT, Interventional Radiology, Conventional Radiology, Nuclear Medecine) - Quality Assurance based on ALARA principle - Occupational Radiation Protection - Patient dose estimate - National Radiation estimate (multi center and multi vendors)	**Researchers :** 3 Full time seniors (Medical physicists with PhD and one with accreditation to supervise researches) Engineers : 7 **Specific equipment :** Detectors and fantoms for medical imaging AQ	- CHU Rangueil, Toulouse - I2MC Inserm UMR1048 - INSERM UA8 : Radiation, Défense, Santé et Environnement	ALARA group Own resources
(Strasbourg) **NEOLYS DIAGNOSTICS** Sandrine Pereira 7 allée de l'Europe, 67960 Strasbourg-Entzheim	**2,3**	- Radiobiology - RT toxicities prediction assays Expertise in development of personalized solutions to define adapted/personalized therapeutic treatments	**Researchers :** Full time seniors researchers: 1 Junior researchers: 1 Technicians: 1 **Specific equipment :** Laboratory Equipments	- Centre Léon Bérard (Lyon) - Inserm UA8 (Lyon) - Centre Eugène marquis, (Rennes) - Instituto del tumori (Milan) - Centre Francois Baclesse (Caen) - Centre François Baclesse (Luxembourg)	ALARA group Own resources
Pharmimage - **Oncodesign (Villebon sur Yvette) Cyril Berthet:** - **CGFL (Dijon) Alexandre Cochet: imagerie et radiotherapie préclinique**	**1,3**	modèles précliniques, developpement de nouvelles molécules en radiothérapie vectorisée imagerie et radiotherapie préclinique	- Oncodesign : 4 - CGFL : 6	numerous contract services and collaborative programs (IMAkinib, IMAPPI, Biocair)	BPI, ANR, Feder…