Appel à candidatures 2018
Structuration de la recherche

Labellisation d'un réseau national de recherche pré-clinique en radiothérapie

Designation of a national Radiotherapy preclinical research network

Dossier de candidature – nouvelle soumission

Date limite de soumission : 7 septembre 2018 -16 heures

Soumission par email : radio2018@institutcancer.fr

Acronym : RADIOTRANSNET	
Nom du réseau de recherche pré-clinique en radiothérapie : Radiotherapy Translational and Preclinical Research Network	
Name of the Radiotherapy preclinical research network: RADIOTRANSNET	
Coordonnateur du réseau (Nom & Prénom) *Network coordinator (Name & first name)*	MAINGON Philippe / MARCHESI Vincent
Budget demandé à l'INCa /*Requested budget to INCa*	200 k€
Organisme porteur de la candidature (bénéficiaire / Funding beneficiary institution	SFRO

Partie I/Part 1

1 Coordonnateur du réseau[1] / Network coordinator

Coordonnateur du réseau (NOM, Prénom) / Network coordinator (NAME, First name)	Dr ☐ Pr **X** Mme ☐ Mr ☐ MAINGON Philippe
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N° RNSR – Information et consultation sur le site / *Information at* : http://rnsr.fr/	

[1] Le coordonnateur du projet assure : - la coordination scientifique du projet – la mise en place et la formalisation de la collaboration entre les équipes participantes, supervise – la production des documents et leur diffusion – les réunions d'avancement du projet – la communication des résultats, la production des documents requis – le suivi du budget global au regard du déroulement du projet.

Co-coordonnateur du réseau (NOM, Prénom) / Network coordinator (NAME, First name)	Dr Pr☐ Mme ☐ Mr x MARCHESI Vincent
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2 Organismes membres du réseau[2]/ Members of the network

Here are listed menbers of the Scientifique Committee and their respective organisms

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. Michel ATTAL Mme Armelle Barelli	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. A. EGGERMONT	Eric DEUTSCH
Institut Curie INSERM / CNRS	Institut Curie – Centre Universitaire - 91405 Orsay Cedex	G. ALMOUZNI	Marie DUTREIX

[2] 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).

SFPM UNICANCER	Service de Physique Médicale - Centre Oscar LAMBRET - 3 Rue Frédéric Combemale, 59000 Lille	Pr. Eric F. LARTIGAU	Thomas LACORNERIE
APHP	Radiation Oncology Department – GHU Pitié-Salpêtrière-Charles Foix – 47/83 bld de l'hôpital, 75013 Paris	M. Serge MOREL	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	M. Vincent BERGER	Paul-Henri ROMEO

3 Organisme porteur de la candidature (bénéficiaire de la subvention) [3]/ Funding beneficiary institution

Nom de l'organisme bénéficiaire de la subvention /*funding beneficiary* : Représentant légal (ou personne dûment habilitée)[4] Legal representative : Nom prénom : (Titre et fonction): Adresse :	Société Française de Radiothérapie Oncologique (SFRO) / French Society of Radiation Oncology MAINGON Philippe Professor SFRO - BP 23266 - 72003 LE MANS Cedex 1
Statut juridique : Code APE : N° SIREN :	Association loi de 1901 851 A 480 625 755000 16
Nom et prénom de la personne chargée du suivi administratif du dossier : Adresse de correspondance : e-mail : Téléphone :	FOURNIGAULT Angélique SFRO – Secrétariat - BP 23266 - 72003 LE MANS Cedex 1 sfro@wanadoo.fr 06.86.96.56.37

[3] 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).

[4] Personne habilitée à signer les conventions

4 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
Labellisation d'un réseau national de recherche préclinique en radiothérapie : RADIOTRANSNET
Mots-clés principaux
Oncologie-radiothérapie, recherche préclinique translationnelle.
Résumé scientifique du projet (max. 3500 caractères espaces compris)
L'ambition du réseau RADIOTRANSNET est de proposer une méthodologie robuste, élaborée sur une base de consensus scientifiques, avec pour mission de créer un consortium de recherche national dédié à la radiothérapie préclinique. Il se propose de mettre en place un agenda de recherches stratégiques portant sur l'état de l'art médical et scientifique, à l'interface de la radiothérapie et de la radiobiologie dans son positionnement préclinique, et de définir une stratégie ayant pour objectif de favoriser les interactions scientifiques et cliniques pour ces approches. Il doit contribuer à coordonner les efforts nationaux de recherche fondamentale et translationnelle en Oncologie-Radiothérapie. Les activités du réseau seront organisées autour de 4 priorités 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 4 axes majeurs seront 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. Le processus sera organisé sous la supervision d'un Conseil de surveillance (incluant des membres de la SFRO, de la SFPM, de la SFR, de la SFMN, d'un représentant des associations de patients) et d'un Conseil Scientifique (dirigé par un coordinateur désigné par la SFRO et un co-coordinateur désigné par la SFPM). Ce Conseil Scientifique va désigner, pour chacun des 4 axes précédemment nommés, trois coordinateurs (un oncologue-radiothérapeute, un physicien médical et un biologiste) qui auront pour responsabilité d'organiser une réunion scientifique basée sur la méthodologie des conférences de consensus afin d'identifier les questions prioritaires qui devront être sélectionnées pour être transmises au Conseil Scientifique. Ces initiatives seront étendues aux collaborations internationales en sollicitant des experts reconnus dans les problématiques discutées. Les thèmes retenus constitueront la base des projets qui seront étudiés et développés en faisant appel, au sein du réseau aux compétences complémentaires de toutes les plates-formes impliquées partenaires. Des propositions d'appels d'offres sélectionnées par le conseil scientifique 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. Une réunion annuelle (assemblée générale) de restitution avec tous les partenaires du réseau et plusieurs autres réunions organisées par les coordinateurs des axes thématiques seront planifiées autour des thèmes spécifiques, en liaison étroite avec les experts de ces différentes questions évoluant au niveau international.
L'ensemble de ces travaux sera publié, diffusé sur les réseaux scientifiques et sociaux, ainsi que sur un site web dédié qui assurera la démarche de consensus entre les quatre axes prioritaires.

Project title

Designation of a national Radiotherapy preclinical research network: RADIOTRANSNET

Principal keywords

Radiation Oncology, preclinical translational research

Scientific abstract (Max. 3500 characters)

The ambition of RADIOTRANSNET is to propose a robust methodology of science-based consensus conference with the view to (i) build a national research consortium dedicated to radiation-oncology, (ii) implement a strategic research agenda based on rigorous scientific and medical state of the art in radiotherapy and radiobiology and (iii) define a road map with the aim to favor existing scientific and clinical interactions. This approach will contribute organizing fundamental and translational national research efforts in radiation oncology. The network's activities must be organized around 4 chosen priorities. These 4 axes are target definition, normal tissue, combined treatments and dose modelling. The sub-targets linked to these 4 major axes are not limited. They include all aspects associated to fundamental radiobiology, preclinical studies, imaging, medical physics research and transversal components obviously associated to these scientific domains such as medical oncology, radio-diagnostic, nuclear medicine and cost effectiveness consideration. It will follow a bottom-up process under the supervision of a steering committee (including SFRO, SFPM, SFR, SFMN and patient representatives) and a scientific committee (led by one SFRO coordinator and one SFPM co-coordinator). The following step will be to appoint coordinators for each main target. One radiation oncologist, one medical physicist and one biologist will have to take the lead as co-coordinators of one of the priorities. They will have to organize, for the 4 above mentioned objectives, dedicated meetings and workshops by using the current possibilities offered by National Scientific Societies such as SFRO, SFPM, DOSEO, French Society of Cancer etc … The purpose of these meetings will be to identify the key points that should be studied including an accurate definition of the tasks taken into account by each partners of the network. These initiatives should be opened to international collaborations. There will be at least one annual meeting (General Assembly) of restitution including all partners of the network and specific annual meetings organized by the WP leaders around specific themes (DNA repair, nanoparticles, mice models and preclinical irradiators and imaging, computing …). The selected key points to be supported in priority will be transmitted to the scientific committee. These themes will be supported by specific funding allocated in reply to scientific calls. They should be the base of the proposition of calls submit to INCa and Academic or Charity Associations in view to provide human and technical resources necessary to conduct in the best conditions translational and preclinical researches in the field of radiation oncology. Dissemination will be made through publications, social networks, as well as a dedicated web site that will ensure the consensus approach between each major axes.

5 Experts récusés /Experts rejected for the review

Si nécessaire, indiquer les experts récusés pour l'évaluation/ If needed, identify the experts rejected for the review

Nom & Prénom /Last name & first name	Pays /country	E-mail	Justification
None			

6 Budget prévisionnel / Estimated budget

6.1 Annexe budgétaire/Bugetary Annex

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

6.2 Budget/ Network financial plan

Adéquation et justification du financement demandé en cohérence avec les objectifs du projet sur la période de **24 mois**. The network will develop a provisional budget for a period of **two** years. The applicant must specify the requested funding and justify the funding adequacy and coherence with the objectives of the project.
200k € over two years This funding will mainly support (89%) the recruitment of a project manager: Emilie BAYART (PhD), senior scientist experimented in the field of oncology, radiobiology and radiotherapy. She will provide support and assistance for the structuration of the network, events organization, timelines, reporting and communication. 6% will be dedicated to events organization (workshops and annual meetings). 1% will be invested in the website building. The 4% remaining correspond to overheads.

Partie II / Part 2

7 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 challenges,
- 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 axes 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…)

Cancer is the second leading cause of death globally, and is responsible for 8.8 million deaths worldwide theses last years. The economic impact of cancer is significant and is increasing. Globally, nearly 1 in 6 deaths is due to cancer and this is as many family concerned with this disease. Cancer plans were elaborated to drive the medical advances and social progress of cancer treatment. 17 operational objectives were identified in the last 2014-2019 cancer plan and many of them directly concerned radiation oncology. In this context, 4 major specific challenges are consensually identified for improving therapeutic index of radiotherapy. These challenges are clarified below and their declension needs to bring together different disciplines including oncology, biology, imaging, pharmacy, information technology, dosimetry and medical physics. Different hospitals and research Institutions develop dedicated objective for improving radiation oncology but suffer from the lack of national coordination. Our proposal is to bring together all these research capacities driven by clinical concerns in the field of radiotherapy for the final patient benefit. The ambition of RADIOTRANSNET is to propose a robust methodology of science-based consensus construction with the view to (i) build a national research consortium dedicated to radiation-oncology, (ii) implement a strategic research agenda based on rigorous scientific and medical state of the art in radiotherapy and radiobiology and (iii) define a road map with the aim to favor existing scientific and clinical interactions. This approach will contribute organizing high-level pre-clinical network able to connect research teams and technological platforms in radiation oncology and increase national and international visibilities. The

scientific missions of the network are described precisely and a methodology for launching and implementing this national network is proposed according to the objectives of the call**.**

- **Scientific challenges**

Cancer is a major health problem in the European Union with about 2.8 M new cases per year and 1.7 M death per year. Among patients suffering from cancer, surgery and radiotherapy, alone or combined with other modalities, are the major contributors to cure cancer (Europe against Cancer). Radiotherapy has a major role in cancer patients cured by local regional treatment. However, anti-tumor efficacy of radiotherapy must increase since about one third of patients dying from cancer will die from local-regional failure. Finally, increasing the efficiency of radiotherapy must be obtained while decreasing radiotherapy side effects on normal tissue.

Thanks to radiobiology which provides numerous tools such as for example:

-more and more efficient microscopy instruments enabling to **analyze temporal and spatial modifications** in cells under various stresses and treatments;

-development of specific antibodies to recognize and monitor protein modifications such as phosphorylation, ubiquitination, sumoylation, parylation, glycosylation, computational genomics and transcriptomics, single cell sequencing; new methods for silencing, knocking-out (CRISP/CAS) or overexpressing genes in different human cell types;

-modelling of pathway regulation and signaling with the help of systems biology;

-the increase of the knowledge in these last years highlighted the complexity of the neoplastic disease and its interaction with the surrounding normal tissue. The role of the immune system and the intestinal microbiota in the tumor response and the toxicity of the treatments define a new area of investigation.

Radiobiology which for long time was restricted to survival analysis has benefit of these progresses to better understand DNA damage signaling DNA repair, cell cycle control and cell death induced by irradiation. However, the role of intercellular signaling and **microenvironment** in the destiny of radiation exposed cells and tissue response is still not completely understood. It is obvious now that to identify new **functional and molecular biomarkers** of prognosis for radio-sensitivity or radio-resistance, all these parameters have to be taken in account. As part of these factors cannot be reproduced in cell cultures or animal models it is essential to associate **concerted analysis from patient samples and clinical data with molecular analysis and preclinical studies**.

The last two decades have seen the development of imaging modalities and radiotherapy (RT) treatment techniques. 3D and 4D imaging modalities allow describing tumors, normal tissues and their motions. Intensity-modulated RT with static, rotational or helical beams, stereotactic or ablative RT and in-room imaging devices allow to deliver accurately highly conformal absorbed doses to the tumor and to spare a large volume of normal tissues. These **technological improvements offer new treatment opportunities such as hypofractionation and voxelization**. However, the impact of these modifications, for example the dose per fraction and total number of fractions, has to be studied at the preclinical level.

In this context, there are 4 major strategies to improve the therapeutic index of radiotherapy:

1) Optimizing the specificity of the absorbed dose distribution of radiotherapy treatments in order to decrease the dose to the 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 that are changing the clinical practice offer new treatment opportunities such as hypofractionation, dose painting or adaptation. These treatment techniques require an efficient quality assurance program in order to increase the safety and to improve the quality of radiotherapy. In addition, to fully develop these opportunities, the target volume has to be better defined. The characterization of tumor heterogeneity can be explored by multimodal imaging aiming to study and more precisely characterize proliferation as well as metabolism including angiogenesis, hypoxia, acidosis, etc... These imaging modalities include MRI (perfusion, diffusion, MRI spectroscopy), of particular interest in brain tumors as well as positron emission tomography (PET) including fluorodeoxyglucose-PET for instance in lung and head and neck cancer but also amino acids (AA)-PET in brain tumors. New tracers have been introduced to study hypoxia, proliferation, angiogenesis, etc. These so-called biological imaging modalities allow not only characterizing the biological heterogeneity of the different tumors as well as their real extension, but also help to understand and follow the tumor response to radiotherapy and to combined chemoradiation. Several axes of research in biological imaging would design and drive clinical trials aiming to study the effect of the dose increase and predict the effect of targeted drugs in combination with radiotherapy. Biological imaging modalities allow studying heterogeneity of the tumors in the aim to either prescribe a suitable dose on voxels according to the metabolic activity (dose painting or voxelization) or follow the effect of irradiation on the studied tumors. Programs of research aiming to study the radioresistance, the genetic profile of such cells are mandatory. Finally, metabolic imaging allows the study of different patterns of relapse (migration, vasculogenesis, etc..) which can be modeled by different mathematical models and be correlated with different biological behaviors and mechanisms of escape to radiotherapy. However, in addition to the spatial localization of radioresistant areas, algorithms of quantitative imaging will be required to convert the metabolic intensity in an amount of dose able to kill tumor cells. Moreover, these biological findings associated to the technological development of treatment devices and treatment planning systems will lead to a new paradigm in terms of planning target volume. The concept of CTV to PTV margin will have to be completely reinvented. Robustness will be necessary to go beyond the in silico studies.

2) Decreasing radiotherapy side effects on normal tissue. Radiotherapy fractionation is mainly based on the differential response of normal versus tumor tissues. This concept has led to conventional scheme of 2 Gy per fraction, 5 fractions per week. In this context, normal tissue complication probabilities have been extensively studied and reported. Technological improvements have modified the clinical practice in terms of margins and ballistics aiming to limit the amount of irradiated normal tissues using advanced irradiation techniques.

As an example, the gain in terms of accuracy allows to develop hypofractionated radiotherapy treatments in stereotactic conditions delivering (very) high dose per fraction in few fractions. It is a high-precision external radiotherapy technique suitable for small volume tumors. Historically indicated for intracranial tumors, the extra-cranial indications of stereotactic radiotherapy are in full development (thoracic tumors, liver tumors, vertebral and bone tumors, abdomino-pelvic tumors). For some indications, the dose per fraction may exceed 10 Gy and sometimes up to 20 Gy. In this context, the use of data from radiobiological models and more precisely the quadratic linear model

based on clonogenic survival is questionable. Dose/volume constraints and tolerance doses of organs at risk are widely documented for "normo-fractionated" protocols. For hypo-fractionation protocols used in stereotactic body radiation therapy (SBRT), these dose/volume constraints change since the biological effects generated on healthy tissues at dose per fraction of 2 Gy and those of more than 10 Gy per fraction are clearly not the same. 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 evolution of radiotherapy practices / techniques.

It is essential to develop new ways to assess and to predict the potential risks of new techniques versus their therapeutic benefit. For these different reasons, it seems necessary to develop new tools to predict the biological effects, their fate and by extrapolation their risks. Consequently, the concept of the differential response of normal versus tumor tissues needs to be reconsidered. New normal tissue complication probabilities should be derived. These studies will require a better knowledge of the dose distribution delivered to the patients. Indeed, up to now, dose-effect relationship is mainly based on planned dose distributions instead of absorbed dose distributions. It means we should be able to accumulate daily dose distributions computed on daily images. Moreover, the evaluation of the biological mechanisms of normal tissue response is key to better understand the impact of novel technologies and novel drug-radiation combination on normal tissue response.

3) Combining new molecular targeted agents and biological modifiers with radiation therapy to increase the anti-tumor efficacy and/or to decrease the radiation effects on normal tissues, i.e. to increase the therapeutic ratio and to enlarge the therapeutic window. Historically, the concept of improving the outcome of radiotherapy in a combined approach has been obtained with radio-chemotherapy and has been validated in large number of randomized trials and meta-analyses. However, whereas radio-chemotherapy is more effective than radiotherapy alone, it is also more toxic, underscoring the need for new combined strategies with enhanced anti-tumor effects without increased toxicity. Combining drugs with irradiation in clinics have resulted in success (Platinum, Temozolomide) and failures (Gemcitabine and Avastin) indicating an absolute need for faster and earlier evaluation of the combined treatments that requires a better understanding of cancer biology and molecular response to ionizing radiation. Surprisingly, very few drugs are specifically developed as radiation sensitizers and the evaluation of drugs as radiation enhancing agents is often considered as an extension of these drugs activity. Moreover, the combination of a new drug with radiotherapy generally occurs relatively **late** in the course of the drug development, although the potential clinical interest could be of major importance for the patients. One of the reasons which leads to late development is the **lack of know how in industrial companies. This outlines the major need for a strong interaction between industrial and academic partners** to develop combined strategies faster and earlier and to find new targets based on enhancement of radiation response.

Using radiotherapy to target cancer cell molecular characteristics and/or tumor microenvironment may have a major impact on radiation response. Proofs of concept have been obtained by targeting microenvironment such as hypoxia or immune cells or by targeting cancer cell characteristics such as a tyrosine kinase receptor but these therapeutics extensions require extensive researches. Finally, abscopal effect of radiotherapy is an important extension that might lead to therapeutic effects of radiotherapy on metastasis.

4) Predicting quickly and accurately 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 in order to develop treatment personalization approaches. Treatment personalization will increase the success of clinical transfer and will justify allocation of resources upon to the specific patient needs.

Such program aiming to address these questions by integrating teams working on radiobiology, biology, mathematics, physics and imaging needs also to be developed. However, the important number of preclinical data that indicate a potential clinical benefit in the field of radiotherapy contrasts with the low number of new drugs approved for concurrent radiotherapy administration during the last 15 years and deserves attention. Fostering innovation and transfer of novel concepts in radiotherapy is thus highly needed and requires preclinical optimization and selection of concepts to be tested into the clinic. The objective **of this project is to set-up a high level pre-clinical network able to connect research teams and technological platforms to test innovative strategies in the field of radiotherapy and to demonstrate their added values.**

- **Overall strategy of the project**

Radiation therapy (RT) is one of the three therapeutic pillars among cancer treatment regimens. Numerous approaches have been tested to improve the therapeutic ratio of RT, and these include increasing the dose delivered to the tumor, altered fractionation schemes, use of heavy ions, combined modality treatments with chemotherapy and, more recently, novel targeted agents However, either treatment efficacy or toxicity may be difficult to predict.

Testing innovative strategies in the field of radiotherapy and demonstrating their added values require inter-disciplinarity. Interdisciplinary research faces with difficulties to ensure its recognition in academic context where huge disciplines outbalance still exist. Inter-disciplinarity is considered as a powerful enriching factor and as a scientific vector in favor of pushing forward boundaries of scientific and medical knowledge and contributing to the emergence of new scientific and medical application. The objective of RADIOTRANSNET proposal is to organize and foster existing cooperation between different disciplines for reinforcing and securing the emergence of innovative cancer treatments and optimizing radiation exposure. The above-mentioned network should gather oncologists, biologists, pharmacists, information technology scientists and medical physicists working on innovative treatments using radiation. The overall RADIOTRANSNET ambition is to demonstrate how national R&D teams of oncologists, biologists, pharmacists, information technology scientists and medical physicists can, in a joint collaborative research effort, achieve innovative results that contribute to enhance cancer treatment.

The long-term success beyond the project will eventually depend on the continued favorable environment to support this science-based collective approach for radiation-oncology development. The INCa, national competent authorities and the involved professions will in particular need to pay attention to provide adequate support to proposal emanating from RADIOTRANSNET.

- **Network's activities**

WP1-Target Definition

- 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 allow describing tumoral and normal tissues and their motions. Intensity-modulated RT with static, rotational or helical beams, stereotactic or ablative RT and in-room imaging devices allow to deliver accurately highly conformal absorbed doses to the tumor and to spare a large volume of normal tissues. However, anti-tumor efficacy of radiotherapy must increase since about one third of patients who die from cancer will die from local-regional failure. This statement demonstrates the need to better define the target.

- Main scientific objectives:

With modern imaging modalities and registration software, the spatial definition of the macroscopic target can be achieved. However, it appears this definition presents weaknesses. From a biological point of view, different phenomena should be included in the 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 in order to produce more consistent volumes whatever the clinician and to pave the way for adaptive radiotherapy.

- WP1 axes and tasks:

The RADIOTRANSNET consortium identifies as a collective goal the progressive implementation of a Strategic Research Agenda (SRA) for the optimization of radiation exposure and the harmonization of practices in radiotherapy. The research topics on “target definition” considered necessary and most urgent are summarized in three themes:

WP1.T1*- Biological volumes at the voxel scale*

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 at defining the target volume or the prescribed dose. Additionally, biological sub-volumes should be spatially registered to the planning images in order to define planning volumes. Despite a great interest on dose calculation on MR images (this topic will be discussed in the specific axis “Dose Modelling”), dose calculation is performed on anatomical CT images. Deformable registration algorithms are already available to fuse different imaging datasets. However, a lot of work has to be done to validate these algorithms. Research should be conducted to better understand biological mechanisms and pathways mandatory to improve the sensibility and the specificity of imaging exams, able to derive accurate and quantitative hypoxia, tumor vascularization or other biomarker maps defining criteria for radioresistance. Considering biological mechanisms that occur at the cellular scale and imaging modalities using comparatively large voxels, studies should also consider this multi-scale problem to fully exploit biological findings. In addition, quantitative imaging should allow converting the detected signal into a required dose to prescribe to these sub-volumes. This quantitative imaging approach is a prerequisite to develop treatments using dose painting by contours or by numbers. All the aspects associated with this issue have been extensively described in section Optimizing of the first chapter of this application. The French Radiology Society and the French Nuclear Medicine Society will be two major partners associated to the calls. They will be incorporated in the network and asked to participate at the meetings and workshops dedicated to this topic.

WP1.T2*-Target volume delineation*

From an anatomical point of view, too many discrepancies still remain between different clinicians in the target volume delineation despite the publication of guidelines. The development of atlas-based auto-segmentation software should allow reducing these discrepancies. A better standardization of delineation is essential in order to improve the consistency of the volumes, and consequently of the

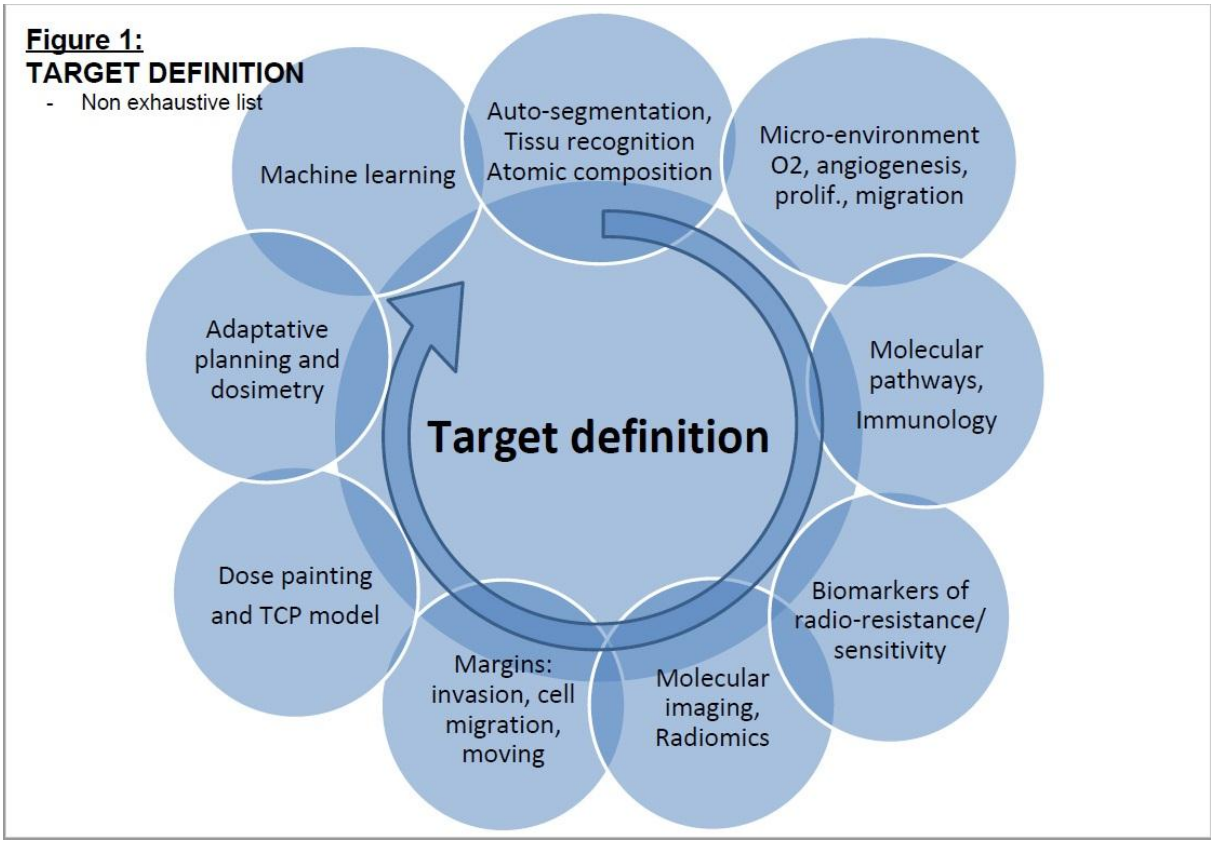
plans. The standardization of delineation is then of great interest to improve the absorbed dose effect relationship. Moreover, this step is fundamental to pave the way for adaptive radiotherapy. Indeed, adaptive radiotherapy is limited due to the necessary interventions of different operators. Fully adaptive radiotherapy could be developed only if progress is made in automation. Many algorithms do already exist and provide satisfactory for some organs, especially when contrast is high. However, they still fail in some situations and always require an expert validation. Research should keep on, including by exploring neural network and machine learning.

***WP1.T3**-Margins*

The new target definition based on biological and anatomical data will raise the problem of the margins. Basically, for modern radiotherapy treatments, the delivery is more accurate and the margins should be reduced. This is much more complex. This former statement is probably true for the CTV to PTV margin if organ motion is well managed. However, it is a non-sense to apply it to the GTV to CTV margin. On the contrary, new or future imaging modalities or biomarkers could lead to an increase of this specific margin. We should speak about tumor control probability modelling instead of increased margins. Combined margin recipe for microscopic disease and geometric uncertainties (CTV+PTV) could dramatically improve the planned dose distribution. High-resolution imaging and collaboration with pathologist and radiologist are needed. Finally, the definition of biological sub-volumes with particular radioresistance could conduct to define many prescribed dose levels, and develop the dose painting technique. The actual standard of margin definition cannot deal with such concepts. Obviously, a large work has to be done on the margin definition. Tumor control probability modelling and probabilistic planning should be considered. Ideally, this work should also integrate the immobilization devices and the positioning management.

Main research issues to improve the target volume definition are listed on figure 1.

Figure 1:
TARGET DEFINITION
- Non exhaustive list



WP2-Normal Tissue

- General background and scientific requirements :

Half of patients with a solid malignant tumor will receive radiation therapy (RT) with a curative or palliative intent during the course of their treatment. Adverse effects impacting normal tissue may result in acute and chronic toxicities that reduce the long-term health-related quality of life of these patients. Considerable progress towards reducing 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 conforms closely to the shape of tumors yielding an improved efficacy/toxicity ratio. However, sophisticated RT cannot definitively prevent toxicity to normal tissues surrounding the target volume, especially as normal tissue constraints are offset by dose escalation or concurrent chemo- or biologically- targeted therapy. In fact, cancer incidence and mortality have been improved during the past several decades, and the number of cancer survivors has almost tripled during the same period ***(Figure 2)***. With an increasing cohort of cancer survivors, efforts to prevent, to diagnose and to manage the adverse effects of cancer therapy, in general, and those of radiation therapy specifically, have to be intensified. New insights into the underlying pathophysiology have to strengthen understanding of the mechanisms of combined tissue-induced toxicity, new diagnostic strategies and management opportunities.

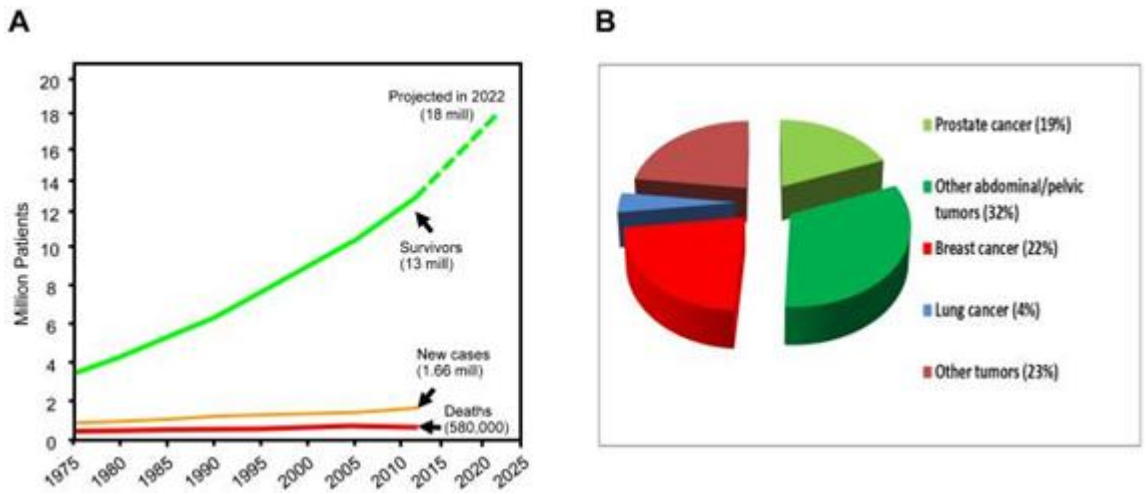


Figure 2 *: Cancer survivors and cancer prevalence rates in the US (Hauer-Jensen et al. Nat Rev Gastroenterol Hepatol. 2014) A) Cancer incidence and death rates have been fairly flat during the past 4 decades, while the cohort of cancer survivors increases by 3% per year, exceeds 13 million in 2013, and is expected to reach 18 million in 2022. B) Approximately half of all cancer survivors are survivors after abdominal or pelvic tumors, many of whom have had or will have radiation therapy.*

- Main scientific objectives:

Reducing the risk of sequelae and second cancer occurrence was identified as one of the 17 objectives of the French "Plan Cancer 2014-2019". Reducing adverse effects represent a major challenge for a better quality of life for long term cancer survivors. Preclinical research investigating mechanistic processes of normal tissue response will pave the way for optimizing radiation exposure and reinforce the emergence of new therapeutic approaches for cancer treatment.

- WP2 axes 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 the harmonization of practices in radiotherapy. The research topics on "normal tissue" considered necessary and most urgent for effective medical care and efficient in terms of radiation protection are summarized in four themes:

WP2.T1*-Non-cancer effects in various tissues and radiobiology-based effect models for morbidity endpoints:*

Radiation-induced morbidity may be observed early (< 3 months) or late (several months or years) after cancer treatment. This result from normal tissues, at the neighborhood or away from the target tumor, exposed at a strong gradient of doses. Sophisticated RT was developed based on complex ballistic, new dose rate and energy spectra in order to increase the benefit/risk ratio. 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. The relative biological effectiveness (RBE) concept of normal tissue response to new radiation modalities has to be reconsidered. Normal tissue tolerance in response to other treatment modalities, particularly chemo- and biologically targeted therapy is currently not well understood. Exploring the role of tissue microenvironment is required to better characterize the normal tissue versus tumor response, a system radiobiology approach will allow the identification of new molecular pathways of normal tissue response. Current morbidity risk model 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 without assumed processes of damage development and lack the evidence of a mechanistic basis. Preclinical model may help to implement NTCP model.

WP2.T2*-Individual patient-tissue response to radiation and early biomarkers of response and morbidity:*

The individual tissue response of patients may be considered in the choice of therapeutic strategies. This can be based on intrinsic factors (age, gender, genomics/epigenetics…) of the normal tissues, but also on concomitant diseases impacting on general or specific normal tissue tolerance. Patient with a high risk for certain, severe, normal tissue response may require a change in dose distribution or in 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 for developing personalized cancer treatment.

WP2.T3*-Radiobiological mechanisms of radiation-induced side effects and protection of normal tissues from the side effects of radiation therapy:*

The biological mechanism of chemo-radio-induced morbidities in normal tissues and organs are very complex and vary between different signs and symptoms of morbidity. For many years, the pathogenesis of radiation -normal tissue injury has been exclusively explained by the severity of the depletion of a specific compartment (i.e. mainly stem cell compartment). A contemporary view of radiation -induced normal tissues pathogenesis integrates and involves multiple cell compartments that interact in a complex sequence of events following the radiation insult. Thus, adaptive and innate immune systems, vascular network, mesenchymal and epithelial cells and even microbiome can contribute to the initiation and progression of radiation injury. Moreover, pathophysiology of radiation-induced normal tissue damages is a multi-faced process involving activation of the coagulation cascade, inflammation, epithelial regeneration, accumulation of granulation tissue and matrix deposition and remodeling. The future challenge in the biological response of normal tissues will be to integrate this complexity in order to 1) identify key compartment/processes and 2) sequences of action for temporal therapeutic intervention. Systems/computational radiobiology approaches and use of up to date localized preclinical modelisation as well as transgenic models able to elucidate the role of different cellular compartments will help to answer the problematic. These mechanisms need to be clarified for specific clinical morbidity endpoints in order to develop specific strategies for protection, mitigation or management of severe radiation side effects to the

organ at risk.

WP2.T4*-Impact of fractionation and radiation particle*

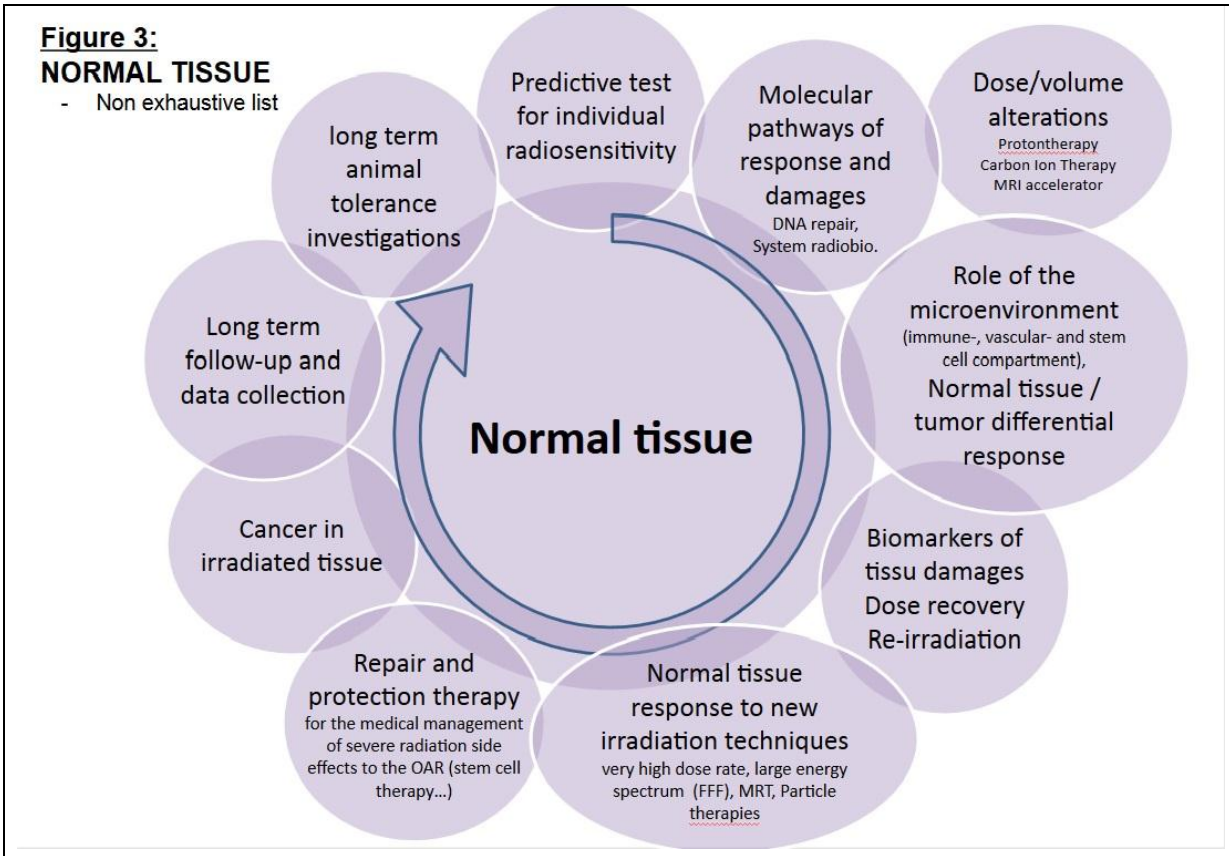
Radiation therapy treatments are mainly delivered by high energy photon beams produced by linear accelerators according to a conventional fractionation. The development of hypofractionated radiotherapy treatments requires a new determination of normal tissue complication probabilities. Biological mechanisms involved after high dose per fraction is controversial. The use of data based on the quadratic linear model is questionable. Dose/volume constraints and tolerance doses of organs at risk are widely documented for "normo-fractionated" protocols. For hypofractionated protocols used in SBRT, these dose/volume constraints change since the biological effects generated on healthy tissues at dose per fraction of 2 Gy and those of more than 10 Gy per fraction are clearly not the same. There is a very significant lack of knowledge of the biological effects associated with both high dose per fraction but also with high dose rate. Preclinical research studies have to be conducted to optimize hypofractionated schemes.

In addition, due to the unfavorable photon percent depth dose profile, the limitation of normal tissue irradiation is obtained thanks to modern treatment techniques based on intensity modulated plans with 5 to 9 static beams, arcs, helical beams or thousands of non-coplanar beams. The use of proton or carbon ion beams allows reducing the number of beams necessary to deliver highly conformal plans. Biological mechanisms involved after particle beam therapy differ from photon therapy. Consequently, radiobiological studies should consider the impact of the particle on normal tissue side effects.

Preclinical research requires dedicated radiation facilities offering representative configuration of clinical use for cancer treatment. Specific action for the identification and networking of the whole national infrastructure will be necessary to favor joint efforts for the upgrading of and open access to dedicated platforms for preclinical radiotherapy research. Several radiation facilities dedicated to preclinical research for radiation oncology including image-guided small animal irradiators, medical linear accelerators, proton and carbon beams… are already available. Numerous platforms have already organized in different networks, for example the Resplandir network (réseau national de plateformes de radiothérapie préclinique) and have been invited to participate to RADIOTRANSNET. Also, management of dose/volume constraints for preclinical modelisation would be necessary (ablative dose, low dose on large volume…) to develop standardized preclinical models with high clinical significance.

A list of main research issues is available on figure 3.

Figure 3:
NORMAL TISSUE
- Non exhaustive list



WP3-Combined Treatments

- General background and scientific needs:

The important number of preclinical data (*in vitro* or *in vivo experiments*) suggesting a potential for clinical benefit in the field of radiotherapy contrasts with the fact that during the last 15 years, very few new drugs were approved for concurrent radiotherapy administration, which deserves attention.

Out of hundreds of clinical trials, 2 compounds went approved for concurrent radiotherapy during this interval: the alkylating agent Temozolomide (Stupp, Hegi et al. 2009), and the anti EGFr Cetuximab (Bonner, Harari et al. 2006). This leads to several interrogations; in particular, there might have been several gaps between experimental models and the clinical reality: i) investigators have often concentrated at the preclinical level on drug responsive models which did not match the great variability of tumor sensitivity in patients. The EGFr sensitive cell lines have been over-represented in preclinical work evaluating the potential for concurrent EGFr inhibition during radiotherapy (Harari and Huang 2004, Loriot, Mordant et al. 2010); ii) Another illustration of these gaps is that chemotherapy is often not considered into preclinical experiments while the drugs enter clinical trials in combination with the therapeutic mainstay, or at least compare to this chemotherapy mainstay in many circumstances. After registration from a positive randomized phase III against radiation alone (Bonner, Harari et al. 2006), the combination of Erbitux to cisplatin based chemoradiation, the current gold standard in locally advanced HNSCC failed to show superiority over chemoradiation alone but an increased toxicity. Similar results were observed in esophagus, anal and cervical cancer (Crosby, Hurt et al. 2013, de la Rochefordiere, Kamal et al. 2015, Levy, Azria et al. 2015).

Only a minority of the various preclinical experiments with targeted therapies and radiotherapy did study the impact of these combinations on normal tissue response. As a consequence of this, the impact of many targeted therapies on normal tissue response was often reported for the first time in

patients, thus underscoring the need for better preclinical modeling of the tumor versus normal tissue therapeutic ratio. Braf inhibitors (Boussemart, Boivin et al. 2013), VEGFr inhibitors (Peters, Richel et al. 2008), mToR inhibitors (Deutsch, Annals of Oncol 2015), EGFr (Budach, Bolke et al. 2007) are examples of the deleterious impact of novel drug radiation combination on normal tissue tolerance which was overlooked by preclinical plans. This raises the question of the need for preclinical pre-requisites (Sharma, Plummer et al. 2016). The anti VEGF antibody Bevacizumab constitutes another illustration since a clinical trial was prematurely closed after the onset of major lung toxicities following radiation (Lind, Senan et al. 2012). In this case, the use of an anti-human VEGF antibody that does not cross react with the respective VEGF murine epitope rendered non-relevant conclusion on normal tissue tolerance. Only the use of an antibody against murine VEGF did recapitulate the negative impact of the combination observed into the clinic (Mangoni, Vozenin et al. 2012).

Several caveats of the preclinical models used for the evaluation of preclinical combinations that should deserve further attention and evolution toward the early clinical steps have to be highlighted. The basis for radiosensitivity assessment, clonogenic cell kill quantification using in vitro clonogenic assays and in vivo tumor growth delays and TCD50 have shown to be robust predictors of the clinical efficacy of so-called conventional cytotoxic radiosensitizers such as cisplatinum, taxanes (Krause, Zips et al. 2006). The transition toward the targeted therapy era has profoundly challenged the value of the preclinical models. A simple “pubmed” search retrieves a major attrition rate between preclinical and clinical phase when novel agents and radiotherapy combinations are considered.

- Main scientific objectives:

Since it is not possible to embrace all these topics in a realistic way in a single project, it is proposed to focus on few combinatory strategies, that should contribute to produce significant advances and novelty in the field, key aspects will then be outlined.

The choice of a pre-clinical axis is relevant in **defining how pre-clinical evaluation of novel combinations would be performed into a network.** Translational research is required in order to validate targets, pathways and to optimize patient selection. Such data will be matched with our preclinical research data in order to define a prioritization list of candidates to be transferred into the clinic. The synergistic activities of partners in such a network should lead to innovative combined strategies in subsequent Phase I and II trials. The project greatly depends on the implication of industrial partners in the field of imaging, radiotherapy and pharmaceutical industry.

WP3 axes and tasks:

WP3.T1*-Combined strategies identification*

One important aspect is to focus on very few key combined strategies among the broad spectrum of potential approaches, based on several selection criteria such as the validity of the rationale, the innovative nature of the topic, the clinical relevance of the question, the practical feasibility both at the pre-clinical and clinical levels, and the existence of an industrial support. In that aim, it will be proposed to develop a strategy to enhance the anti-tumor effect of radiotherapy, focusing on various concepts of combinatory approach such as targeting the tumor cells intrinsic signals, DNA damage and response pathways involved in resistance to radiation, targeting the interplay between the tumor and the vascular network, targeting the cellular dynamics, motility and plasticity involved in resistance to radiation and targeting the interplay of the cancer cell and the immune host.

Preclinical requirements for a drug to be selected as a radiation sensitizer candidate should have been previously characterized based on the existence of a synergy and the respect of a therapeutic

window. This methodology has been widely used for so called 'classical' radiosensitizing agents evaluation (example of platinum, 5FU, Tirapazamine) and also for radioprotectors such as Amifostine.

WP3.T2*-Read outs standardization*

The validity of the retained concepts will be evaluated using a **standardized and innovative methodology** taking into account the **latest laboratory technologies** available such as using functional genomics for target validation and target selection, or in vivo imaging. Harmonization of the end points (tumors growth delay, biomarkers expression, vascularization, immune response) and the standardization of the methods are crucial for comparison of data obtained in the context of a large network. The multi-disciplinarity (Scientists specialized in radiobiology, immunology, functional genetics, methodologists, radiation oncologists, medical oncologists, imaging specialists, pathologists …) and exchange of knowledge within this consortium makes it a unique platform to develop innovative set up for robust pre-clinical evaluation, in immune-competent and orthotopic tumor models.

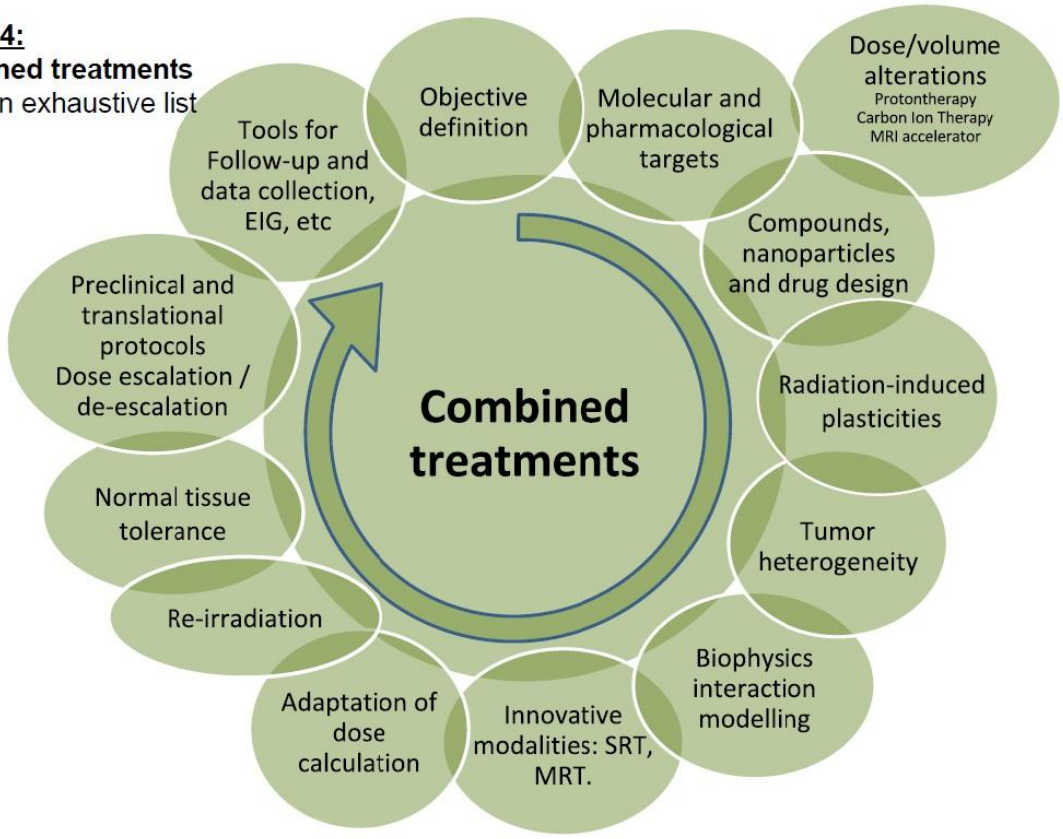
WP3.T3*-Set up of protocols the preclinical evaluation*

The recent example of the Bevacizumab radiation combination that has been halted after the event of fatal lung cases in a phase II trials not only addresses the questions of safety issue in phase I trials but also underscores the critical need for normal tissue toxicity data accumulation at the preclinical stage. We will focus of 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 the immune effects of radiotherapy require relevant of appropriate murine models to evaluate the systemic immune effects of radiotherapy. Response to highly specific targeted agents often relies on pre-existing mutations. The molecular profiling of tumors, the data from the TCGA are underscoring the emerging needs for more relevant models of tumors reflecting *the diversity of the molecular subtypes.* In the same way, cellular models coming from the patients and fully characterized in term of genomic profile and clinical response to irradiation will be used to study the efficacy of targeted drugs directed against activated pathways involved in radio-resistance.

A list of main research domains is summarized in figure 4.

Figure 4:
Combined treatments
- Non exhaustive list



The selection of candidates to be transferred into the clinic will integrate translational molecular, genomic and imaging data demonstrating the target engagement in order to ensure clinical relevance of the hypothesis and to 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.**

Beside the potential benefits of the foreseen structuration are the followings:

- Faster and earlier testing in combination with RT of some drugs early in development of the pipeline based on scientific rationale (preclinical data showing that the target is of interest as well as clinical data showing that the target of the drugs has a clinical significant relevance in term of radiation response)
- Access to a pre-clinical 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 that could lead to faster registration of the drugs in combination with RT that would ultimately benefit to the patient.

WP4- Dose Modelling

- General background and scientific needs:

Radiotherapy treatments are mainly based on a single in silico tridimensional dose calculation using patient-specific CT images and contours. Modern analytical “type b” algorithms allow computing accurate dose distributions, including in complex heterogeneous geometries. In frequent situations, Monte Carlo (MC) simulations should be preferred. Indeed, the dose modelling by advanced statistical methods is of great interest in some circumstances. Monte Carlo (MC) simulations is considered as the most advanced and appropriate answer to the expressed needs: they allow computing accurately organ doses, for every patient using computational 3D models based on the CT images of the patient.

However, dose distributions are usually calculated on a snapshot of the living and breathing patient.

It appears that dose modelling should go further to be able to calculate the absorbed dose by the patient at the voxel scale during the treatment delivery. 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, re-irradiations, adaptive radiotherapy and clinical outcome in order to derive dose-effect relationships. However, scientific problems are still unsolved, especially validation of deformable registration algorithms, measurement or computation of the daily dose and dose accumulation.

Since reducing the risk of sequelae and cancer in irradiated area is a major objective, the use of MC simulations can address various issues related to the radiotherapy and associated imaging techniques (kV- and MV-imaging, radiology), such as out-of-field dose estimation or the determination of patient dosimetry caused by imaging CT examinations for treatment preparation, delivery and follow-up. Hence, accurate knowledge of out-of-field doses and imaging doses is important to better understand the dose-carcinogenic effect relationship. Dose modelling will allow estimating accurately for each patient and treatment the out-of-field doses delivered by the therapeutic beam and the imaging positioning procedure used for IGRT.

Moreover, dose calculation is 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 lead researches on dose calculation on MR images instead of CT images.

Furthermore, dose modelling can be used to solve current issues such as the simulation of the innovative treatment like nanoparticles by as example the determination of the dose enhancement factor, ultra-high dose rate treatment, protons...

- Main scientific objectives:
Reducing adverse effects represents a major challenge for a better quality of life for long-term cancer survivors. To achieve this objective, a precise knowledge of the doses delivered for each technique, each patient, and each organ is essential.

Achieving the optimization of radiation exposure and the harmonization of practices in radiotherapy and understanding the biologic effects require a better knowledge of the physical dose and the characteristics of the ionizing radiation (type, energy). The computation of the daily delivered dose by analytical or advanced statistical methods during radiotherapy courses will answer this challenge. These calculations should take into account the geometry of the day, and should be able to accumulate daily dose distributions in single reference geometry.

In addition, commercial treatment planning systems (TPS) used in RT provide adequate dosimetric accuracy for in-field and near-field calculations. However, current TPS are not commissioned for out-of-field dose calculations making them hence irrelevant to estimate correctly these doses.

Additional dose including imaging sessions for planning and follow-up such as CT and PET-CT but also in-room imaging such as CBCT should also be computed. Even if some MC-based software packages were already developed to calculate organ doses from CT exams, no simulation tool is today available in clinical routine.

There are no internationally recognized recommendations/protocols on how to plan radiotherapy to minimize the risk of cancer in irradiated tissue. Also, during the entire treatment, dose to the patient due to different diagnostic procedures is not always recorded and added. Moreover, the addition of physical doses from orthovoltage and megavoltage energy beams is controversial. Indeed, biological effects may vary according to the energy range of the incident beams. Relative biological effectiveness of kV beams needs to be deeper investigated to be able to express cumulative doses.

This question of dose summation can be extended to successive courses of radiotherapy. A patient may undergo plans of different modalities including photon beam radiotherapy, brachytherapy, proton beam radiotherapy or even molecular radiotherapy during his cancer care. New models of biologically effective dose are required to accumulate doses and to take into account previously absorbed dose in case of re-irradiation. Linear-quadratic model is far from sufficient.

The main ambitions of the RADIOTRANSNET consortium for this purpose are: to calculate delivered dose to patients instead of planned dose to derive dose effect relationships; to develop a new and reliable software built-in tool to estimate accurately and rapidly out-of-field doses for 3DRT and IMRT treatments, and also imaging doses due to 2D-kV or kV-CBCT imaging procedures; to develop mathematical models to sum biological doses or calculate biologically effective doses from successive treatments delivered by various beams during years of care.

- WP4 axes and tasks:

The RADIOTRANSNET consortium identifies as a collective goal the progressive implementation of a Strategic Research Agenda (SRA) for the optimization of radiation exposure and the harmonization of practices in radiotherapy. The research topics on “Dose Modelling” considered necessary and most urgent are summarized in five themes:

WP4.T1*-Minimalizing the complications of healthy tissues*.

During the last decade, an intensive research was performed to quantify 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. The technological progress accomplished by the new medical accelerators allows a better conformation of the dose deposited to the tumor. Despite doses received by organs outside the treatment field have decreased, parts of organs may still be highly irradiated depending on the distance to the target volume. Intensity-modulated RT (IMRT) and volumetric modulated arc therapy (VMAT) are known to increase the number of monitor units by a factor of 2-3, hence increasing the whole-body exposures from leakage radiation in comparison to conventional RT. However, there is a great disparity in the out-of-field dose depending on the type of machine used. The adaptation of "the least irradiant technique reasonably achievable" is therefore of major interest, especially in pediatric cases where life expectancy for surviving subjects may be sufficiently long for a second cancer to develop. Research should also include proton and carbon ions beams.

In addition to out-of-field doses, we should also pay attention to additional doses delivered by X-ray imaging systems used in Image-Guided RT for patient positioning, called imaging doses. Indeed, recent studies showed that use of intense imaging regimens (e.g. daily CBCT) for normo-fractionated courses might lead to doses to organs at risk (OAR) and normal tissues surrounding tumor site from 1 to 2 Gy, delivered either at the skin or in large volumes outside the target area, especially in bony structures due to high photoelectric effect at orthovoltage energy. This topic may be of less interest for hypofractionated treatments. However, SBRT uses intra-fraction imaging sessions, and consequently, even if the additional imaging doses will be reduced, they have to be evaluated. Out-of-field and imaging doses both contribute to a significant increased dose to whole body, which is of major concern for patients at risk, such as children and young adults.

RADIOTRANSNET consortium will focus on the assessment of out-of-field doses and to concomitant doses due to positioning imaging procedures during radiotherapy. The development of a module to consider them for further treatment planning using TPS and hence, to minimize the risk of secondary cancer in radiation therapy without lowering the probability of tumor control can be considered.

WP4.T2-Doses delivered during diagnostic and positioning imaging procedures

Currently, more than 50% of the cumulative radiation exposure to patients in diagnostic radiology comes from CT scanners. Due to rapid technological evolutions of multi-slice CT technology, the number and relative contribution of CT examinations has considerably increased over the past 15 years. Optimization in CT imaging involves a carefully set balance between the best image quality ensuring a reliable diagnostic and the lowest radiation exposure. Both aspects and methods should provide patient a specific indication approach which adheres to clinical practice. The systematic optimization of CT imaging is today limited because the delivered dose is mainly estimated using global dose indicators. Comprehensive optimization tools for clinical routine are lacking.

Modelling Monte Carlo simulations will be used in order to evaluate accurately the dose-to-organs for each patient. However, dose cannot be minimized without considering the clinical imaging task and it is necessary to try to reduce the dose while keeping an image quality sufficient enough for the clinical purpose. Mathematical model observers, such as the Non-Pre-Whitening Eye Filter model, have been recently developed. Their main feature is that they present a good correlation with the human eye for clinical tasks, such discrimination and detection of tumoral lesions. This type of model observer will be studied and will enable to get the best image quality while maintaining the delivered dose to the lowest level, for the required clinical task.

WP4.T3*- Track structure characteristics and biological outcomes prediction*

The quantity used at present for a clinical prescription in radiotherapy deliveries is absorbed dose to water. 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 nano-scopic sub-cellular scale, i.e. the particle track structure. 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. This factor generally depends on properties of the radiation and various biological factors whose measurement lacks traceability to metrological standards.

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 track structure of ionizing radiation in mixed radiation fields. They are related to the biological outcome of the mixed field in a direct manner. They can be the basis for future treatment planning systems with biological optimization based on nanometric characteristics of particle track structure.

Research projects exploring the practical use in treatment planning systems of nanodosimetric quantities related to track structure for characterizing radiation quality in terms of biological effects are still needed. These projects will also explore the impact of the dose rate that is neglected by commercially available treatment planning systems.

WP4.T4*-Clinical Decision Support System creation*

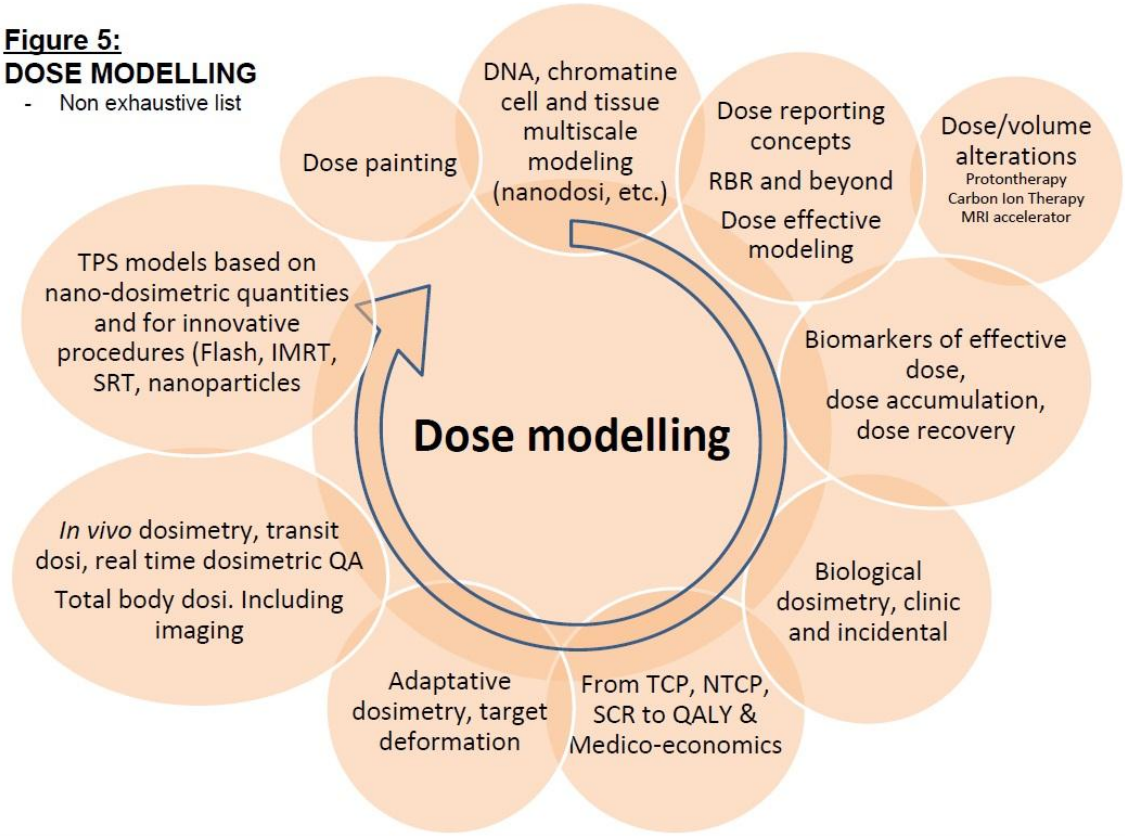
Only 3% of adult patients are included in clinical studies, a long time before launching is mandatory, clinical results are complicated to register. Finally, the results are often not relevant considering the evolution of practice and knowledge. Therefore, it is necessary to use treatment data of all patients to get feedback and improve clinical practice. The main issue **to create a machine learning database** is the poor quality of the data which are not standardized ... To build an efficient Clinical Decision Support System in radiotherapy able to correlate toxicities and tumor control probability to treatment data, truly delivered dose is requested. Functional imaging after or during treatment will improve disease response assessment; registration of these images with dose distribution is an active area of research. These registrations are necessary to enable quantitative evaluation of the response

of the tumor or normal tissue to radiation. Solutions exist to measure dose delivered but not for all techniques and for all machines. Furthermore, we still do not know if it is appropriate to deform dose and there is no consensus on how to accumulate dose delivered at each session. Many parameters related to biological effect should be considered and tracked during the treatment duration in combination with radiobiological experiments or preclinical research.

WP4.T5- *The dose accumulation during an overall treatment* is of major importance to derive dose effect relationships, tumor control probabilities and normal tissue complication probabilities. Nevertheless, this concept only considers physical dose. Altered fractionations or modified treatment modalities require considering biologically effective dose. In clinical practice, the linear-quadratic model and the equivalent dose to 2 Gy fractions (EQD2) are used to compare different fractionations. These models present weaknesses in modern radiotherapy while reduced overall treatment duration and a high dose per fraction have been introduced. Moreover, time is usually neglected, and recovery factor ignored. There is an important need of mathematical models willing to deal with modern radiotherapy cancer care. Patients undergo several treatments, more and more patients benefit from re-irradiations. Clinicians need to know how to take into account previously absorbed dose. Models aiming to derive dose/volume constraints in a context of re-irradiation are fundamental. Preclinical radiobiological studies are necessary. These investigations should also consider relative biologically effectiveness according to the linear energy transfer of particles.

Key issues on dose modelling are listed on figure 5.

Figure 5:
DOSE MODELLING
- Non exhaustive list



Concrete actions contributing to the structuration of radiotherapy in France:

First, the project manager, in charge to coordinate the actions decided by the scientific committee, will establish an exhaustive list of partners in the most inclusive way. A preliminary list of partners willing to participate at this initiative, their orientation inside the project as well as their expertise

and specific equipment is provided in section 8.2 of this application.

Second, all of the partners will be questioned to identify and describe their field of expertise, regarding the 4 identified challenges mentioned above. All existing authorities and bodies and all existing networks will be asked to participate at this effort. This process will be associated to identify the resources and the funding capacities of each actor involved in that purpose.

Third, in the same period of time, the scientific committee will appoint moderators for each 4 main challenges. One Radiation Oncologist, one medical physicist and one scientist/biologist will have to take the lead as co-coordinators of one of the 4 priorities.

Moderators of the work packages (WP) will then have to organize, for the 4 above mentioned objectives, dedicated meetings and workshops. The purpose of these meetings, planned by using consensus conference methodology, will be to identify the key points that should be the axes of research in the next coming years in the field of preclinical and translational research in radiation oncology. Firstly, the priorities as well as the respective contributions of different partners will be identified under the supervision of the 4 WP moderators. All the identified partners will have to take part in the projects by using the existing competences and the relevant platforms in a complementary basis within the network. An annual restitution meeting, including SWOT analysis, will favor transparency, interactions and the efficiency of the network. It will provide relevant tools and arguments to the scientific committee for the elaboration and implementation of the Strategic Research Agenda (SRA) regarding the main topics identified and the road map of the project. A final web consultation will be proposed to refine the SRA and proposed road map. In parallel to the SRA, a statement on a short to medium term research agenda will be build up to improve scientific basis for improving cancer treatment.

The selected key points to be supported in priority will be transmitted to the scientific committee. The priorities will have to be supported by specific funding allocated in reply to scientific calls. They should be the base of the proposition of calls submit to INCa and Academic or Charity Associations in view to provide human and technical resources necessary to conduct in the best conditions translational and preclinical researches in the field of radiation oncology.

Identified deliverables	• Appointment of the moderators of the WP • Inventory analysis of the national expertise and infrastructures • Strategic research agenda definition • 4 Annual workshops reports • Swot analysis • Roadmap definition • Proposition of calls

Description of collaborations and synergies between the teams and members of the network:

Synergy between clinical and scientific relevance will drive the elaboration of the SRA. As described above, a scientist with a biology background, a clinician and a medical physicist will lead the implementation of the Strategic Research Agenda for each of the four axes. This will include Workshops organization and working group definition. To assure an open and inclusive discussion and the development of the SRA, the contribution from a large number of clinicians, and physicists will be expected (National Scientific Societies such as SFRO, SFPM, DOSEO, French Society of Cancer

etc. …). At least, two joint seminars will be organized together with the medical and physics societies covering practice in radiotherapy (SFRO and SFPM). Moreover, SFPM organizes annual international workshop for young scientists about scientific topics. All existing research institute and networks will be associated to this task (CEA, IRSN, DOSEO, CNRS, INSERM, Cancéropôles and SIRICs …). Most of them are identified and expressed their interest in working in this network for the above mentioned purpose (see annex 8.2). It is planned to develop a living document and to identify research areas of joint interest where progress may benefit from contributions from advanced dosimetry, radiobiology, system biology, physics and mathematics developments. Patient associations will be also asked to take part in these open discussions. The SRA will be on open access on the RADIOTRANSNET website and open for large consultation and implementation.

International relevance

The proposed national strategy for radiotherapy will be highly interconnected thanks the preselected members of the scientific committee and their respective affiliation in European medical and scientific associations. Under the supervision of the moderators of each axes, the organization of the workshop will include the participation of the international community to exchange facts and opinions so that the discussions and the SRA implementation will take into account national and international views on radiotherapy practice. 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 network, Enlight, PTCOG, CERN and other dedicated scientific networks including other specialists. Also, interaction with EU existing research platforms including EURADOS, EURAMET, EURAMED ... will be developed to anchored the national view of preclinical research for radiation oncology in the European landscape. This will increase RADIOTRANSNET's impact and avoid duplication of efforts and improve RADIOTRANSNET dissemination and consensus-building efforts.

Expected outcomes (collaborations, synergy, visibility…)

Several reports and specific meetings aiming to identify the strengths of French research in radiation oncology pointed out the dynamism and originality of the achievement of researches in radiobiology and in medical physics. The major weaknesses are well known such as the spreading of the human and technical resources, the lack of funding and dedicated academic or industrial calls, particularly considering the translational and preclinical axes. In this context, the initiative taken by the French National Society for Radiation Oncology (SFRO) and the French National Society for Medical Physics (SFPM) devoted to all partners and structures involved in this purpose is a major opportunity to structure translational research in the field of Radiation Oncology preparing clinical research through large studies aiming to benefit to the patients.

A large scientific community, including experts in the field and representatives of research institutes (CEA, CNRS, INSERM, IRSN), health professional associations (SFRO, SFPM) and federations of public and private hospitals (SNRO, FHF, Unicancer) will take care about creating networks around these challenges organized around the 4 proposed major issues of clinical practice in radiation oncology: target definition, normal tissue, combined treatments and dose modelling. The sub-targets linked to these 4 major axes are not limited. They include all aspects associated to fundamental radiobiology, preclinical studies, imaging, medical physics research and transversal components obviously associated to these scientific domains such as medical oncology, radiology, nuclear medicine and

cost effectiveness consideration. A bottom-up process under the supervision of a steering committee and a scientific committee is proposed by the RADIOTRANSNET proposal to promote inter-disciplinarity, gathering existing national research initiatives, promoting synergies and favoring connection between research groups and technological platforms.

As described above, active collaboration between clinical and scientific relevance will drive the elaboration and implementation of the SRA regarding the four major topics identified. Synergy between advanced dosimetry, radiobiology, system biology, physics and mathematics will enhance clinical practice and radiation protection in the medical field. This should also allow standardization and harmonization of methods and endpoints. The SRA will be on open access on the RADIOTRANSNET website for large consultation and implementation. A second step will be dedicated to the proposal of a roadmap as an expected outcome of this project. Moreover the publication of RADIOTRANSNET reports and recommendations on good practice for better radio-oncology and communications during national and international congress will increase RADIOTRANSNET's impact.

The final objective of RADIOTRANSNET is to give itself the means to develop new strategies for better patient care with radiotherapy. Besides the structuration of the scientific and medical community, RADIOTRANSNET aim to increase partnerships with pharma in order to facilitate drug development for combined therapy and clinical trial initiation.

In order to achieve the objectives of the project and to 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 (researcher, students, research organization in the field of radiobiology, oncology, physic…), national and international platforms (EURADOS, EURAMED, MELODI, EURAMET…), medical community (clinicians, including oncologist, radiation oncologists, medical physicist, specialist in cardiology, pneumology, neurology, general practitioners), National and European medical scientific societies (SFRO, ESTRO, SFPM, EFOMP, …), healthcare authorities and regulators (DGS, ASN …), patients and patients organization (ARC, LNCC, European Patient's Forum, …).

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

8.1 Organization of the network

The application must present well-defined and detailed governance, in which responsibilities and tasks are clearly ascribed.

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.

- **<u>Organization of the network</u>**

The application is led by one coordinator. During the next coming 2 years, the coordination will be managed by Professor Philippe MAINGON, Chairman of the French Society of Radiation Oncology. He will organize and supervise the activities of the scientific committee. The background and the CV of the coordinator are exposed in the section 11.1 of this application.

1- Coordinator:

During his chairmanship of the Radiation Oncology department in Centre Georges-François Leclerc in Dijon, the coordinator developed several preclinical research activities in the field of imaging. He worked on researches in immunology of the environmental normal tissue. He coordinated the SARI national PHRC project dedicated to study the clinical, biological and dosimetric predictive factors associated to the occurrence of sarcoma developed in irradiated area.

He was appointed as 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 offered to pharmaceutical companies the opportunity to study in a selected network of institutions working in the field of radiobiology, radiosensitivity of tumoral cells, radio-resistance and interaction with normal tissue during the early introduction of combined treatments for various tumoral localizations in which chemo-radiation demonstrated their superiority over radiotherapy alone.

2- Steering committee:

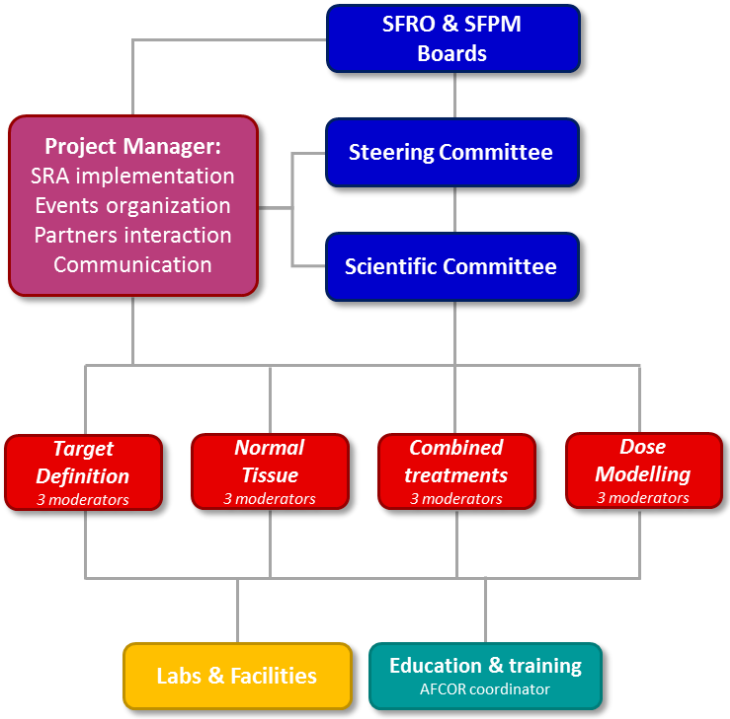
A steering committee will have a supervisory role in the definition of the topics developed by the network. Three representatives of SFRO; one for Unicancer (Pr Marc-André Mahé), one for the CHU (Pr Philippe Giraud) and one for the private practice (Dr Fabrice Denis) and three representatives of the SFPM to be nominated will be members of the steering committee. Other national medical society such as the French Radiology Society or the French Nuclear Medicine Society will each appoint one representative. One representative of the "End users" (patient associations) will be

nominated as member of the Steering Committee. The chair (or the co-chair) of the Scientific Committee will be invited as well as INCa representatives as observer. It will check whether the activities of the scientific committee are running as expected by the SFRO and the SFPM boards. It will have a look at the use of the funding provided by INCa to launch RADIOTRANSNET and will meet every year. All members will be appointed for 2 years. Their mandate might be renewed only once.

3- Scientific committee

The Scientific committee will develop and promote consensus approach for the elaboration of a SRA and associated road map relevant to preclinical research for radiation oncology. In the framework of RADIOTRANSNET, a scientific committee has been created in order to reply to the INCa call on behalf SFRO and SFPM. It is composed of 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 section 2).

- The scientific committee will have the responsibility to nominate the 4 WP moderators including one medical doctor, one biologist and one physicist. The participation of several international experts to exchange facts and opinions will be organized so that the discussions and SRA implementation will take into account national and international views on radiotherapy practices.
- At the beginning of the project, a kick-off meeting will allow the scientific committee to define in a more detailed way the priority objectives within the 4 previously identified challenges and define with accuracy the methodology that will be applied to harmonize the activities of the network. Also, the format of the deliverable (workshops report) will be defined. The purpose of the 4 workshops will be to identify the targets that should be studied by using the network of complementary competences previously listed. A preliminary list of partners is provided in section 8.2 of the application. They will have to define under the supervision of the moderators the list of priorities and who and where the tasks will be conducted.
- The scientific committee will arrange measures for receiving feedback from coordinators regarding research programs that will be submitted to the scientific committee.
- Implementation of participative web-consultations (through RADIOTRANSNET website) will help to get feedback from members of the network.
- The scientific committee will formulate the final version of the SRA and associated road map on the basis of the 4 workshop reports. The main challenge will be to get benefit from a large panel of competences and attract experts not only from the radiotherapy - radiobiology community, recognizing that those non - radiation experts may bring new thoughts and different views and may consider preclinical research for radiotherapy from different angles.
- The mandate of the members of the Scientific Committee will last 2 years. After this period, the Steering Committee will have the opportunity to renew or to ask for a new chair and a new co-chair of the Scientific Committee. They both will have to revise the list of the Scientific Committee members.



Coordinators	Time commitment
Philippe MAINGON	15%
Vincent MARCHESI	10%
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%

Organizational scheme of the RADIOTRANSNET network and time commitment of the scientific managers

4- Working groups

Four exploratory workshops bringing together experts representing a wide range of disciplines will be organized to explore the 4 key scientific questions raised by challenging innovative radiotherapy treatments, to identify the most promising preclinical research lines and to provide recommendations for the future. Organizers of the 4 consensus workshops will largely diffuse the information to assure transparency and inclusivity. All existing research Institute (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 …) and patient associations will be associated and invited to participate at this meetings as well as). Organizers will in addition make a selection of scientific and medical experts to ensure a large representativeness of disciplines concerned by the 4 exploratory workshops and to keep the scientific level of the conference as high as possible. Also young scientist including post-doc and PhD students will be invited to participate in the framework of AFCOR.

During the 4 workshops, the work will be planned in working group sessions where the distribution of experts among the group will be decided to ensure well - balanced representativeness of competences in each group. Each working group will choose its leader in charge of the preparation of the working sub-group report able to summarize the answers to questions and the differences expressed between experts. Finally, chairperson will present topic by topic the findings of the different working sub-groups, commonalities as well as differences to build the consensus. This step-by-step approach will allow the scientific committee to propose a Strategic Research Agenda (SRA) for radiation oncology based on the 4 previously described topics. SRA will be accessible on the RADIOTRANSNET website for a final amendment period. The SRA will be amended every years and a road map could thus be adapted.

5- Project Manager

The project manager will be in charge of providing support and assistance for the coordination and structuration of the network, maintain contact with scientific societies and partners and assist the

project coordinators for their reporting to INCa. Emilie BAYART will be recruited as project manager.

- The project manager will provide a particular attention on the timelines of the project, particularly on workshops organization and strategic research agenda implementation. She will help the axis coordinators in the organization of scientific events.
- The project manager will also promote the interaction between (radio) biology, imaging modalities and dosimetry within each defined research axis and between the four axes.
- The project manager will ensure dissemination through social networks, a specific website dedicated to these activities. This website will facilitate web-consultations at the different step of the project.
- The project manager will organize all RADIOTRANSNET meetings, at least one meeting per year. There will also be specific annual meetings organized by the WP leaders around specific themes (DNA repair, nanoparticles, mice models and preclinical irradiators and imaging, computing …).
- The project manager will be in charge of the facilitating formal liaison and communication at the European level with ESTRO and EORTC, with the EU platform including EURADOS, EURAMED, … and also with similar European incentives and networks (UK: CR-Rad, Germany –DKTK…).

The major weaknesses for such a network are well known, particularly the spreading of the human and the technical resources, which could make it difficult communication between partners and harmonization of the methods. However, this bottom-up organization should help the RADIOTRANSNET coordinators to circumvent these bottlenecks. Regular SWOT analyses will help to counteract emerging difficulties and favor transparency, interactions and the efficiency of the network. It will provide relevant tools and arguments to the scientific committee for the elaboration and the implementation of the Strategic Research Agenda.

- **<u>Education & training</u>**

1- Teaching

SFRO (SFJRO) and SFPM are involved in the organization of several education and training activities respectively in brachytherapy, radioanatomy, radiophysic and radiobiology for the SFJRO and at least 3 EPUs (enseignement post-universitaire) per year for the SFPM. Several already organized teaching and training activities related to radiotherapy involve other partners of this consortium and are mostly listed on SIRlaF's website (Société Internationale de Radiobiologie de Langue Française, http://sirlaf.free.fr/liens/cours.htm):

- DU (Diplôme Universitaire) de radiobiologie et radioprotection (Univ. Paris Sud)
- DU (Diplôme Universitaire) de radiobiologie et radioprotection (Univ. Lille2)
- DU (Diplôme Universitaire) 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)
- 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)

- Diplôme de qualification en Physique radiologique et médicale (DQPRM) (INSTN)
- DIU Thyroïdologie / DIU tumeurs endocrines (Univ. Paris Sud/Univ. Lille2)

Moreover, many institute partners of RADIOTRANSNET give access to e-learning, MOOC and seminar retransmission.

The educational and training program that should be associated to the development of RADIOTRANSNET would be planned and organized with AFCOR, in charge of the training program of French radiation oncologists, in close relationship with the coordinators of the 4 main axes. AFCOR will appoint one corresponding member who will coordinate the training program.

2- Training

Several national incentives for training in biology of physics will contribute to the support of students such as the Maurice-Tubiana grant from SFRO, and, at the local level, institutional specific PhD grants from institutions such as IRSN, CEA, Curie, Gustave Roussy, Fondation de France, ARC….

Training possibilities should be increased and supported by call proposals coming out from RADIOTRANSNET orientations based on SRA.

- **Ethics**

The RADIOTRANSNET wished to endow itself with an ethics charter that embodies the principles to which it adheres. The radiotherapy transnational network seeks to affirm by the present charter its commitment to perform research according to the ethics rules recognized by the national community. This network is at the interface of research, public health, radiation therapy, teaching and training and patients. Research undertaken in RADIOTRANSNET extents to many different fields in both basic research and its application. This charter aims to set force the rules to which the RADIOTRANSNET adheres. RADIOTRANSNET wishes to reaffirm the necessity of inscribing transnational research and the resulting progress in rigorous ethical framework that contributes to the enforcement of ethics rules for research, living subject and to the respect of human dignity and human rights. All research on human beings is inscribed in the framework of the ethics rules establish by the International community. Furthermore, all research must conform to laws and regulation in effect in France where it is conducted (Jardé's law). This charter aims to retain Personal of the legal and regulatory documents that various internal services must maintain to ensure that Personnel remain well informed. Seems the else of the patients must always be the primary concerning his or her Doctor and or scientific researcher, the interest of persons participating in biochemical research must always take precedence over the interest of sciences and society. In this regard, the benefit obtained through research must be evaluated with respect to the risks assumed by all persons concerned irrespective of whether there are research subjects in good or bad health or scientific medical or paramedical personnel. All structures, involved in preclinical or transnational research promoted by RADIOTRANSNET provided Personnel with guidance on legislative and regulatory directives applicable to research using human biological samples. This texts protected the person from whom samples were taken with respect to the inventory of samples maintain by health and research authority and including the protection of Personnel working on the samples. French law and regulatory statutes imposed strict procedures for informing patients and obtained in their consent or no 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 used for this purpose.
Research studies using human stand cells of embryonic or fetal origin must adhere strictly to legislation and regulatory statutes. A person our genetic characteristic is to be examined must be

informed previously to giving his or her consent which personal must duly comply. Moreover, RADIOTRANSNET would like to draw the attention of the Personnel to the ethical questions that often arise in a course of research on genetic predisposition and vulnerabilities.

The use of live vertebrates in biochemical research is currently supervised by the European directive 86-609 transposed into French law in 1987. This directive was revised in 2010 and its transposition is in preparation. The use of animal models for biochemical research is an essential step in the scientific activities, preceding research on human being. Research in the field of RADIOTRANSNET in the scope of the present charter should be in coherence with the regulatory text currently in force. The French text required that all establishment performing animal experimentations be approved that lead investigators in charge of protocol be authorized to perform that experiment and that all persons involved animal experiment receive appropriate training. Certain protocols must be declared and justified at the prefecture before any research can begin. Finally, any person possessing none domestic species must have a certificate of capacity. Moreover, the RADIOTRANSNET scientific council expects personnel working with animals to be aware of good practices in a development of research protocols for use on vertebrates.

Statutory operating procedures member groups of the RADIOTRANSNET network pledge to answer the following their statutes with the possibility of supplementing them with internal rules of procedure or another document:

- Creation of scientific committee for RADIOTRANSNET
- Creation of a steering committee charge with steering the SFRO, SFPM and other authorities and bodies the transnational preclinical research in Radiotherapy project.
- Creation of teaching and training program for translational and preclinical research in Radiotherapy,
- Favoring the contribution or the participation of all members reeling to promote support and participate in the design and implementation of preclinical research protocols.
- The SFRO/SFPM steering committee pledged to implement procedure that guaranty the independence of the scientific council members, transparency and management of conflict of interest.
- All members working in this RADIOTRANSNET network pledged to respect the following principal: no executive operations will be paid; no profits of any form will be directly or indirectly distributed; no group members will receive any assets.
- Effective management.

The RADIOTRANSNET commit to using management mess-ups design to optimize their use a founding accorded to them for research. In this context, it will implement procedure and checks answering appropriate and effective management of their operational research structures. It will be objective as possible in their choice of service providers and suppliers.

<u>Academic communication of all results :</u>

The members group of the RADIOTRANSNET network commits to the goal of a publishing progress in medical research in conducting research project. All results from their research project, even if negative, must be published and should be brought to the attention of the scientific community institution and public. RADIOTRANSNET is in charge with communicating their activities in a way that is both academic and transparent rendered as widely and easily accessible as possible. Every publication should mention the role of INCa in the process. The coordinator will have to remain this request to all coordinators and leaders of projects. All scientific exploitations of data are under the responsibility of the principal investigator of the study.

Financial transparency:

The members group of the RADIOTRANSNET network pledged to produce annual accounts and summary document and to answer authorities and bodies.

Role of responsibilities of the scientific committee:

The role of scientific committee of RADIOTRANSNET is to provide independent effective leadership in supervising a management of network. The responsibility of the scientific committee included: adopting a strategic planning process, answering that procedure in favor for the management of the research in the access of trial defined by the council. It should renew on approve annual operating plan on budget.

Scientific committee will adopt measures for receiving feedback from coordinators regarding research program that 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 program.

8.2 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 to have a complete overview of the partnership available with RADIOTRANSNET, including orientations of the partners in the four major topics, expertize, available equipment's, ongoing collaborations (national, international, academic and/or industrial) and funding.

Quality of the network:

RADIOTRANSNET aim to federate actors in the field of radio-oncology at all institutional levels.

- At the time of this application, RADIOTRANSNET is accounting for more than 80 research teams included in about 70 research groups or units. It includes experts in the field and representative of research institutes from public and private statutes (CEA, CNRS, INSERM, IRSN, Universities), federations of public and private hospitals (SNRO, CHU, CRLCC, Unicancer) and several specific institutions as Cancéropôles, SIRIC, IRBA,…etc, that 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 to these health professional associations or other academic societies in the field (DOSEO, French Society of Cancer, SIRIaF, …etc.).
- Additionally, activity of many of these groups are supported and labelled by patient's associations (LNCC, ARC, FRM, Fondation de France, …etc), showing that those associations are aware and sensitized to some of the radio-oncology problematics. It will facilitate their participation to the reflection and exchange on the topics to be supported in priority and

how to finance them.

The activities of such a network should lead to innovative strategies and subsequent Phase I and II trial propositions. The project greatly depends on the implication of industrial partners in the field of imaging, radiotherapy and pharmaceutical industry. Many Teams have developed partnerships with dozens of industrials (as listed in the provided annex) at their individual level. The structuration of RADIOTRANSNET and the convergence of priorities should reinforce industrial partnerships at the all network level, allowing better promotion of early clinical trials.

National and international scale:

The RADIOTRANSNET network aim to involve actors at all territorial levels. The scientific community already identified (hospitals, research institutes and platforms) is spread all over France. A summary of each team is given in the table provided in the annex where they are ranked by cities of location in France, showing that all regions represented. Existing local, regional or national groupings or identified, and often labelled, collaborations are mentioned and recalled in the annex. Actually, several regional collaborations are existing, in particular thanks to Cancéropôles network and on which RADIOTRANSNET will also rely on, showing the rising effort of collaboration. The national and international scale of some teams is obvious viewing their existing collaborations that are detailed. RADIOTRANSNET will use this ongoing dynamic to reach its own goal of federation at the national scale, being in contact with national authority (INCa, Ministry of higher education and research, Ministry of health and associated funding instruments). This is a very valuable chance to draw all the RADIOTRANSNET quickly at an international level of quality and visibility. In addition to the existing collaboration, this will rely on participation to recognized international congress, such as ESTRO, ASTRO, AACR, PTCOG,…etc., and on liaison and communication with EORTC and similar international incentives and networks (CR-Rad, DKTK, EURATOM, LIFE SCIENCE, EURAMET …).

The added-value of the network through the active synergies and complementarities will be easy to establish, since this overview, almost exhaustive, of the French teams acting in the preclinical research domain shows the similarities and the complementarities related to radio-oncology: radiotherapy, chemotherapy, targeted therapy, radiobiology, radio-pathology, genetic, system biology, stem cell biology, immunology, vascular biology, physics, dosimetry, imaging, mathematics, machine learning,...etc. The similarities will urge to work together, to build critical mass in critical domains and to converge on specific tasks. The complementarities will allow strengthening multidisciplinary domains and here also to gain critical mass to succeed in the collaborative activities. The provided table is the initial tool addressed by joining teams to RADIOTRANSNET to structure the network to address its scientific objectives.

Relevance, originality of the network

The objective of this project is to set-up a high level pre-clinical network able to 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 RADIOTRANSNET initiative is driven by health professional associations. This organization ensures to point out the critical problematics related to radio-oncology to which the medical community and patients are faced during cancer treatment. All the identified partners will have to take part in the projects by using the existing competences and the relevant platforms in a complementary basis within the network. Many teams have added originalities, in particular regarding their specific equipment (imaging equipment, source types, preclinical facilities, equipment for specialized biological analyses, simulation algorithms) and their local collaborations. In particular, the very multidisciplinary figure of preclinical research in radiotherapy is largely demonstrated by the participation of all the scientific bodies of France. This network will make easier the development of collaboration that will be often the extension of

already existing collaborations. The organization and the richness of the RADIOTRANSNET should allow the implementation of high quality and efficient preclinical research.

9 Calendrier et étapes clés du projet / Schedule and milestones

1) The **scientific committee** will **nominate** one medical doctor, one biologist and one physicist as **co-coordinators of each** above defined **axis**.

2) At the beginning of the project, a **kick-off meeting** will allow the scientific committee to define in a more detailed way the priority objectives within the four axes and define with accuracy the methodology that will be applied to harmonize the activities of the network.

3) A dedicated website will be created to ensure visibility, consensus approach between the 4 major axes, web-consultations and communication and transparency on RADIOTRANSNET actions.

4) **Four exploratory workshops** bringing together experts representing a wide range of disciplines (radiotherapy, chemotherapy, targeted therapy, radiobiology, radio pathology, genetic, system biology, stem cell biology, immunology, vascular biology, physics, dosimetry, imaging...) **will be organized**. The purpose of the 4 workshops will be to define the research directions that should be explored creating a multidisciplinary approach of the topic and taking advantage of the network of complementary competences as previously listed. A consensus methodology will be defined by the scientific committee. During the 4 workshops, the work will be planned with moderators among sub-groups to ensure well-balanced representativeness of competences. The chair will summarize the answers to questions asked by each working sub-group and highlight as much as possible the differences expressed between experts. Researchers produce consensus statements will be expected on objective evidence-based opinions.

5) **Chairpersons** of each working group **will report** to the scientific committee topic by topic the findings of the different working sub-groups, commonalities as well as differences to find a consensus.

6) Based on 4 consensus conferences reports, **the scientific committee will build a Strategic Research Agenda** (SRA) for radiation oncology based on the 4 workshop reports. This research strategy agenda will be refining through large web-consultation. The final version will be exposed and validated during the annual general assembly of the RADIOTRANSNET network.

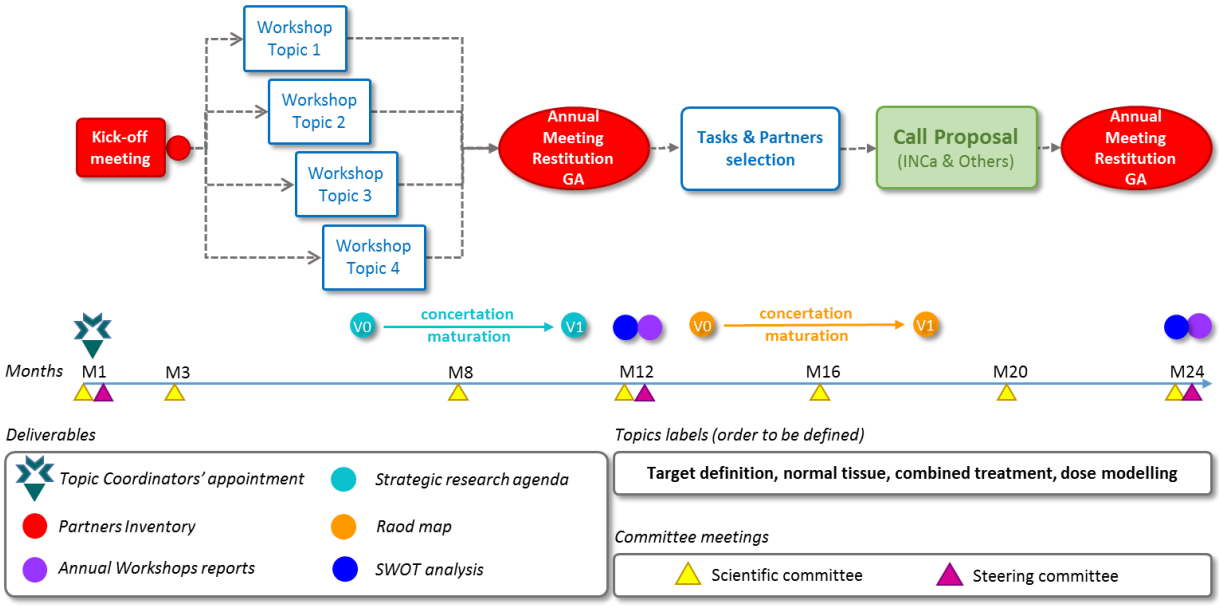
7) Following the 4 workshop reports and consistent with the SRA, a **road map** will be proposed by the scientific committee before a final large web consultation and defined using the network of complementary competences.

8) This step-by-step approach will allow **the scientific committee** to **select targets to be supported in priority**. It will be the **basis of the proposition of calls** submit to INCa and Academic or Charity Associations in view to provide human and technical resources necessary to conduct in the best conditions translational and preclinical researches in the field of radiation-oncology.

9) Depending on funding instruments supports, SRA and road maps will be amended during annual meeting.

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	7 Septembre 2018	Defined by INCa
Appointment of the **moderators of the 4 axis** by the Scientific Committee	October 2018	One month required for moderators' appointments after RADIOTRANSNET validation from INCa
Kick-off Meeting with moderators of the 4 axis	November 2018	One month required to plan kick off meeting with all moderators
Workshops	January - April 2019	2-4 months required to organize 4 workshops with partners (some involved in several axis)
Selection of the priorities transmitted to the Scientific Committee	May - August 2019	Concertation and maturation for SRA generation (4 months)
Restitution meeting	September 2019	Restitution will be performed during the general assembly (annual meeting)
Selection of tasks and partners	October 2019 - January 2020	3-4 months required to define road maps
Calls proposal to INCa and others funding instruments	February 2020 – July 2020	6 months required to exchange with moderators of funding instruments on radio-oncology priorities
Restitution meeting	September 2020	Annual meeting and general assembly



Representative scheme of key steps and timelines

10 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 concerning RADIOTRANSNET ongoing activities will be made through **social networks**, a **specific web page** and **email newsletters**, which will be monitored by the project manager.

At least, one annual **restitution meeting** and a **general assembly**, including the steering committee, will be organized. An **annual report** will be provided to the steering committee and **transmitted** to INCa after validation. It will be **published** and **transmitted to** the knowledge of the **public health authorities**, and will be available on the website of RADIOTRANSNET, the SFRO and the SFPM websites.

There will be **formal liaison and communication at the European level** with ESTRO and EORTC, the European plateforms (EURADOS, EURAMET, EURAMED …) and also with similar European incentives and networks (UK : CR-Rad, Germany –DKTK…).

Each consensus **meeting report** will be **published in scientific and medical journal** (for example the Cancer Radiotherapy journal) for scientific dissemination for the medical and scientific community.

The **SRA** and **roadmap will be published** on the RADIOTRANSNET website and open for large consultation and public implementation during the maturation phase under the supervision of the scientific committee. They will be finally published, as a scientific and medical review, for French as well as for international community, following the Recorad model from SFRO, in radio-oncology oriented journal.

Results will be **presented during international meetings** including NCI-AACR-EORTC new drugs meeting, ESTRO, ASTRO, AACR, PTCOG and many others encompassing session dedicated to radiotherapy. Translational research and clinical research will be performed under the umbrella of collaborative groups such as EORTC, UNICANCER and organ oriented groups such as GERCOR, FFCD, GORTEC, IFCT ... There will be a yearly meeting in the form of a specific session during the SFRO annual meeting and SFPM international meeting. Altogether, the actions implemented by the RADIOTRANSNET, through **the structuration of a network focused on radiotherapy challenges**, should lead to the **synergistic activity of actors from many disciplinary fields**: dosimetry, radiobiology, system biology, physics and mathematics developments. RADIOTRANSNET aimed to **reinforce existing collaborations** and to **federate new ones** to develop new strategies for better management of cancer with radiotherapy. This should result in **an increase of scientific production** and might be illustrated by **scientific and medical publications**, **patent registrations** and, hopefully for patients, **clinical trial initiations.**

11 Compétences et expertises /Skills and expertises

11.1 Coordonnateur / Coordinator

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

CURRICULUM VITAE

Philippe MAINGON

Date and place of birth: February 9th, 1957, Reims, France.

ACADEMIC TITLE
Professor in Radiation Oncology

ADDRESS
Radiation Oncology Department
Groupe Hospitalier Universitaire La Pitié-Salpêtrière-Charles Foix
47-83, boulevard de l'hôpital
Pavillon Antonin Gosset
75013 Paris

1.1 PRESENT POSITION

Radiation Oncologist
Head of Radiation Oncology Department

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

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

ADMINISTRATIVE APPOINTMENTS

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 - 2017	Medical Expert in Radiation Oncology for Dijon Appeal Court
2013 - 2017	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 - 2017	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	Editorial Board Member for Radiotherapy & Oncology
2015	Editorial Board Member for Frontiers Head and Neck Cancer

CLINICAL ACTIVITIES

1990	Patients treated in a clinical research protocols: 925
1999	Member of the Scientific Committee of the French foundation: Fondation Française de Cancérologie Digestive (FFCD)
2010 - 2015	Investigator in clinical research protocol: 28 studies Number of patients included: 269 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

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 - 2017 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.

ICH GCP training validated on 1999, 2013, 2015.

Principales publication 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. New challenge of developing combined radio-drug therapy
   Maingon P, Govaerts AS, Rivera S, Vens C, Shash E, Grégoire V.
   Chin Clin Oncol. 2014 Jun;3(2):18.2304-3865

2. The role of telomeres in predicting individual radiosensitivity of patients with cancer in the era of personalized radiotherapy.
   Mirjolet C, Boidot R, Saliques S, Ghiringhelli F, **Maingon P**, Créhange G.
   Cancer Treat Rev. 2015 41(4):354-60.

3. Creating a data exchange strategy for radiotherapy research: towards federated databases and anonymised public datasets.
   Skripcak T, Belka C, Bosch W, Brink C, Brunner T, Budach V, Büttner D, Debus J, Dekker A, Grau C, Gulliford S, Hurkmans C, Just U, Krause M, Lambin P, Langendijk JA, Lewensohn R, Lühr A, **Maingon P**, Masucci M, Niyazi M, Poortmans P, Simon M, Schmidberger H, Spezi E, Stuschke M, Valentini V, Verheij M, Whitfield G, Zackrisson B, Zips D, Baumann M.
   Radiother Oncol. 2014 113(3):303-9.

4. The radiosensitization effect of titanate nanotubes as a new tool in radiation therapy for glioblastoma: a proof-of-concept.
   Mirjolet C, Papa AL, Créhange G, Raguin O, Seignez C, Paul C, Truc G, **Maingon P**, Millot N.
   Radiother Oncol. 2013 ;108(1):136-42

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 Role of radiotherapy fractionation in head and neck cancers (MARCH): an updated meta-analysis.

Lacas B, Bourhis J, Overgaard J, Zhang Q, Grégoire V, Nankivell M, Zackrisson B, Szutkowski Z, Suwiński R, Poulsen M, O'Sullivan B, Corvò R, Laskar SG, Fallai C, Yamazaki H, Dobrowsky W, Cho KH, Garden AS, Langendijk JA, Viegas CMP, Hay J, Lotayef M, Parmar MKB, Aupérin A, van Herpen C, **Maingon P**, Trotti AM, Grau C, Pignon JP, Blanchard P; MARCH Collaborative Group. Lancet Oncol. 2017 (9):1221-1237.

2 Prognostic Factors for Local Control in Breast Cancer After Long-term Follow-up in the EORTC Boost vs No Boost Trial: A Randomized Clinical Trial.

Vrieling C, van Werkhoven E, **Maingon P**, Poortmans P, Weltens C, Fourquet A, Schinagl D, Oei B, Rodenhuis CC, Horiot JC, Struikmans H, Van Limbergen E, Kirova Y, Elkhuizen P, Bongartz R, Miralbell R, Morgan DA, Dubois JB, Remouchamps V, Mirimanoff RO, Hart G, Collette S, Collette L, Bartelink H; European Organisation for Research and Treatment of Cancer, Radiation Oncology and Breast Cancer Groups. JAMA Oncol. 2017;3(1):42-48.

3. Short Androgen Suppression and Radiation Dose Escalation for Intermediate- and High-Risk Localized Prostate Cancer: Results of EORTC Trial 22991.

Bolla M, **Maingon P**, Carrie C, Villa S, Kitsios P, Poortmans PM, Sundar S, van der Steen-Banasik EM, Armstrong J, Bosset JF, Herrera FG, Pieters B, Slot A, Bahl A, Ben-Yosef R, Boehmer D, Scrase C, Renard L, Shash E, Coens C, van den Bergh AC, Collette L. J Clin Oncol. 2016;34(15):1748-56.

4 Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer.

Poortmans PM, Collette S, Kirkove C, Van Limbergen E, Budach V, Struikmans H, Collette L, Fourquet A, **Maingon P**, Valli M, De Winter K, Marnitz S, Barillot I, Scandolaro L, Vonk E, Rodenhuis C, Marsiglia H, Weidner N, van Tienhoven G, Glanzmann C, Kuten A, Arriagada R, Bartelink H, Van den Bogaert W; EORTC Radiation Oncology and Breast Cancer Groups. N Engl J Med. 2015;373(4):317-27.

5 Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial.

Bartelink H, **Maingon P**, Poortmans P, Weltens C, Fourquet A, Jager J, Schinagl D, Oei B, Rodenhuis C, Horiot JC, Struikmans H, Van Limbergen E, Kirova Y, Elkhuizen P, Bongartz R, Miralbell R, Morgan D, Dubois JB, Remouchamps V, Mirimanoff RO, Collette S, Collette L; European Organisation for Research and Treatment of Cancer Radiation Oncology and Breast Cancer Groups. Lancet Oncol. 2015;16(1):47-56.

6 Pathological response and safety of two neoadjuvant strategies with bevacizumab in MRI-defined locally advanced T3 resectable rectal cancer: a randomized, noncomparative phase II study.

Borg C, André T, Mantion G, Boudghène F, Mornex F, **Maingon P**, Adenis A, Azria D, Piutti M, Morsli O, Bosset JF. Ann Oncol. 2014;25(11):2205-10.

7 Outcome impact and cost-effectiveness of quality assurance for radiotherapy planned for the EORTC 22071-24071 prospective study for head and neck cancer.

Weber DC, Hurkmans CW, Melidis C, Budach W, Langendijk JH, Peters LJ, Grégoire V, **Maingon P**, Combescure C. Radiother Oncol. 2014;111(3):393-9.

8 Fluorouracil-based adjuvant chemotherapy after preoperative chemoradiotherapy in rectal cancer: long-term results of the EORTC 22921 randomised study.

Bosset JF, Calais G, Mineur L, **Maingon P**, Stojanovic-Rundic S, Bensadoun RJ, Bardet E, Beny A, Ollier JC, Bolla M, Marchal D, Van Laethem JL, Klein V, Giralt J, Clavère P, Glanzmann C, Cellier P, Collette L; EORTC Radiation Oncology Group. Lancet Oncol. 2014 ;15(2):184-90.

9 Development of clinical trial protocols involving advanced radiation therapy techniques: the European Organisation for Research and Treatment of Cancer Radiation Oncology Group approach.

Fairchild A, Bar-Deroma R, Collette L, Haustermans K, Hurkmans C, Lacombe D, **Maingon P**, Poortmans P, Tomsej M, Weber DC, Gregoire V. Eur J Cancer. 2012;48(7):1048-54.

10 Radiotherapy and androgen deprivation for prostate cancer.

Créhange G, Bolla M, **Maingon P**. N Engl J Med. 2011 ;365(14):1354-5.

11.2 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)*

Co-Coordinator / CURRICULUM VITAE

Vincent MARCHESI

5 September 1974
Married, 2 children

Institut de Cancérologie de Lorraine
Radiation Therapy Department, Medical Physics Unit

Phone: 03 83 59 85 36
Email: v.marchesi@nancy.unicancer.fr

Professional experience

May 2003 - … : **Medical Physicist**, Radiotherapy, Institut de Cancérologie de Lorraine, Vandoeuvre les Nancy (0,8 FTE).
April 2007 - … : Head Medical Physicist, Centre Hospitalier Emile Durkheim, Epinal (0,2 FTE).
2001-2003: Part time **Medical Physicist** (replacement during holidays of the full medical physicist), Centre d'Oncologie de Gentilly, Nancy.

Education

2003: PhD **(Thèse de Doctorat spécialité Rayonnements et imagerie en médecine**). "Problématique du Contrôle de qualité en RCMI". Institut National Polytechnique de Lorraine. Nancy.

2001: Medical Physicist Certification (**DQPRM**), Hôpital des Armées du Val de Grâce, Paris.
1999: Post-Graduate degree in Medical Physics (**DEA Physique Médicale**), Université de Toulouse.
1999: Biomedical Engineer Diploma, Ecole Supérieure d'Ingénieurs de Luminy, Université Aix-Marseille.
1998 : Master 1 in Physics Sciences, Université de Nice-Sophia-Antipolis.

Societies

2016-... : President of SFPM
2011-2016: Vice -president of SFPM in charge of training matters.
2016: Chairman of the Scientific Committee of SFPM Annual Meeting
2015: Member of the Scientific Committee of SFPM Annual Meeting
2011, 2012, 21013, 2014, 2016 : Member of the Scientific Committee of Enseignement Post-Universitaire on IMRT for SFPM (Rennes)
2011, 2012, 2013 : Co-chairman of training course on IMRT (SFRO/AFCOR/SFPM)
2013, 2014 : Co-chairman of training course on Stereotactic Radiation Therapy (SFRO/AFCOR/SFPM)
2003 - 2011 : Co-chairman of the Medical Physics Group of GORTEC (Head and Neck Oncology Radiotherapy Collaborative Group)

Teaching activities

Medical Physicist Certification (DQPRM), Institut National des Sciences et Techniques Nucléaires, Saclay
Graduation of Medical Physics (Master 2), Université de Toulouse
Graduation of Biomedical Engineer School, Université de Lorraine, Nancy
Radiologic Technologist School, Nancy

CURRICULUM VITAE

David AZRIA

Citizenship, Age: French, 46 years old
Current Positions:
Head of the Radiation Oncology Department (Montpellier Cancer Institute)
Scientific Director of Montpellier Cancer Institute
E-mail: david.azria@icm.unicancer.fr
Fields of competence: Radiation Oncology, Radiobiology, Medical Oncology.

University Education

2006: Research Director Habilitation in Radiobiology (HDR), Faculty of Medicine, Montpellier
2004: PhD Degree, Faculty of Medicine , Montpellier
2001-2002: Fellowship, University of Lausanne, Switzerland
2001: Radiation Oncology specialization
2001: Doctorate of Medicine, Montpellier University
2000: Master of radiobiology, Faculty of Medicine Kremlin Bicêtre, Paris
1999: Master of science, Faculty of Medicine, Montpellier

Professional Cursus

2016-2019: President elected of the National Council of Teachers in Oncology (CNEC)
Since 2016: Scientific Director of the Montpellier Cancer Institute
2015-2018: President elected of the UNICANCER Committee of Research and Development in

Radiation Oncology (UNITRAD)

Since 2013: Head of the SIRIC Radiobiology research program

Since 2012: Head of the Radiation Oncology Department (Montpellier Cancer Institute)

Since 2012: Europe clinical lead of the FP7 research program REQUITE (European Commission)

2011-2016: President of the Medical Council (Montpellier Cancer Institute)

Since 2009: Medical Professor in Radiation Oncology (First Class)

Administration, Scientific, Clinical or industrial Expertise & responsibilities

Founder of the start-up "NovaGray"

Head of project of tumor immunotargeting and radiobiology applied in oncology, Inserm U1194, cancer institute ICM Montpellier-France

Head of project of the phase I Department combining new drugs with ionizing radiation (label from the French national cancer institute, INCa)

Teaching experience (including Dissemination of Scientific Information)

President of the National College of Teachers in Oncology

Head of the Oncology program at the Montpellier University (students in Medicine)

Founder of the website: http://www.nova-gray.com/

Editorial Board and Participations in National and International Scientific Networks

Board Member of:

- 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
- Radiation Oncology
- Radiotherapy and Oncology
- Cancer Radiothérapie

Patents, Industrial Exploitation & consulting

- 5 patents in radiotherapy
- Research collaboration contracts with industry: Roche, Bayer, Genentech

Awards

French Ministry of Research: i-lab2016 Laureate

American Society for Radiation Oncology (ASTRO) Abstract Award 2015, San Antonio

Prevot Fondation Award, Geneva 2013, Switzerland

Prevot Fondation Award, Geneva 2012, Switzerland

Prevot Fondation Award, Geneva 2011, Switzerland

Prevot Fondation Award, Geneva 2010, Switzerland

The Swiss Society of radiobiology and Medical Physics (Varian Award), December 2008

Research in Radiobiology Award, Paris, November 2008, France

Research in Radiobiology Award, Paris, June 2007, France

Prevot Fondation Award, Geneva 2004, Switzerland

Research in Radiobiology Award, Paris, June 2004, France

GEFLUC Clinical Research Award, Montpellier 2003, France
Breast Research Award, Journées Françaises de pathologies mammaires, Nice 2002, France
Lilly Oncologie 2002 Award Special Mention, Eurocancer, France
University Award Gold Medal Paul-Sabatier 1995
University Award Gold Medal Paul-Sabatier 1994
University Award Silver Medal Paul-Sabatier 1993

Memberships

Member of the French National Society of Radiation Oncology Executive Board (SFRO)
Member of the European Society for Medical Oncology (ESMO)
Member of the European Society for Radiotherapy and Oncology (ESTRO)
Member of the American Society of Clinical Oncology (ASCO)
Member of the American Society for Radiation Oncology (ASTRO)
Member of the Clinical Research Program in Oncology Board (PHRC) of the French National Cancer Institute (INCa)
Member of the Clinical Research Program in Pediatric Oncology Board (PAIR PEDIATRIE) of the French National Cancer Institute (INCa)
Member of the International Radiogenomic Consortium (RGC)

Scientific Production

396 publications : H Factor: 32; number of citations: 3793

CURRICULUM VITAE

JACQUES BALOSSO

Citizenship: French
Date of birth: 10 December 1960
Current address:
Service de Radiothérapie
CRLCC François Baclesse
3 rue du Gral Harris
F-14000 CAEN

N° RPPS : 10000537505
N° ADELI : 38 10 71 02 6
N° CNOM : ex 38/07102

Phone: +33(0)2 31 45 50 50**/**5845
E-mail: JBalosso@chu-grenoble.fr

Education & University positions

- **1986:** Nomination à l'Internat de Montpellier, inter-région Sud, 2/167;
- **1988:** D.E.A. des "Bases fondamentales de l'oncogenèse",
- **1990:** Thèse de doctorat de Médecine à Montpellier.
- **1990:** Diplôme d'Etudes Spéciales d'Oncologie option Radiothérapie.
- **1990:** Chef de clinique assistant à la Faculté St-Antoine (Paris 6) et l'Hôpital Tenon, Paris.
- **1996:** Diplôme d'Etudes Spéciales Complémentaires de Cancérologie.
- **1997:** Doctorat es Sciences l'Université Paris VII.

- 2001: Habilitation à diriger des Recherches, Université Joseph Fourier, Grenoble1 (UJF)
- 2003: Professeur des Universités en cancérologie radiothérapie à l'UJF
- 2017: Détachement à temps complet auprès du Centre François Baclesse à Caen

Scientific experience & project Managment

1988-89: Unité INSERM 350, Institut Curie, DEA étude des interactions Chimiothérapie- Irradiation. Poursuite dans ce laboratoire des travaux au retour des USA.
1991-1993: 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
1995-98: - Activités d'évaluation scientifique: membre nommé de la Comm. Scientif. Spé. n°2 de l'INSERM
Since 1999: Coordonninateurde 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.
2007-2014: Directeur du Groupement de coopération sanitaire GCS-ETOILE (www.centre-etoile.org)
2013-2017: Fondateur et coordonnateur de l'infrastructure nationale de recherche France HADRON
2011-2016: President of the Medical Council (Montpellier Cancer Institute)
Since 2018: - Coordonnateur scientifique du projet ARCHADE de recherche en hadronthérapie

Clinic Activities

- 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 CNAMTS

Principal teaching activities

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

Publication

About 90 international publication since 1991

CURRICULUM VITAE

Marc BENDERITTER

8 July 1966

Institut de Radioprotection et de Sûreté Nucléaire
31, avenue de la Division Leclerc
BP17- 92262 Fontenay-aux-Roses

Phone: 33 (0)1 58 35 91 36

Email: marc.benderitter@irsn.fr

Professional experience

Head of the Department of Radiobiology and Regenerative Medicine in IRSN. Extensive experience in radiobiology and radiopathology (up to 100 scientific publication).

Education

PhD in Pathophysiology and Pharmacology.

Societies

Chairman of the International Association of Radiopathology. IRSN representative for the World Health Organization (WHO) collaborating Centre for Radiation Protection. Senior expert for the International Atomic Energy Agency of (IAEA) in case of Radiation Emergency Medical Preparedness & Assistance, participated in the management of up to 10 radiological accidents (Chile-2006, Belgium-2007, Senegal-2007, Tunisia-2008, Ecuador-2009, Venezuela-2010, Gabon-2010, Bulgaria-2011, Peru-2012 and Peru-2014). Member of the European Radiation Research Society (ERRS) board.

Grants

Currently,
Task leader of the EU project "Implications of Medical Low Dose Radiation Exposure" (MEDIRAD, 2017-2020), 10 Meuros.

Leader of the ANR-RSNR project "Repeated stable Iodine prophylaxis in accidental situation" (PRIODAC 2014-2019), 6 M euros.
Contributor of the INCA project "Clinical phase II trial evaluating the efficacy of systemic Mesenchymal Stromal Cell (MSCs) injection on the symptomatology of severe and chronic in radiotherapy-induced abdomino-pelvic complications (pelvic radiation disease, PRD) refractory to standard therapy" (PRISME, clinical trial NCT 02814864), to the "Early clinical and biological predictors of radiotherapy-induced cardiac toxicity in breast cancer" BACCARAT and "Etude épidémiologique de la neurotoxicité liée à la radiothérapie pour un gliome cérébral de haut grade" (EPIBRAINRAD) project.

Contributor of the ANR project "Generation of hematopoietic stem cells from non-hematopoietic iPS in patients with acute irradiation syndrome an innovative therapeutic strategy of hematopoietic syndrome" (GIPSI, 2015-2017) and the ANR project "EXOsomes des Cellules souches pour le Traitement des brûlures radiologiques" (EXOCET, 2017-2019).

CURRICULUM VITAE

Elizabeth COHEN-JONATHAN, M.D., Ph.D.

Married Name : MOYAL

Head of the Radiation Oncology department of IUCT-O and Head of the translational research team on Glioblastoma Radioresistance , INSERM UMR1037, CRCT.

Office Address: Department of radiation Oncology-IUCT-Oncopole-1 avenue Irene Joliot Curie-

31059 Toulouse Cedex-France
Email : moyal.elizabeth@iuct-oncopole.fr

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 Full Professor in Radiation Oncology
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
- Head of the Radiobiology team INSERM U1037, CRCT, Toulouse, France
- Head of the Brain tumor committee of the Cancer University Institute (IUCT),Toulouse, France
- Radiotherapy of the central nervous tumors
- Head of the oncology teaching for the students in School of medicine
- Head of the regional teaching for the residents in Radiation Oncology
- National and local teaching for students in Biology (Master, PhD)
- National Teaching for students in neuro-oncology

Scientific and administrative functions

- Member of executive board of the European Neuro-Oncology society (EANO)
- Member of the National scientific committee (CSS2) of the French National institute for medical research (INSERM)
- Member of the national scientific committee of the Foundation for Cancer Research (ARC)

- Member of the board of direction of the Toulouse Research Cancer Center (CRCT)
- Member of the medicine faculty council of Toulouse Purpan
- Member of the scientific committee of the Comprehensive Cancer Center Claudius Regaud, France
- Member of the research group of the French Society of Radiation Oncology
- 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

Membership

- European Association of Neuro-Oncology (EANO)
- Brain tumor group of European Organization of Research and Treatment of Cancer (E.O.R.T.C)
- European Society for Therapeutic Oncology and Oncology (E.S.M.O.)
- European Society for Medical Oncology (E.S.T.R.O.)
- American Society for Therapeutic radiology and Oncology (ASTRO)
- American Association for Cancer Research (A.A.C.R.)
- French Association of Neuro-Oncology (A.N.O.C.E.F.)
- French Society of Radiation Oncology (S.F.R.O)

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

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 recuurent glioblastoma.
- National MoGLImaging project (7 teams): Modeling of Glioblastoma treatment-induced resistance and heterogeneity by multimodal imaging

Lectures by invitation (since 2009)

Invited to more than 25 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.

CURRICULUM VITAE

Grégory DELPON

30 may 1975
Married, 2 children

Institut de Cancérologie de l'Ouest
Centre René Gauducheau
Medical Physics Department

Phone: 02.40.67.99.52. / 06.14.09.84.91.
Email: gregory.delpon@ico.unicancer.fr

Professional experience

From Jan 2018 : Head of Medical Physics Department, Institut de Cancérologie de l'Ouest Centre René Gauducheau, Nantes Saint-Herblain, and member of team 14 U1232 (ex 892) INSERM (Centre de Recherche en Cancérologie Immunologie Nantes Angers)
2011-2017: **Medical Physicist**, Radiotherapy, Institut de Cancérologie de l'Ouest Centre René Gauducheau, Nantes Saint-Herblain, and member of team 14 U1232 (ex 892) INSERM (Centre de Recherche en Cancérologie Immunologie Nantes Angers)
2004-2011: **Medical Physicist**, Radiotherapy, Institut de Cancérologie de l'Ouest Centre René Gauducheau, Nantes Saint-Herblain
2003-2004: **Medical Physicist**, Radiotherapy and Nuclear Medicine, Centre Jean Bernard, Le Mans
1999-2003: Part time **Medical Physicist**, Nuclear Medicine, Centre Hospitalier Montluçon

Education

2017: Habilitation to conduct researches (**HDR**). Image-guided radiotherapies. Université de Nantes.
2002-2003: Medical Physicist certification (**DQPRM**), Centre René Gauducheau, Nantes Saint-Herblain

1999-2002: PhD **(Doctorat de Physique Médicale**). Optimisation of quantitative imaging protocols for iodine 131 radioimmunotherapy clinical trials. INSERM U463, Nantes, Université de Toulouse.
1998-1999: Post-Graduate degree in Medical Physics (**DEA Physique Médicale**), Université de Toulouse
1997-1998: Master of Physics (**Maîtrise de Physique**), Université du Maine, Le Mans. ERASMUS at Sheffield (United Kingdom)

Societies

2016: Member of the Task Group Quality Control in CBCT EFOMP/ESTRO/IAEA.
2015: Member of the Scientific Committee of SFPM Annual Meeting
2015: Member of the Scientific Committee of the 3rd Physics Forum ESTRO
2014: Coordinator of Enseignement Post-Universitaire entitled IGRT for SFPM
2013: Coordinator of Enseignement Post-Universitaire entitled IGRT for SFPM
2012: Coordinator of Task Group dedicated to Image-Guided Radiotherapy for SFPM
2012: Coordinator of the Scientific Committee of SFPM Annual Meeting
2011: Coordinator of the Scientific Committee of SFPM Annual Meeting
2010: Member of the Scientific Committee of SFPM Annual Meeting
2007: Member of the Scientific Committee of SFPM Annual Meeting
2004-2016: President of Association des Physiciens de la Région Ouest (APRO).

Grants

2016: Laureate of a Ligue Contre le Cancer grant
2015: Partner of an ANR project led by Delphine Lazaro (CEA, Saclay)
2015: Partner of an INCA/INSERM project led by Nick Reynaert (Centre Oscar Lambert, Lille)
2012: Laureate of an INCA/INSERM project
2012: Laureate of a SFPM grant
2010: Prizewinner of best Medical Physics Poster at Annual Meeting of Société Française de Radiothérapie Oncologique

Teaching activities

Medical Physicist Certification (DQPRM), Institut National des Sciences et Techniques Nucléaires, Saclay
Graduation of Medical Physics (Master 2 Applications et Recherche Subatomique), Université de Nantes
Radiologic Technologist School, Nantes

CURRICULUM VITAE

Eric DEUTSCH
Date of birth: 30/05/1968
Nationality: French
Contact: eric.deutsch@gustaveroussy.fr

Current position :

- PUPH in oncology radiotherapy
- Executive director of 2018-2023 SIRIC project of Gustave Roussy
- Position Chairman of the Radiation Oncology Department and INSERM 1030 "Molecular Radiotherapy"
- Fields of interest: Molecular predictors of the efficacy of anti-cancer therapy,

immuno-oncology, early drug development, radiomics, preclinical and translational research in onco radiotherapy

- h index: 39 (Google Scholar, July 2017)

Short biography

Prof. Deutsch trained as a radiation oncologist (Université Paris VII). He gained a PhD degree in the fundamental basis of oncogenesis in 2003 (Université Paris-Sud, Parix XI), and completed his training with a post-doctoral fellowship in the Department of Radiation Oncology of the University of Pennsylvania, Philadelphia, USA. Prof. Deutsch became a tenure-track and full time cancer specialist at Gustave Roussy and was primarily involved in preclinical and translational radiation oncology. He became a Professor of Medecine and Medical Oncology at South-Paris University in 2010. Prof. Deutsch was appointed head of the radiation oncology department at Institut Gustave Roussy in 2012 and is a part of the early drug development department (DITEP). In 2012, he was appointed Head of the INSERM1030 Molecula Radiotherapy unit. He is member of the cluster of Excellence ('Labex') LERMIT, funded by the French 'Investment for the future' program, supported by the French Ministry of Research and Education. It combines the best research teams and laboratories in the field of drug development sciences. Prof. Deutsch is also member of the board of the medical school of the Paris Sud University.

He is an active member of the EORTC, as PI of trials in the radiotherapy group and is directly involved in the CT-RAD project, a reflexion group that aims at defining the research and translational priorities in the field of radiation oncology. He is also involved in ESTRO. Prof. Deutsch is currently a member of the Editorial Board of Radiotherapy and Oncology, the journal of ESTRO. Since 2012, he is co-leader of the DNA repair axis of the SIRIC program of Gustave Roussy.

Scientific and Academic Degrees

- **2001**: MD Thesis, specialization in radiation oncology
- **2003**: PhD in Cell Biology: (option: Radiation biology), University Paris XI
- **2003**: PhD « influence of BCR-ABL tyrosine kinase activity on DNA repair »
- **2009**: Habilitation for Research Direction, University Paris XI

Academic and Scientific Career

- **2000-2003**: PhD program UPRESEA2710: influence of Brc-Abl on DNA repair
- **2002-2004**: Assistant professor (chef de Clinique) radiothérapie IGR
- **2004-2005**: Post-doc: University of Pennsylvania, Philadelphia USA: modulation of PI3K activity to increase tumor response to ionizing radiation
- **Since 2006**: Tenure track position at IGR in radiation oncology with protected time for research
- **2009**: Creation of the INSERM 1030 unit
- **2010:** Full professor of radiation oncology
- **2011**: Board director of the excellence network of laboratories “Labex-LERMIT”
- **Since 2012**: Co Chair of the INSERM 1030 unit “Molecular Radiotherapy”
- **Since 2012**: Chair of the radiation therapy department of Gustave Roussy

Awards

- 2001: Prix de l’innovation de l’université Paris XI
- 2010: Prix Paul Mathieu de l’académie de médecine
- 2016: AWARD for the ESTRO-ICTRE teaching lecture

Patents

- **1999**: European patent N PCT/EP00/11246: Abdulkarim, Deutsch, Bourhis:

"combination of antiviral agents cidofovir for the treatment of cancer".

- **2003**: US extension of the patent N PCT/EP00/11246.
- **2011**: EGFR inhibitor and antiviral agent for simultaneous, seperate or sequential use in treatment and/or prevention and/or palliation of cancer PCT/EP2011/054548.
- **2011**: Triple combination of a vascular disruptive agent and CDDP + radiotherapy, WO 2013018017 A1.
- **2011**: Triple combination of a vascular disruptive agent and EGFR inhibitors + radiotherapy WO 2013018018 A1.
- **2013**: Use of cancer cell cannibalism as a biomarker EP 2867368 A
- **2015** : Combined vaccination/radioterapy for cancer treatment EP 3058956 A1.
- **2016**: Use of a thermoreactive gel to deliver free radical scavengers in order to prevent mucositis after irradiation.

Editorial Board, Scientific Societies and Expert

- Editorial board: academic editor for Radiotherapy and Oncology.
- Scientific societies: member of the scientific committee of European Society of Therapeutic Radiation Oncology ESTRO, member of the EORTC, member of Société Française de Radiothérapie Oncologique (SFRO), member of AACR. NCI-EORTC- new drugs meeting 2012: member of the annual meeting scientific board.
- Expert: member of the scientific committee of EDF (Electricité de France), member of the scientific comitee of ARC (association de recherche contre le cancer), expert for INCA, Belgian and Dutch research leagues (FNRS and ZonMW), Fond Suisse contre le cancer and CRUK

Lectures 2013 to 2017

- TAT Targeted Anti cancerTherapies, 4-5 mars 13, PARIS– Marriot Hotel
- SICRO vii7ème Shanghai International conference on radiation Oncology, 22-24 mars 13, Shanghai Fudan University Chine
- ICTR PHE 2014, Combination of Vascular, 12-13 février 14, Genève,
- Université Catholique Louvain – Séminaire, 26 février 14, Louvain
- ESTRO, 4- 8 avril 14, Vienne
- ESMO, 27-29 septembre 14, Madrid
- EORTC NCI AACR, 20 novembre 14, Barcelone
- SFNano et NanoSMS, 11 décembre 14, Nancy
- CERRO, 17-24 janvier 15, Les Menuires,
- ESTRO, 24-27 avril 15, Barcelone,
- University of Oxford, 14 septembre 15, Oxford
- ECCO 18, 25-27 septembre 15, Vienne
- ESGO, 24-26 octobre 15, Nice
- 12th Conference on Radiation Oncology, 29 octobre, 1er novembre 15, CHEN DU, Chine
- AERO Conference, 5 février 16, Paris,
- ICTR, 17-19 février 16, Genève
- ESTRO, 3 mai 16, Turin
- MACC 10, 8 juillet 16, St Paul de Vence
- International Conference on Immunology and radiotherapy, 22-23-24 septembre 16, Villejuif,
- SFRO, 3-8 octobre 16, Paris Palais des Congrès
- Esmo Congress, 7-11 octobre 16, Copenhague
- NCI-AACR-ENA, 29-2 decembre 16, Munich
- SEOR, 1er février 17, Madrid

- EORTC Rog Meeting, 20 février 17, Bruxelles
- ESTRO Turin, 5-9 mai 17, Vienne

- BIGART, 13-15 juin 17, Aarhus, Dannemark

CURRICULUM VITAE

Marie DUTREIX, Ph.D.

Head of the team"Recombination , Repair and Cancer", Institut Curie-Unit ETIC , INSERM U1021, CNRS UMR 3347, University Paris-Saclay.

Office Address: Institut Curie, centre universitaire, 15 rue Georges Clemenceau, 91405 Orsay

Email : marie.dutreix@curie.fr

Education

1980 : DEA de Microbiologie (Université de Paris XI)
"Isolement et caractérisation de mutants de délétion du phagemide lambda-miniF"
1983 : Doctorat de 3ème cycle de Microbiologie (Université de Paris XI)
"Etude in vivo de la régulation de l'induction lysogénique chez E. coli"
1988 : Doctorat ès Sciences (Université de Paris XI)
"Caractérisation des activités de la protéine RecA impliquées dans la régulation de la réparation des lésions et dans la mutagénèse"

Post-graduate Training and Fellowship Appointments

1984: Laboratoire du Dr. Gallibert (Laboratoire de la mutagénèse, Centre Hayem, Hôpital Saint-Louis, Paris)
1988-1991 : Séjour post-doctoral dans le laboratoire du Pr Charles Radding (Department of Human Genetics, School of Medecine, Yale University, CT91940 New-Haven).

Faculty Appointments

1978-1979 : Technicienne en génétique de la Drosophile (CNRS) dans le laboratoire du Dr Zalokar, (Centre de Génétique Moléculaire, CNRS, 91198- Gif-sur-Yvette).
1985-1988: Chercheur (CR2) au CNRS dans le Laboratoire du Dr Raymond Devoret
1992-1999: Chercheur (CR1) au CNRS (Section de Recherche, UMR 144, Institut Curie, 26 rue d'Ulm, 75231 Paris cedex 5)
1999-2007 : Direction de l'équipe « recombinaison et instabilité des génomes » (UMR 2027, Institut Curie , centre Universitaire, 91405 Orsay cedex)
2001: Directeur de recherche (DR2) au CNRS
2007- : Direction de l'équipe « Reparation, Recombinaison & Cancer », Département de Transfert , Institut Curie .
2014- : Directeur de recherche (DR2) au CNRS (UMR3347, U1021, Institut Curie, centre Universitaire, 91405 Orsay cedex)

Scientific and administrative functions

- 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 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)
- President of the Société Française du Cancer

Patents:

12 Patents (main inventor in 11)

Most recent Patents: 2012-2017

- PCT/EP2012/059799

« Cancer treatment by combining DNA molecules mimicking double strand breaks with hyperthermia» Déposants IC , CNRS, INSERM, DNA Therapeuctics

- EP13305518, le 19/05/2013

"Inhibition of DNA damage repair by artificial activation of PARP with oligonucleotide molecules" Déposant DNA Therapeutics, IC, CNRS

- EP15306201, le 23 /07/ 2015

« Use of a combination of Dbait molecule and PARP inhibitors to treat cancer" Déposant IC

- EP16305234.3, le 01 /03/ 2016

"Treatment of cancer by systemic administration of DBAIT molecules" Déposant IC, DNA Therapeutics

- EP 16305503.1, le 29/04/2016

"A method of predicting a response to an anti-tumor treatment" Déposant IC, DNA Therapeutics, INSERM, CNRS

Awards and Honors:

2003 Concours national d'aide à la création d'entreprises de technologies innovantes
2005 2ème prix national de la catégorie "Création - Développement" du Ministère de l'Industrie et de la Recherche
2006 Prix 2006 de la valorisation de la recherche de l'Université de Paris XI
2006 Grand prix 2006 de Science de la Vie de l'Inserm-Transfert
2006 Trophée 2006 de Science de la Vie du 8ème Concours « Tremplin Entreprise » organisé par le Sénat et l'ESSEC
2009 Prix 2009 de la « Fondation Antony Bernard contre le Cancer », Ligue Contre le Cancer
2013 Décorée Chevalier de l'ordre National du Mérite
2013 Biovision Next Gem Award for innovation
2016 Prix Lazothes de l'Académie des Sciences
2017 Décorée Chevalier de la légion d'honneur

CURRICULUM VITAE

Thomas LACORNERIE

Citizenship, Age: French, 49 years old
Current Positions:
Head of the Medical Physics Department (Lille Cancer Center)
E-mail: t-lacornerie@o-lambret.fr
Fields of competence: Radiation Oncology, Stereotactic Radiation Therapy.
ORCID : https://orcid.org/0000-0001-8994-5999

University Education

2001: Master of Computer Science, University of Strasbourg
1991: Master of Medical Physics, University of Toulouse

Professional Cursus

Since 2017 : Head of the Medical Physics Department, Lille Cancer Center
2003-2017 : Medical Physicist (Lille Cancer Center)
1994-2003 : Medical Physicist, Department of Radiotherapy, Strasbourg Cancer Center

Administration, Scientific, Clinical or industrial Expertise & responsibilities

Participant to 2 research projets PhysiCancer (INCa) :

- Mechanical Nanotweezeers and Microfruidic Setup for the Direct Assay of DNA (2012-2014)
- MRI based Monte Carlo treatment planning for hypofractionated extracranial stereotactic radiotherapy (2015-2017)

Teaching experience (including Dissemination of Scientific Information)

Master of Medical Physics- University of Lille

Diploma for Qualified Medical Physicist - French National Institute of Science and Nuclear Technics

Editorial Board and Participations in National and International Scientific Networks

Board Member of:

- European Journal of Medical Physics
- Cancer Radiothérapie

Reviewer of: European Journal of Medical Physics, Cancer Radiothérapie, Journal of Applied Clinical Medical Physics, British Journal of Radiology, Radiation Oncology

Award

Medal of Pierre et Marie Curie, Académie du Languedoc, 2012

Memberships

French Society of Medical Physics, SFPM (Vice-President and EFOMP Delegate)

European Society for Radiotherapy & Oncology, ESTRO

Scientific Production

58 articles

CURRICULUM VITAE

Paul-Henri ROMEO

***Business address**:* Institute of Cellular and Molecular Radiobiology CEA/DSV
18, Route du Panorama
92265 Fontenay-aux-Roses-BP6
Tel: 33 1 46548585
Mail: paul-henri.romeo@cea.fr

Degree

1978: Engineering graduate of the Ecole Polytechnique

1983: Ph.D. Thesis in Biochemistry

Present position

INSERM Exceptional Class Research Director

Head of the Institute of Cellular and Molecular Radiobiology at the DSV/CEA

Head of the Inserm UMR967 « Genetic Stability, Stem Cells and Radiation »

Positions and Employment

1984-1989	CR1 Inserm
1989-1995	Director of Research Inserm
1990-2001	Professor of Biology, Ecole Polytechnique
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

2006-	Head of the CEA/DRF Institute of Cellular and Molecular Radiobiology
2008-	Director of Research Exceptional Inserm
2008-2014	Director of the ITMO "Immunology, Hematology and Pneumology"
2009-	Head of the Inserm UMR967 CEA « Genetic Stability, Stem Cells and Radiation

Consulting Activities

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 ISTC European Commission
Member of the Scientific Board of the French Institute for Universities (IUF)
Co-President of the Scientific Board of the IRCAD
President of the ARC Scientific Commission 1

Scientific Awards

Prix MONTYON of the French Science Academy	**1992**
Prix de la Ligue contre le Cancer	**1993**
Prix de la Ville de Paris	**1995**
Chevalier dans l'ordre des Palmes Académiques	**2003**
Prix Rosen of FRM	**2008**
Member of « Tohoku Medical Society » (Sendai, Japon)	**2009**

Co-Coordinator / CURRICULUM VITAE

Emilie BAYART

04/01/1980
French

Groupe Source de Particules par Laser
Laboratoire d'Optique Appliquée
828 bvd des Maréchaux,
91762 - Palaiseau CEDEX

Phone: +33(0)1 69 31 97 73
Email: emilie.bayart@ensta-paristech.fr
eb.radiotransnet@gmail.com

Professional experience

April 2018…	**Radiotransnet Project Manager :** revision of Radiotransnet Network project proposal, organization and structuring of the network, communication
Summer 2012 - to date	**Radiobiology Project Manager: Laboratoire d'Optique Appliquée** – CNRS7639 – ENSTA – Ecole Polytechnique / **Gustave Roussy** (Villejuif), INSERM U1030 (radiotherapy department) **Multidisciplinary** and **multisite** project: evaluation of new radiotherapy protocols involving X-rays filtration and ultra-intense laser-pulsed particles (protons, electrons, photons) beam.

	Partnerships: - **Memorandum of Understanding « ultra-intense laser technology for medical applications »** co-organization with Oncoray, Helmholtz-Zentrum Dresden-Rossendorf - **IRS Paris-Saclay NANOTHERAD** - **OSEO - SAPHIR project** : 6M €, 8 partners (academic and **industrial)** - **Institut Curie Proton Therapy Center** (ICPO) - **ESRF Synchrotron** Medical beam line (Grenoble, France), - **Physicians**, **medical physicists** (including LNHB, for X-rays and proton QC)
Autumn 2010 **Summer 2012**	**Senior researcher (R&D):** Laboratoire de Biologie et Pharmacologie Appliquée (LBPA), Ecole Normale Supérieur de Cachan (France) **Development:** design, production and *in vitro* validation of new **recombinants lentivectors** dedicated to **gene therapy** and the generation of **induced pluripotent stem cells** taking account the cancer predisposition of Fanconi Anemia cells. **Partnerships:** European Network of Excellence **CliniGene-NoE** (http://www.clinigene.eu), 12M €, 38 academic and industrial partners.
2007- **Summer 2010**	**Junior researcher (R&D):** Centre Génétique Moléculaire (CGM, Gif sur Yvette, France) **Development** of **yeast strains** and **expression vectors,** automation of molecular biology protocols for **purification** and functional understanding of a multiprotein complex whose human homologue is involved in cerebellar ataxia type 2 development.
2001-2006	**Master and thesis in Oncology**: UMR 8126, Gustave (Villejuif, France) and UMR 2027, Institut Curie (Orsay, France) with Dr M. Amor-Guérêt ***Project:*** Carcinogenesis Mechanisms *in* Bloom syndrome - Cellular and Molecular Aspects during mitosis **Development** of ***in vitro* protocols** to study cell and DNA damages repair pathways signaling involved after genotoxic stress (γ-irradiation) during mitosis.

Education

2001-2006	**Master** and **PhD** in **Oncology - Cellular and molecular biology,** Paris Sud – XI University (France)**,**
1997-2001	**BSc** in **Biochemistry,** University of Sciences and Technology of Lille (France)

Memberships

2018… : Member of the Radiobiology Committe of PTCOG

2015…: Member of the SIRIaF's (Société Internationale de Radiobiologie de Langue Française)

2012-2014: Treasurer of AJCi (young researchers association of Gustave Roussy)

2008-2009: Treasurer of CéGéM (association of young researchers of CGM)

2006-2007 : Member of the Scientific Board of the University of Paris XI

2005-2006 : Member of the Executive Committee of the ADIC (Association of Graduate Students and Young Doctors of Institut Curie).

Partie III / Part 3

12 Engagements et signatures

12.1 Organisme porteur de la candidature

Nom de l'organisme porteur de la candidature (destinataire de la décision de labellisation et bénéficiaire de la subvention)**:** ***Société Française de Radiothérapie Oncologique (SFRO)***

Je, soussigné(e), Philippe MAINGON
Représentant légal **X**
Personne dûment habilitée ❒

(cocher la case correspondante) Cette personne est soit le représentant légal de l'organisme, soit toute autre personne dûment habilitée et bénéficiant d'une délégation de pouvoir ou de signature établie par le représentant légal. En cas de délégation de pouvoir ou de signature, joindre la copie de délégation.

- Déclare avoir pris connaissance :
  - de l'appel à candidatures 2018 «**Labellisation d'un réseau national de recherche préclinique en radiothérapie**» ;
  - du règlement n°2014-01 relatif aux subventions allouées par l'INCa (consultable à : http://www.e-cancer.fr/Institut-national-du-cancer/Appels-a-projets/Reglement-des-subventions/Subventions-attribuees-apres-le-01-janvier-2014) ;
  - du dossier de candidature complet;
- M'engage à ce que l'organisme que je représente respecte l'ensemble des dispositions de ces textes qui concerne l'organisme que je représente, notamment le règlement n°2014-01 susvisé sous réserve des éventuelles dérogations qui y seraient apportées dans l'acte attributif de subvention conclu entre l'INCa et l'organisme que je représente;

- accepte le mandat confié par les organismes membres du réseau identifiés au 12.3 ci-après et, par conséquent accepte, notamment, de porter la candidature du réseau intitulé **RADIOTRANSNET** ;
- désigne M Philippe MAINGON en qualité de coordonnateur du réseau et lui donne tous pouvoirs pour mener les missions décrites dans l'appel à candidatures ;
- m'engage à ce que l'organisme que je représente :
  1) mette en œuvre les missions décrites dans l'appel à candidature et assure leur coordination
  2) mène les actions prévues dans le dossier de candidature et, le cas échéant, tienne compte des recommandations du comité d'évaluation et propositions de l'INCa,
  3) transmette à l'INCa un rapport annuel d'activité sur l'état d'avancement de ces différentes missions ;
- lorsque l'organisme que je représente agira en qualité de représentant du réseau labellisé, je m'engage à ce qu'il le mentionne expressément en citant le nom du réseau ;
- Certifie exactes les informations contenues dans ledit dossier ;
- M'engage à ce que l'organisme que je représente mobilise, dans les meilleurs délais, les crédits obtenus dans le cadre du présent appel à candidatures ;
- Déclare que l'organisme que je représente est en règle au regard de l'ensemble de ses obligations administratives, comptables, sociales et fiscales (déclarations et paiements correspondants).

Fait le : 26/07/2018
Cachet et Signature

Pr. Philippe MAINGON
Oncologie radiothérapie
Chef de service
N° RPPS : 10002148178
N° FINESS : 750100125
Tél. RDV : 01 42 17 61 84
Télécopie : 01 42 17 82 50
GH Pitié Salpêtrière
83, Bd de l'hôpital - 75651 Paris cedex 13
Tél. secrétariat : 01 42 1

12.2 Coordonnateur du réseau

Engagements du coordonnateur du réseau

Je, soussigné(e) : **Philippe MAINGON**,
Agissant en qualité de coordonnateur du réseau

- Déclare avoir pris connaissance :
  - de l'appel à candidatures 2018 «**Labellisation d'un réseau national de recherche préclinique en radiothérapie**» ;
  - du règlement n°2014-01 relatif aux subventions allouées par l'INCa (consultable à : http://www.e-cancer.fr/Institut-national-du-cancer/Appels-a-projets/Reglement-des-subventions/Subventions-attribuees-apres-le-01-janvier-2014);
  - du dossier de candidature complet (annexes incluses) ;

- M'engage à respecter les dispositions qui me concernent et à mener les missions coordonnateur du réseau telles que décrites dans l'appel à candidatures.

Fait le : 26/07/2018
Cachet et Signature

Pr. Philippe MAINGON
Oncologie radiothérapie
Chef de service
N° RPPS : 10002148178
N° FINESS : 750100125
Tél. RDV : 01 42 17 61 84
Télécopie : 01 42 17 82 50
GH Pitié Salpêtrière
83, Bd de l'hôpital - 75651 Paris cedex 13
Tél. secrétariat : 01 42 1

Engagements du co-coordonnateur du réseau

Je, soussigné(e) : **Vincent Marchesi**,
Agissant en qualité de coordonnateur du réseau

- Déclare avoir pris connaissance :
  - de l'appel à candidatures 2018 «**Labellisation d'un réseau national de recherche préclinique en radiothérapie**» ;
  - du règlement n°2014-01 relatif aux subventions allouées par l'INCa (consultable à : http://www.e-cancer.fr/Institut-national-du-cancer/Appels-a-projets/Reglement-des-subventions/Subventions-attribuees-apres-le-01-janvier-2014);
  - du dossier de candidature complet (annexes incluses) ;
- M'engage à respecter les dispositions qui me concernent et à mener les missions coordonnateur du réseau telles que décrites dans l'appel à candidatures.

Fait le : 02/08/2018
Cachet et Signature

Vincent MARCHESI, Ph D
Unité Radiophysique Médicale
INSTITUT DE CANCEROLOGIE DE LORRAINE
6 avenue de Bourgogne - CS 30519
54519 Vandoeuvre-lès-Nancy cedex
T. 03.83.59.84.27 - F 03.83.59.83.91

12.3 Organismes membres du réseau

A répéter autant de fois que le nombre de membres impliqués dans le réseau
Veuillez ajouter autant d'engagements que de membres

Nom de l'organisme membre du réseau : *Commissariat à l'Energie Atomique et aux Energies Alternatives (CEA)*

Je, soussigné(e), BERGER Vincent *(indiquer nom, prénom)*

Représentant légal •

Cette personne est soit le représentant légal de l'organisme, soit toute autre personne dûment habilitée et bénéficiant d'une délégation de pouvoir ou de signature établie par le représentant légal. En cas de délégation de pouvoir ou de signature, joindre la copie de délégation.

- certifie exactes les informations contenues dans le dossier de candidature ;
- donne mandat à la SFRO pour porter la candidature du réseau de recherche pré-clinique en radiothérapie intitulé RADIOTRANSNET
- donne tous pouvoirs à Philippe MAINGON pour agir en qualité de coordonnateur du réseau et mener les missions décrites dans l'appel à candidatures
- m'engage, en cas de labellisation par l'INCa, à ce que l'organisme que je représente contribue aux activités du réseau telles que décrites dans ce dossier de candidature et dans l'appel à candidature et ce, pendant toute la durée de la labellisation.

signature :
et Cachet de l'organisme

Le 14.12.2017

Responsable scientifique au sein de l'organisme membre du réseau :

Je, soussigné(e), ROMEO Paul-Henri,

Agissant en qualité de responsable scientifique au sein de l'organisme membre du réseau

- Déclare avoir pris connaissance :
  - de l'appel à candidatures 2017 «**Labellisation d'un réseau national de recherche préclinique en radiothérapie**» ;
  - du règlement n°2014-01 relatif aux subventions allouées par l'INCa (consultable à : http://www.e-cancer.fr/Institut-national-du-cancer/Appels-a-projets/Reglement-des-subventions/Subventions-attribuees-apres-le-01-janvier-2014);
  - du dossier de candidature complet (annexes incluses) ;
- M'engage à respecter les dispositions qui me concernent et à mener les missions du réseau telles que décrites dans l'appel à candidatures.

Fait le : 11/12/17
Signature :

P. H. ROMEO

N

Nom de l'organisme membre du réseau : Institut de Radioprotection et de Sûreté Nucléaire (IRSN)

Je, soussigné(e), NIEL Jean-Christophe

Représentant légal •

Cette personne est soit le représentant légal de l'organisme, soit toute autre personne dûment habilitée et bénéficiant d'une délégation de pouvoir ou de signature établie par le représentant légal. En cas de délégation de pouvoir ou de signature, joindre la copie de délégation.

- certifie exactes les informations contenues dans le dossier de candidature ;
- donne mandat à la SFRO pour porter la candidature du réseau de recherche pré-clinique en radiothérapie intitulé RADIOTRANSNET
- donne tous pouvoirs à Philippe MAINGON pour agir en qualité de coordonnateur du réseau et mener les missions décrites dans l'appel à candidatures
- m'engage, en cas de labellisation par l'INCa, à ce que l'organisme que je représente contribue aux activités du réseau telles que décrites dans ce dossier de candidature et dans l'appel à candidature et ce, pendant toute la durée de la labellisation.

signature : Le 11/12/2017

et Cachet de l'organisme

INSTITUT de RADIOPROTECTION et de SÛRETÉ NUCLÉAIRE
B.P. N° 17
92262 FONTENAY-AUX-ROSES CEDEX
Tél. : (33) 01 58 35 88 88

Responsable scientifique au sein de l'organisme membre du réseau :

Je, soussigné(e), BENDERITTER Marc,

Agissant en qualité de responsable scientifique au sein de l'organisme membre du réseau

- Déclare avoir pris connaissance :
  - de l'appel à candidatures 2017 «**Labellisation d'un réseau national de recherche préclinique en radiothérapie**» ;
  - du règlement n°2014-01 relatif aux subventions allouées par l'INCa (consultable à : http://www.e-cancer.fr/Institut-national-du-cancer/Appels-a-projets/Reglement-des-subventions/Subventions-attribuees-apres-le-01-janvier-2014);
  - du dossier de candidature complet (annexes incluses) ;

- M'engage à respecter les dispositions qui me concernent et à mener les missions du réseau telles que décrites dans l'appel à candidatures.

Fait le : 12 decembre 2017

Signature :

ANNEXE

Section 8.2 – Annex: Partnerships

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-(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
3-(Bordeaux) **POPRA : Programme Optique, Physique Radiothérapie en Aquitaine)** Pr Guy Kantor Consortium: • **Institut Bergonié,** • **CHU Bordeaux** • **CELIA** (University, CNRS,	**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	• **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	• National : – Pôle de compétitivité laser (RLH) – Canceropôle GSO (axe technologie et santé) – Oncopôle Toulouse, – Centre Antoine Lacassagne de Nice – CEA – ICMCB (nano chemistry)	Conseil Regional Nouvelle-Aquitaine (co-funding) and European FEDER funds University of Bordeaux ; CNRS ; CEA ; IDEX; ANR; Canceropôle GSO

CEA) • **CENBG**(CNRS IN2P3, University) • **INRIA** (équipe Monc, IMB) **LaBRI**		• **Comparative dosimetry** • **Nano medicine 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	Post-doc (2 Past) • **LaBRI** : 0,5 ETP; 1 doc • **Inria** : 2 doc (past)	– Aquitaine sciences transfert (AST/SATT) – Industrial partnership International: Univ of Dresden (Germany)	European PM Curie program
4-(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
5-(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
6-(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.			
7-(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
8-(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
9-(Caen) **LARIA** **Laboratoire d'Accueil pour la Recherche sur les ions Accélérés** Yannick Saintigny **IRCM /CEA/GANIL**	**Cf (Fontenay-aux-roses, CEA) IRCM**				
10-(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
11-(Clermont-Ferrand) (hors LabEx PRIMES, cf plus loin) **UMR 1240 INSERM** **IMoST : Imagerie**	**1,2,3,4**	• Targeted Radionuclide Therapy, • External radiation therapy, • Radiobiology,	**20 FTE:** Senior researchers : 12 Doc : 7 Post-Doc : 1 **Specific Equipment** Plateforme d'imagerie	• National : IRCM - Montpellier UPS- Strasbourg ISA - Lyon LPC – Clermont Fd Cyclopharma-Clermont Fd	UCA INSERM CRLCC Centre Jean Perrin Ligue Contre le Cancer

Moléculaire et Stratégies Théranostiques **<u>Directrice :</u>** D[r] E Miot-Noirault **<u>Directrice adjointe :</u>** P[r] Frédérique Penault-Llorca **<u>Equipe 1 :</u>** *Cibles et outils pour l'imagerie et la thérapie* D[r] F Degoul **<u>Equipe 2 :</u>** *Recherche translationnelle en imagerie fonctionnelle, radiopharmaceutiques et biomarqueurs théranostiques* P[r] F Cachin **UCA : Université Clermont Auvergne ; CRLCC Jean Perrin ; INSERM ; CHU Clermont Fd**		Dosimetry, • Metrology, • Chemistry, Radiochemistry.	<u>préclinique</u> : IVIA : PET, 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	Caminnov, Alès CLB – Lyon ILM – Lyon ISPB/UCBL – Lyon IPHC – Strasbourg UCBL – Lyon - EA3738 Institut de Cancérologie de L'Ouest, Nantes	INCA/PRTK CPER FEDER ANR
12-(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
13-(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		• ANR Générique "SINCOLISTIN" • ANR PRCI "2DPS"

			Nanoparticle synthesis		• 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
14-(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
15-(Lille) **Plasticity and Cancer »** X Le Bourhis **INSERM U908 « Cell**	**2**	Stem cells Preclinical models (Zebra, transgenic mice)	2 researchers		• INSERM • Centre Oscar Lambret
16-(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
17-(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)
18-(Lyon and Auvergne-Rhône-Alpes) **LabEx PRIMES** Françoise Peyrin 8 teams		**Physique, Radiobiologie, Imagerie Médicale et Simulations**	Federates 16 teams including 8 teams directly involved in preclinical research in radiotherapy		Each team has its own funding and the LabEx has specific ANR funding

19-(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
20-(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
21-(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
22-(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
23-(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
24-(PRIMES Grenoble) Rayonnement Synchrotron et Recherche Médicale (RSRM) EA 7442 Pr Sam Bayat **Univ. Grenoble-Alpes**	**1,2,3**	• In-vitro and in-vivo micro imaging, • Experimental synchrotron radiation therapy (SSRT, MRT), • Nanoparticle preclinical studies.	9 pers, 5,5 FTE, team located at ESRF/ID17	• National : LabEx PRIMES, CEA • International : European MRT coll., Australian Synchro., Daegu Synchro. (Korea)	Labex PRIMES, INCa/DGOS, UGA, FRM, Région AuRA

25-(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
26-(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
27-(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
28-(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
29-(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)
30-(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)
31-(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 and radiotherapy combinations • Preclinical and clinical dosimetry	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) - Other national thematic networks (SFRO, GETUG, SFPM, …) - Regional Univ.	• Institutional funding: INCa, DGOS • Charities: League against cancer, ARC Foundation, FRM • Industry contracts (Roche, Genentech,

				Federation of Radiation Oncology (ICM and CHU of Nîmes) • International : - European FP-7 Requite consortium - International RadioGenomics consortium (RGC) - Univ. of Arizona, Mount Sinaï Hospital of New-York (US) - CHUV, Lausanne (Switzerland)	Novartis, Varian) • Territorial authorities: Montpellier Metropole "Health Capital", Occitanie Region
32-(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)	4 FTE: 1 senior researcher 2 engineers 1 physicist **X-ray irradiator** (SARRP Lite Xenx - XStrahl)	• National : - ITMO-Cancer PROUST network • International : - European FP-7 Requite consortium • Industrial collaborations: 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
33-(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
34-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	• National SIRIC Montpellier Cancer CEA (Fontenay-aux-roses) • International University of Leicester	• SIRIC Montpellier Cancer • Labex MabImprove • Plan Cancer (Proust) • GEFLUC
35-(Montpellier) Radiobiology and targeted radiotherapy Dr Jean-Pierre Pouget	**1,3**	• Radiobiology of targeted radiotherapy (ovarian and colorectal cancers) • Development of radiopharmaceuticals for theranostic approaches of ovarian cancer	2 senior researchers 1 MCU 2 MCU-PH 1 PH 1.5 post-doc 2 PhD student • Specific equipment SPECT-CT/PET-CT	• National collaborations ONIRIS Nantes CRCT Toulouse IBMM Montpellier INSERM Clermont Ferrand • International Queen Mary University London NRG Petten Netherlands NECSA South Africa ITU Karslruhe Germany	• Nordic Nanovector, Oslo Norway • Physicancer • SIRIC Montpellier • Labex MabImprove/ Labex Chemisyst • Others: Bionov, EDF, LNCC,

					Canceropole (CGSO), GEFLUC
36-(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
37-(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)
38-(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 (NANCYCLOTEP)	• <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 AFREThi EU (INTERREG)
39-(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).	<u>14 FTE:</u> 4 senior researchers (INSERM, CNRS, CEA) 1 faculty researcher, 2 MD, 4 engineers /tech., 4 Doc., 1 Post-doc. <u>Specific equipment</u> micro SPECT/CT imaging, nuclear imaging and radioisisotope handling, animal care facility, animal models, cellular biology,	• <u>National</u> IRSN; IRBA; CEA Saclay & Cadarache ; CLCC Baclesse, Caen ; INRIA & IPMC at Sophia Antipolis, Inserm (Nice). • <u>International</u> Colombia, Madrid, USA. • <u>Industrial</u> : Theraguix, Lyon.	- CEA/PTTox, DRF impulsion - ANR PRIODAC - Cancéropôle Sud-Est - Plan Cancer ….

			spectrometric platform. Access to medical irradiators: EBRT (Cyberknife, protontherapy: Medicyc 65 Mev, ProteusOne 235 MeV) in the Centre Antoine Lacassagne.		
(Paris, Ile de Fr)					
(Institut Curie)					
40-Institut Curie Department of medical physics; Alejandro Mazal **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
41-Institut Curie Department of radiation oncology; Pr Philip Poortmans **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
42-Institut Curie Marie Dutreix **Centre de Recherche, Orsay**	**1,2,3**	• Preclinical models, normal and tumor tissue differential index • FLASH irradiation (high dose rate irradiation) • Protons • Development of new radiosensitising molecules • Preclinical studies on combined treatments • biomarkers	5 teams 7 senior researchers, 3 post-doc, 4 doc, 8 engineers, technicians	• National. F. Lemoine, CHU Salpétrière, Paris ; E. Charafe, IPC,Marseille NANOTHERAD network • European: 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. • USA: S. Bhaskara, Huntsman Cancer Center,Utah,USA	Institut Curie foundation, INSERM, CNRS, Institut Curie centre de recherche, Univ. Paris-Saclay, INCA, Onxeo, EU
43-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	Staff permanent position: 1 radiation biologist 1 Medical physicist 3 engineers Specific equipment: - XRAD320(X-rays) - SARRP (Xrays + imaging + TPS) - CIXD (double x-rays) - GSRD1 (^{137}Cs) - KINETRON (HDR Linac) - Medical proton beamline (ICPO)	• National: RESPLANDIR network Y Prezado (IMNC/IN2P3) C Laurent (ToxEMAC ABTE, univ. Caen) Khe Hoang-Xuan (ICM/APHP) • International : F Lebrin (Leiden univ. medical center, NL) Han Tun (Mayo Clinic, Jacksonville, FL, USA)	Recurrent resources – Invoicing – institutional Research contract – INCA (PRT-K, canceropole IDF2016) – ITMO Cancer – Equipement (2015regional funding) And 4 Industrial contracts
(AP-HP)					
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:** Prediction of efficacy of radiotherapy and combined radiotherapy to new drugs Prediction and prognostic of radiation-induced damage in healthy tissues		

44-GRRAP Member: Recombinaison DNA repair and cancer: "de la molécule au patient" Laurent Quéro **Inserm U1021 / CNRS UMR3347**, Orsay (lab of M Dutreix, cf Institut Curie just above)	**3**	• DNA repair • Anticancer drugs combination • Translational research	6,5 FTE: 3 Seniors researchers 1 Professor 2 Doc 1 Post Doc	Pharma Industry Paris VI university	Institut Curie CNRS INCa
45-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
46-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)
47-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
48-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)
49-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					
50-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
51-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.
52- 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
53-(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);
54-(Villejuif) Molecular radiotherapy Pr Eric Deutsch **INSERM 1030** Gustave Roussy (IGR)	**1,2,3**	• Preclinical models, normal and tumor tissue differential index, Lung and head and neck models • Radiomics and functional imaging • Biomarkers • Immunotherapies combined to radiotherapy	2 senior researchers, 6 doc., 4 post-docs	• Nationale: - Ecole central Paris, - LOA école polytech., - Dosisoft, IRSN, CEA, - A Boissonnas UPMC-INSERM, - P Sansonetti Institut Pasteur, - I Buvat, SHFJ CEA Orsay. - J Galon U1138 (immunology)	INSERM, FRM, Ligue contre le cancer, ARC, EDF, INCA. NanoH, Nanobiotix, + pharma

55-(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
56-(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
57-(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,
58-(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. • Radiophotolumine scence (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
59-(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 medical imaging.	**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 platform • TPS VOLO Tomotherapy • TPS PRECISION CyBerknife • TPS Raystation	**National** INSERM, Villejuif Curie Institute, Paris Dosisoft, Cachan Equal-Estro, Villejuif Raysearch ELEKTA **International** IAEA	INSERM Plan Cancer Inca European Commission

			(VMAT) • 10 Linacs • Brachy dedicated TPS. • PLANETDose (Targeted Radionuclide Therapy)		
60-(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 **<u>Specific Equipment</u>** : 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)	• <u>National</u> collaborations through several ANR and Inca programs • <u>International</u> collaborations Japan, EU, USA • <u>Industrial</u> collaborations AREVA, EDF	2017 Recurrent : Logistic : 1,8 M€ Contracts : 3 M€ Plateforms : 0,75 M€
61-(Fontenay-aux-roses, CEA, suite) **PROCyTox,** Michelle Ricoul	**2**	• New approaches in molecular cytogenetics including telomere length measurements. • Biological dosimetry with cytogenetics biomarkers. • International intercomparison exercices for dose estimate.	<u>4,2 FTE</u>: 1,2 researchers, 2 technicians, 1 Post-doc <u>Specific equipment</u> cellular and molecular cytogenetics, image analysis with Metasystems set-up. <u>PROCyTox acts as a platform</u> for characterization of genotoxic damages.	• <u>National</u> -Neurospin, Saclay Joliot/SPI/ LERI Saclay -CEA/BIG/Grenoble -IGR Radiotherapy -INSERM Nantes • <u>International</u> - 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-roses, IRSN)					
62-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. <u>Equipment:</u> Medical Linear accelerator, Metrological photon and beta calibration laboratory, ESR spectrometers. OSL/TLD dosimetry capabilities; Calculation cluster	EURADOS members, Geant4-DNA/Geant4 collaboration, European project MEDIRAD, EURAMED, EURAMET	IRSN recurrent resources; EU

63-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
64-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
65-Unité d'expertise medicale Cécile Etard **IRSN, Fontenay**	**1, 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;
65-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;
67-(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 dosimeters. **Experimental measurements**: dose, in vivo dosimetry.	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€
68-(Palaiseau, X)	**2,3,4**	• Protons	4 FTE:	• National :	CNRS, ENSTA,

Laboratoire d'Optique Appliquée (LOA), team SAPHIR, Alessandro Flacco, **CNRS-7639, ENSTA-PARISTECH, Ecole Polytechnique**		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)	2 senior researchers (1 physicist, 1 radiobiologist), 1 Doc 1 engineer SAHIR Laser facility: pulsed protons (electrons and X ray coming) Cell culture lab	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)	Ecole Polytechnique, IRS Nanotherad, EDF
69-(Orsay) **New Approaches in Radiotherapy,** Yolanda Prezado, **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.	• National : – ICPO (Institut Curie) – RadExp (Institut Curie) – IR4M (Paris Sud) – Human path and animal models (Instit. Pasteur) – Institut Neurosciences Paris Saclay – LOA • International : – ALBA synchrotron – Centro nacional de Microelectronica – Univ. de Santiago de Compostela – Hospital Clinico de Santiago (Spain) – HIMAC (Japan) – Univ. medizin Berlin	• CNRS
70-(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...
71-(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:	recurrent resources: INSERM research contract: INCa ANR- Labex CominLabs & CAMI IResP CGO Industrial

				LIST-CRIBs, SouthEast University, Nanjing, China; CSIRO, Australia; Ryerson University, Toronto, Canada; UNET, Tachira, Venezuela; UNC-Universidad Nacionale de Colombia, Bogota	partners: ANSYS (Lyon), AQUILAB (Lille), EDAP (Vaulx-en-Velin), ELEKTA (Paris), KEOSYS (Nantes), THERENVA (Rennes), PHILIPS (Aachen, Best), SIEMENS (Forchheim, Paris), GE (Horten, Norway).
72-(Strasbourg) Département de Radiobiologie, Hadronthérapie et Imagerie Moléculaire: DRHIM Patrice Laquerière **IPHC: Institut Pluridisciplinaire Hubert Curien,** CNRS, Univ. de Strasbourg. **73-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.
74-(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
75-(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	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	• 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	• Plan cancer/ITMO/Aviesan (HTE program) • INSERM (Gros équipement) • ARC • Ligue contre le Cancer • RITC / Region • PHUC

		glioblastoma heterogeneity • In vitro and in vivo 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	by an animal irradiator for precise irradiation as well as in vito irradiation	radioresistance signature of the patients included in the national POLA data 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)	
(Réseaux)					
(Réseau régional, 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)
(Réseau national) **Réseau de plateformes de radiothérapie préclinique (hadrons et photons)** **RESPLANDIR (GDR-Mi2B) (Mickael Beuve, David Brasse, Céline Mirjolet, Frédéric Pouzoulet, Marc Rousseau) :**		• <u>Translational research</u> • <u>Medical Physics</u> • <u>Preclinical radiation therapy</u>	<u>Constitution</u> : 36 ETP - Radiobiologists - Radio physicists - Technicians - Students <u>Specific equipment</u>: - 3 Xrad320 - 4 SARRP - 2 linac - neutron generator: E<2.5 MeV - neutron generator: 2.5<E<14 MeV - protons generator: E< 3.5 MeV - protons generator: E<25 MeV - 1 CIXD - alpha generator 17MeV<E<70 MeV - deuton generator - ^{12}C, Ions lourds: E< 95 MeV/n - micro-faisceau alpha/proton: E< 3MeV Access to proton medical beam line	**RESPLANDIR** is a National Network that federates 14 teams -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	Each team has its own funding to perform their research activity but currently, RESPLANDIR has not specific funding

				Saintigny - Biobeam 8000 (Centre Paul Strauss, Strasbourg) : Hélène Burckel - IRCM, Strasbourg, Muriel Brengues	
(Réseau national) **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)
(Réseau national) **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 international reference in cancer research	7 Cancéropôles : - Nord Ouest - Ile de France - Grand Ouest - Est - 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.

Date limite de soumission / Submission deadline : 7 septembre 2018 (16h)

ATTENTION

Le dossier de candidature (Cf. trames « dossier » et «annexe budgétaire ») doit comprendre l'ensemble des éléments requis et nécessaires à l'évaluation scientifique et technique du projet.

Le dossier finalisé est soumis sous forme électronique (soumission en ligne) et sous forme papier, les deux formes sont identiques excepté les signatures et les documents complémentaires qui ne sont exigées qu'en version originale papier.

Le dossier complet en format papier doit comporter tous les documents et toutes les signatures des partenaires, en **version originale** pour les coordonnateurs du projet et les représentants légaux des organismes bénéficiaires de la subvention INCa. Les dossiers ne satisfaisant pas à ce critère ne seront pas soumis à évaluation et ne pourront faire l'objet d'un financement.

➢ Soumission du format électronique :

Le format électronique comporte le présent dossier de candidature **(fichier Word97-2003)**

n'excédant pas 4Mo), **ne pas ajouter de signatures scannées**, et l'annexe budgétaire (**fichier Excel97-2003**) dument complétés.(PAS DE FORMAT PDF).
L'ensemble est transmis en ligne par téléchargement via le site de soumission. :

Adresse unique pour l'appel à projets :

http://www.e-cancer.fr/Institut-national-du-cancer/Appels-a-projets/Appels-a-projets-en-cours/radiotherapie2017

ET

➢ Soumission du Format papier :

- un original du présent dossier, comprenant les signatures originales et non scannées et l'annexe budgétaire et les documents complémentaire si applicable (Cf. check-liste ci-après);
- Un relevé d'identité bancaire de l'organisme bénéficiaire de la subvention INCa

à l'adresse suivante (cachet de la poste faisant foi) :

Institut National du Cancer
AAC RADIOTHERAPIE- 2018
52, avenue André Morizet
F - 92513 Boulogne-Billancourt cedex

Contact pour tout renseignement scientifique ou technique:
Madame Caroline DREUILLET **cdreuillet@institutcancer.fr** (Dpt Recherche Clinique-Pôle Recherche et Innovation)

Check-list de constitution du dossier papier complet original

Attention ci-dessous la liste de contrôle concerne TOUS LES ORGANISMES

Quels documents fournir	Signature obligatoire	Commentaires	Quoi faire	Check liste
Conformité du dossier de candidature				
Dossier de candidature		Le dossier doit être complet et la partie projet conforme au document électronique	Vérifier que la dernière version sans marque de correction est conforme à la version électronique soumise sur le site. Vérifier que le montant demandé est en adéquation avec l'annexe budgétaire Vérifier que la liste des équipes est en conformité avec les engagements requis	☒ ☒ ☒
Conformité des engagements et des signatures : attention les signatures et cachet des organismes doivent être conformes aux précisions indiquées ci -après				
Engagement du représentant légal de l'organisme porteur de la candidature et bénéficiaire de la subvention	A signer Joindre l'original	L'engagement est signé par le représentant légal de l'organisme mentionné dans le dossier de candidature et qui bénéficiera de la subvention en principal. Le représentant légal est le président ou le directeur général de l'organisme ou tout autre personne ayant reçu une délégation expresse de signer en lieu et place. Attention : un chef de service ou un responsable de laboratoire ou d'unité de recherche n'est pas un représentant habilité	Compléter le document : - titre du projet, - nom et qualité du signataire, - date, - signature -apposer le cachet de l'organisme et éventuellement de la personne signataire Vérifier que le signataire est habilité à signer	☒
Délégation de signature du représentant légal de l'organisme bénéficiaire de la subvention		Si le représentant légal ne signe pas l'engagement alors fournir le document de délégation de signature	Si le représentant légal ne signe pas l'engagement alors joindre le document de délégation de signature du représentant légal à la personne qui va signer en lieu et place	☒
Engagement du coordonnateur du réseau	A signer Joindre l'original	L'engagement est signé par le coordonnateur du réseau qui est celui mentionné dans le dossier de candidature	Compléter le document : - titre du projet, - nom, - date, - signature	☒

Quels documents fournir	Signature obligatoire	Commentaires	Quoi faire	Check liste
Engagement(s) des organismes membres du réseau IRSN ☑ CEA ☑ SFRO ☑ SFPM ☑	A signer Joindre original ou copie	Les organismes membres du réseau telles que listées dans le dossier de candidature doivent compléter les documents d'engagement : - Signature du représentant légal de l'organisme Le représentant légal est le président ou le directeur général de l'organisme ou tout autre personne ayant reçu une délégation expresse de signer en lieu et place Attention : un chef de service ou un responsable de laboratoire ou d'unité de recherche n'est pas un représentant habilité	Vérifier la liste des organismes membres du réseau avec le nombre d'engagement à fournir Nombre de membre : Vérifier que le signataire est habilité à signer Compléter le document : - titre du projet, - nom et qualité du signataire, - date, - signature -apposer le cachet de l'organisme et éventuellement de la personne signataire	Nbre membre : _4__ ☒
Délégation de signature du représentant légal de l'organisme partenaire bénéficiaire d'un reversement la subvention		Si le représentant légal ne signe pas l'engagement alors joindre le document de délégation de signature du représentant légal à la personne qui va signer en lieu et place	Si le représentant légal ne signe pas l'engagement alors joindre le document de délégation de signature du représentant légal à la personne qui va signer en lieu et place	☐
Engagement du responsable scientifique pour le projet de la organisme membre du réseau		Signature de la personne qui met en œuvre la partie du projet concerné		
Conformité annexe budgétaire				
Annexe budgétaire		Compléter l'annexe budgétaire en indiquant tous les coûts liés au déroulement du projet, coût total et coût demandé à l'INCa. Les calculs doivent être vérifiés et conforme aux indications du document	- Vérifier le nom de l'organisme et du représentant légal de l'organisme bénéficiaire de la subvention. - Vérifier les calculs : équilibre des budgets (voir code couleur dans le document excel) - Vérifier que les frais de gestion ne dépassent pas les 4% et sont calculés sur l'addition des postes équipement, fonctionnement et personnel	☒

Quels documents fournir	Commentaires	Quoi faire	Check liste
Pièces complémentaires pour les associations et organismes privés à but non lucratifs			
RIB - Un relevé d'identité bancaire	Vérifier que le nom du bénéficiaire est en cohérence avec le nom de l'organisme bénéficiaire sinon veuillez justifier	A joindre	☒
Une copie signée des statuts à jour		A joindre	☒
Une copie de la publication au JO de la déclaration de constitution de l'organisme) et éventuellement des mises à jour	Vérifier que les adresses actuelles du siège de l'association sont conformes au document du JO et du statut	A joindre	☒
Le dernier rapport d'activité		A joindre	☒
La liste des membres du Conseil d'administration		A joindre	☒
La liste des membres du bureau (pour les associations)		A joindre	☒
Les comptes approuvés du dernier exercice clos		A joindre	☒
Le ou les rapports du commissaire aux comptes pour les associations qui en ont désigné un, notamment celles qui ont reçu annuellement plus de 153 000€ de dons ou plus de 153 000 € de subvention		A joindre	☒

- Je confirme que les documents listés et cochés figurent dans le dossier de candidature et sont joints au dossier original papier et sont conformes aux exigences de l'appel à projet et du dossier de candidature ;

Date le 20/08/2018

Signature :