I2BM - Institut d'imagerie biomédicale

Rapport Hcéres

agence d'évaluation de la recherche
et de l'enseignement supérieur

Section des Unités de recherche

AERES report on the research unit

Institut d'Imagerie biomedicale

From the

CEA

May 2010

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CEA

Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

May 2010

Research Unit

Name of the research unit: Institut d'Imagerie biomedicale (I2BM)

Requested label : CEA Institute

N° in the case of renewal

Name of the director: Ms. Malgorzata TKATCHENKO

Members of the review committee

Committee chairman

Mr. Andrew TODD-POPROPEK, University College London (UCL), England

Other committee members

Mr. Jacques BARBET, University of Nantes

Mr. Alexander HAMMERS, Imperial College of London, England

Mr. Maxime GUYE, University of Aix-Marseille 2

Mr. Irene BUVAT, CNRS, Orsay

Mr. Gregoire MALANDAIN, INRIA, Sophia Antipolis - Méditerrannée

Mr. Luc BUEE, INSERM, Lille

Ms. Barbara BARDONI, University of Nice

Mr. Charles Henri MALBERT, INRA, Rennes

Mr. Bernard GALLEZ, Catholic University of Louvain (UCL), Belgium

Committee members suggested by CNU, CoNRS, CSS INSERM, CSS INRA, INRIA, IRD

Observers

AERES scientific advisor

Mr. Christian BARRILLOT

University, School and Research Organization representatives

Mr. Jacques NEYTON (CEA)

Ms. Anne FLURY-HERARD (CEA)

Mr. Gilles BLOCH (CEA)

Ms. Nathalie LERESCHE (CNRS)

Mr. Christian VINCENT (CEA)

Report

1 • Introduction

- Date and organisation of the visit:

The committee arrived on site on the afternoon of the 10th of February, 2010. Site visits, interviews and discussions went on throughout the 10th, 11th and 12th of February. Most of the discussions took place at the SHFJ ; there were site visits at Neurospin and Mircen by the Committee in the afternoon of the 10th. On the 11th in the afternoon, the Committee split, and 3-4 Committee members concentrated on one of each of the three sites. There was no site visit as such to the facilities at the SHFJ.

- History and geographic localisation of the service and a synthetic description of the domain of its activities :

I2BM is a research Institute which is one of the eight institutes within the Life Sciences Division of the French Atomic Energy Agency (CEA). It was founded in 2007. It is a virtual institute comprising three large services – SHFJ, NeuroSpin and MIRCen all three located at differrent sites within the south suburban Paris region. These three service were those that were evaluated in this visit. Each of these three services are about 30 minutes travelling distance from each other. In addition the Institute also includes the service SRHI working in the domain of haematological immunology located at the Hospital St Louis in central Paris which was not evaluated and the Service CI-NAPS/ GIN currently located at Caen, also not evaluated but in the process of reorganisation and probably relocation.

The administration of the I2BM institute is currently co-located with the SHFJ on the Orsay site.

The domain of activities is to study (1) Normal brain function, (2) Neurodegenerative diseases and their treatment, (3) Psychiatric diseases and their treatment, and (4) Cancers and their treatment.

It is clear that the emphasis of the research undertaken by the components of the Institute is neurology. However in particular at the SHFJ, located in close vicinity to the Orsay Hospital, there is a general nuclear medicine service which does include study in addition in the area of oncology.

The desciption of the three services evaluated and their domain of activities is given in the specific reports of those three services. Note that in confirmance with CEA terminology the term 'Service' is used to describe what might more conventionally be called 'Unit' each of which is composed of 'Teams' or 'Equipes'.

- Management team

The Head of the Institute is Ms. Margo Tkatchenko

- Staff members (on the basis of the application file submitted to the AERES)

	Dans le bilan ETP 30/06/09	Dans le projet ETP 01/01/11
N1 : Nombre d'enseignants-chercheurs (cf. Formulaire 2.1 du dossier de l'unité)	37	40
N2 : Nombre de chercheurs des EPST ou EPIC (cf. Formulaire 2.3 du dossier de l'unité)	74	80
N3 : Nombre d'autres enseignants-chercheurs et chercheurs (cf. Formulaire 2.2 et 2.4 du dossier de l'unité)	13	12
N4 : Nombre d'ingénieurs, techniciens et de personnels administratifs titulaires (cf. Formulaire 2.5 du dossier de l'unité)	155,7	169
N5 : Nombre d'ingénieurs, techniciens et de personnels administratifs non titulaires (cf. Formulaire 2.6 du dossier de l'unité)	39,1	23,1
N6 : Nombre de doctorants (cf. Formulaire 2.7 du dossier de l'unité)	67	72
N7 : Nombre de personnes habilitées à diriger des recherches ou assimilées	65	66

2 • Overall appreciation on the Institute

- Summary :

The role of the Institute in adding value to the combination of constituent services was not entirely clear to the committee. The individual services were all judged to be either excellent or very good. While the individual services stated their association and linkages within the institute were considered to be very important by staff consulted, it is possible that this benefit could still be achieved even if the institute did not exist. The role of the institute in directing the strategy of the overall and individual structures is not entirely clear. The structures for managing the institute and its component parts seem to require reorganisation and if the institute is to continue to be of value, reinforcement. In additional the relationships between the institute, the service and the Orsay University campus including the role of the Institute in the 'Plan Campus' need to be carefully considered and probably reinforced.The overall scientific quality of the components of the institute is in general excellent, as is the output. The ongoing and new projects of the services evaluated are relevant with in general good originality quality and impact.

- Weaknesses and threats

Management at the institute level needs to be improved in particular with respect to communications between the institute and all the staff and students within the constituent services and teams. The role as association between certain services not evaluated such as SRHI and GIN is a risk and needs careful consideration at the strategic level. This also holds for the links between the research and the provision of clinical service at both SHFJ and NeuroSpin.

- Recommendations to the director of the institute:

It is important that the role of the institute, its strategy and its overall management be clarified and where appropriate reorganised in particular by the establishment of addition management and other institute wide committees. Likewise an appropriate mechanism for the allocation and prioritisation of resources should be established with appropriate participation at all levels. Communications between staff and students in the different service could be improved. The sharing and management of resources such as but not only animal facility should be reinforced to provide value at the institute level and corresponding economies of scale. Again the role of the institute in the 'Plan Campus' are likely to be very important in particular linkages with certain key units based at the Orsay University.

3 • Specific comments

Since the institute is virtual, the bulk of the appreciation must be considered with the detailed appreciations of the three constituent evaluated services.

- Appreciation on the results

In general the scientific quality and quantity of the output of the Institute as a whole is very good and substantial. The quality and quantity of the two services NeuroSpin and MIRCen are excellent while that of the SHFJ was judged by the committee also to be very good.

It is clear that the output of the Institute being that of the three services is highly relevant in the area of neuroscience, of high quality and impact. The output in terms of other application areas such as oncology and cardiology seems to have less impact. This is treated in the individual service reports.

The quantity and quality of the publications and communication is very satisfactory. A reasonable number of doctoral students have completed theses which appear to be of good quality. A significant number of patents have been obtained.

The contractual relationships with the supervising organisations, primarily CEA and CNRS appear to be strong and well maintained.

- Appreciation on the impact, the attractiveness of the research unit and of the quality of its links with international, national and local partners

The ability to recruit staff, post docs and students of high quality seems very reasonable, but not uniform within the three services. There are some notable areas where there is a lack of staff and resources to support ongoing and planned projects that are reported in the individual service reports.

Within the context of French research, the ability of the institute and the service to raise funding is good. In particular there are some excellent industrial collaborations.

The participation of the services in national and international collaborations is good, both at the individual level for example with other research group and in participation within EU projects. These are also reported in the three service reports.

Valorisation of research and socio-economic or cultural relationships looks fine but is not uniform within the three services.

- Appreciation on the strategy, management and life of the research unit

At the level of the team by and large the management and internal communications looks fine with some variability within the whole organisation. Again the management at the level of the services appears to be fine, but

with some indications of problems of communications internal to the service. Although there are some committees that are established for the management of the institute as a whole, the participation of the team leaders in this overall management does not appear to be happening, and there was some significant indication of concern in the process when discussions took place with various members of staff. In addition there seems to be a lack of some important structures at the institute level for example of a general management committee with elected representative from all types of staff, a lack of a good method for distributing resources, the lack of an Ethics committee, etc. The services appear to function largely in an autonomous manner in particular with respect to the distribution of resources and in external communications. There are however apparently regular meetings between the direction of the Institue and of the individual service directors. There is a good scientific animation again mostly based at the team and service level. It is not clear that the structures necessary to assess the risks that are likely to happen and to plan an appropriate strategy are well established at the Institute level. The establishment of the scientific projects appears to be primarily at the service level and it would be advisable that the projects should also be assessed and in particular prioritised at the institute levels.

- Appreciation of the project:

The existence, pertinence and feasibility of the scientific projects is excellent at the service level, but there does not appear to be a corresponding plan at the institute level.

The strategy at the service level is fine (with some weakness at stated in the individual service reports and in particular the relationship between the research and clinical groups at the SHFJ.

The strategy of the institute as a whole and the allocation or reallocation of resources between the services does not appear to be well established.

The originality of the projects at the service level seems in general to be very good, as reported in the individual service assessments. The role of the institute as such is not entirely clear.

4 • Appreciation on the MIRCEN research unit

- History and geographic localisation of the service and a synthetic description of the domain of its activities :

The URA 2210 is the continuation of the URA CEA-CNRS 1285 that was renewed twice on January 2000 and January 2008. It includes four teams : 1) Cell-cell Interactions in Neuronal and Glial Degeneration ; 2) Preclinical Therapies for Neurodegenerative Diseases ; 3) Preclinical Brain Imaging ; 4) Clinical Imaging for Neurodegenerative Diseases. In 2009, the vast majority of the members of the URA 2210 unit moved to MIRCen (Molecular Imaging Research Center) which is CEA service and a Common Research Center (CRC CEA-INSERM) located at Fontenay-aux-Roses. This resulted into the effective gathering of all preclinical research activities of the URA 2210 in one building while clinical activities of the URA remain located at Henri Mondor Hospital for the clinical assessments and at Service Hospitalier Frederic Joliot (SHFJ) for PET/MRI imaging in patients.

The main topic of the URA 2210 is centered on the development of experimental models of neurodegenerative disorders such as Huntington disease. It has been pionner in different clinical and preclinical trials (gene and cell therapies).

Each team has its specificity : experimental models, viral vectors (lentivirus and AAV) ; preclinical assays with neuroimaging approaches (MRI, PET) and clinical validation of preclinical experiments.

- Management Team :

M. Emmanuel Brouillet is the director of URA 2210 that is composed of four teams. The four heads are Gilles Bonvento, Nicole Déglon, Vincent Lebon et Philippe Remy.

- Staff members:

	Dans le bilan	Dans le projet
N1 : Nombre d'enseignants-chercheurs (cf. Formulaire 2.1 du dossier de l'unité)	2	1
N2 : Nombre de chercheurs des EPST ou EPIC (cf. Formulaire 2.3 du dossier de l'unité)	9	10
N3 : Nombre d'autres enseignants-chercheurs et chercheurs (cf. Formulaire 2.2 et 2.4 du dossier de l'unité)	4	4
N4 : Nombre d'ingénieurs, techniciens et de personnels administratifs titulaires (cf. Formulaire 2.5 du dossier de l'unité)	15	17
N5 : Nombre d'ingénieurs, techniciens et de personnels administratifs non titulaires (cf. Formulaire 2.6 du dossier de l'unité)	2	2
N6 : Nombre de doctorants (cf. Formulaire 2.7 du dossier de l'unité)	11	9
N7 : Nombre de personnes habilitées à diriger des recherches ou assimilées	8	7

4.1 • Overall appreciation on the research unit

- Global Opinion

URA 2210 has an international recognition with an outstanding translational research. It starts with basic neuroscience with energy metabolism, cell interactions among neurodegenerative disorders (Team 1). Then, it includes methodologies for gene transfer and PET analysis in brain (Teams 2 and 3). They use both rodents and non-human primates as animal models. They apply these technologies to study two neurodegenerative diseases: Hungtinton's and Parkinson's diseases and to evaluate pre-clinical treatments for these pathologies (Teams 2 and 3). As an exemple, based on a preclinical dopamine gene therapy study in non-human primate model of Parkinson's disease, a phase I clinical trial has also been started at Henri Mondor Hospital and PET scan examination is performed by team 4.

Such expertise in translational research has been brought to the scientific community through the MIRCen patform (Inserm/CEA) with animal facilities with biological safety levels 2 and 3, neuroimaging and preclinical trials.

- Strong point and opportunities:

- Unique animal facility allowing for neuroimaging in A2 and A3 biological safety levels;

- High quality projects;

- Animal ethics committee and animal experiment habilitation (for all PhD students involved in animal experiment);

- Good laboratory atmosphere.

- Points to improve and risks:

- Speed up the set-up of executive and scientific boards (Conseil de labo);

- Lack of users committee on platforms. The nature and the role of the MIRCen meetings are not clearly defined;

- Lack of focus in clinical research.

- Recommendations to the director of the service:

- Reinforce Alzheimer axis through collaborations and/or arrivals of new scientists. Such input should be done especially in team 1.

- Human ressources are highly needed for MRI and PET platforms in team 4.

- Staff levels and productivity :

A1 : Nombre de produisants parmi les chercheurs et enseignants chercheurs référencés en N1 et N2	11
A2 : Nombre de produisants parmi les autres personnels référencés en N3, N4 et N5	2
A3 : Taux de produisants de l'unité [A1/(N1+N2)]	1
A4: Nombre d'HDR soutenues	8
A5 : Nombre de thèses soutenues	13

4.2 • Specific comments

- Scientific Quality and quantity:

Original translational research highly relevant in the field of neurodegenerative disorders that results in applications in gene and cell therapies. Major findings of the 2005-2009 period are (1) the demonstration that mitochondria, excitotoxicity and neuron-astrocyte interactions are key pathogenic mechanisms in Huntington's disease; (2) the assessment of the efficacy of gene transfer-based therapeutic strategies in particular those using small interfering RNA for Huntington's disease and increased sustained dopamine delivery/synthesis for Parkinson's disease; (3) the development of new methods for image processing and anatomical reconstruction; and (4) first phase I/II clinical trials assessing the potential therapeutic efficacy of neuronal grafting in Huntington's disease patients and dopamine replacement gene transfer for Parkinson's disease and the demonstration of a key role of PET imaging, NMR spectroscopy and MRI for understanding Huntington's disease and Parkinson's disease pathophysiology.

URA2210 has published over 120 peer-reviewed publications since 2005.

During the past period, the unit has also developed excellent translational research with teams from hospitals and industries.

- Influence, attractiveness and integration of the team and the project in its environment :

Participation to national and international meetings often as invited speakers

URA 2210 scientific production also involved the collaboration with many other national and international academic laboratories. The URA is involved in teaching and research training related to Paris area Universities and the RTRA "Ecole des Neuroscience de Paris". Many postdoctoral scientists, many coming from abroad, work in URA and some of them have been hired on permanent positions.

Financial support of URA research originates from national (ANR, FRC grants, ACI, GIS and "Pôle de Compétitivité" Medicen Santé programs), and international (FP6 / FP7 European STREP and Network of excellence, NIH R01) funds.

Several collaborations have been also conducted on translational research programs with industrial groups (Oxford Biomedica, Servier, Ipsen-Beaufour, Sanofi-Aventis).

- Appreciation of the strategy, management and the life of the service:

In such short period of time, work has been organized between URA and MIRCen allowing for a clear input of the URA scientists to operating aspects of the MIRCen platform.

Excellent organization on animal's facilities and neuroimaging in preclinical studies (sharing of veterinarians and scientists with other platforms in I2BM). Excellent formation with animal experiment habilitation for all personals involved in preclinical studies. Nevetheless, executive/scientific boards (Conseil de labo) and users committee on platforms have to be quickly operational. Task force groups should be set up to define clear protocols on radioactivity and biology safeties. The nature and the role of the MIRCen meetings are not clearly defined.

Although regular seminars occur at MIRCen, there are not enough talks and seminars among teams. These latter may help to keep a good dynamic among teams and the good atmosphere.

Unique animal facility combining imaging and experimental animal models where all URA scientists bring their expertise and thus it provides a real asset for users.

- Evaluation of the project:

URA 2210 is still exploring preclinical and clinical researches developed in the former project. It is going deeper in the exploration of Huntington's diseae experimental models by electrophysiological and transcriptomics approaches. URA2210 is also broadening its expertise on translational research to other neurodegenerative disorders than Huntington and Parkinson's diseases. It has started preclinical research on Alzheimer's disease. It is a very promising study for identifying new biomarkers and may have further benefits in the understanding of neurodegenerative disorders and innovative therapeutic approaches.

An input of all teams should be given to the Alzheimer's disease project to facilitate its development.

The project Huntington's disease is a follow up of the former one but will explore new aspects of the disease through new experimental models and methodologies. As described above, Alzheimer's research area is new and URA 2210 has many assets to bring an excellent contribution to this field.

4.3 • Appreciation team by team

Team 1: Cell-cell interaction in neurodegeneration

Team leader: Mr. Gilles Bonvento

- Staffing levels

	Dans le bilan	Dans le projet
N1 : Nombre d'enseignants-chercheurs (cf. Formulaire 2.1 du dossier de l'unité)	0	0
N2 : Nombre de chercheurs des EPST ou EPIC (cf. Formulaire 2.3 du dossier de l'unité)	3	3
N3 : Nombre d'autres enseignants-chercheurs et chercheurs (cf. Formulaire 2.2 et 2.4 du dossier de l'unité)	0	0
N4 : Nombre d'ingénieurs, techniciens et de personnels administratifs titulaires (cf. Formulaire 2.5 du dossier de l'unité)	5	5
N5 : Nombre d'ingénieurs, techniciens et de personnels administratifs non titulaires (cf. Formulaire 2.6 du dossier de l'unité)	0	0
N6 : Nombre de doctorants (cf. Formulaire 2.7 du dossier de l'unité)	2	2
N7 : Nombre de personnes habilitées à diriger des recherches ou assimilées	2	2

- Scientific Quality and quantity:

This team has an international recognition on Huntington's disease with a main interest on defects in mitochondria and energy metabolism. Moreover, another aspect of the project is the analysis of Complex cell-cell interactions between neurons and astrocytes that regulate energy metabolism and promote glutamate homeostasis. This basic research is directly at the origin of innovative therapeutic strategies in Huntington's disease that are now evaluated in preclinical works. This work results in 43 high quality publications and a large number of communications in national and international meetings.

- Influence, attractiveness and integration of the team and the project in its environment:

Team members are regularly invited to national and international conferences (ECNP, Gordon conference, Japan Neuroscience Society…).The team has hired different scientist at post-doctoral level and a CNRS research scientist was recently recruited. Numerous funds are obtained from national and international sources (HiQ Foundation, USA; Hereditary Foundation, USA; MEDICEN pole de compétitivité…)

- Appreciation of the strategy, management and the life of the service:

The project is at the interface between cell-cell communications and Huntington's disease and is a continuity of the former project. The team has PhD students but should hire a post-doctoral fellow. This team has a large number of collaborations with laboratories in the South-East of Paris-Ile de France.

- Evaluation of the project :

The project is mostly focussed on Huntington's disease and links between neurons and astrocytes. It is a nice project exploring new experimental models with more methodologies (transcriptomics, electrophysiology…). A follow-up project is an understandable choice at the level of the team. However, it is more difficult to understand it when teams 2 and 3 will open up their project to the Alzheimer's field. It may be related to the organization of URA into 4 teams and not to the quality of the project.

- Conclusion:

Internationally recognized team in the field of Huntington's disease with a good project in the continuity of the past project.

- Strong Point and Opportunities:

- Exploration of a new experimental model of Huntington's disease;

- Involving electrophysiology in the project;

- Unique environment with complementary collaborations within MIRCen.

- Points to improve and risks :

- Two strong leaders in the same team;

- No open up on other neurodegenerative processes/diseases.

- Recommendations :

- Reinforce links with other teams that are developing a strong Alzheimer's disease research.

Team 2 : Preclinical therapeutics for neurodegenerative diseases

Team leader : N. Déglon

- Staffing levels

	Dans le bilan	Dans le projet
N1 : Nombre d'enseignants-chercheurs (cf. Formulaire 2.1 du dossier de l'unité)	0	0
N2 : Nombre de chercheurs des EPST ou EPIC (cf. Formulaire 2.3 du dossier de l'unité)	2	2
N3 : Nombre d'autres enseignants-chercheurs et chercheurs (cf. Formulaire 2.2 et 2.4 du dossier de l'unité)	0	0
N4 : Nombre d'ingénieurs, techniciens et de personnels administratifs titulaires (cf. Formulaire 2.5 du dossier de l'unité)	8	8
N5 : Nombre d'ingénieurs, techniciens et de personnels administratifs non titulaires (cf. Formulaire 2.6 du dossier de l'unité)	1	1
N6 : Nombre de doctorants (cf. Formulaire 2.7 du dossier de l'unité)	1	1
N7 : Nombre de personnes habilitées à diriger des recherches ou assimilées	2	2

- Scientific Quality and quantity:

The research projects of team 2 during the past 4 years were focused on: i) methodologies for gene transfer in brain and ii) methodologies for PET analysis. They applied these technologies to study two neurodegenerative diseases: Hungtinton (HD) and Parkinson (PD) diseases and to evaluate pre-clinical treatments for these pathologies. They used non-human primates as an animal model. It is important to underline that in the context of the URA2210, projects of other teams rely on the activity/methodology of team 2.

This research effort resulted in 62 peer-reviewed publications, many of them in high impact factor journals (e.g. PNAS; J. Clinical Invest.; J. Neurosci.; Hum. Mol. Genet.; Mol. Biol. Cell.; Lancet Neurol.). The ability to handle a unique technology, the originality of the strategy of work and the important results obtained place this team in a leader position on a world wide scale.

- Influence, attractiveness and integration of the team and the project in its environment :

International visibility is certified by the high number of invitations to international meetings, national/international collaborations and by the European grants obtained (5 EC-FP6 and 2 EC-FP7).

The high relevance of their translational approach is also underlined by the interest that industries display for their technology and results. Indeed, two main industrial contracts have been obtained.

- Appreciation of the strategy, management and the life of the service:

The team is well organized and perfectly integrated in the Institute. A good teaching activity accompanies a relevant evaluation/reviewing activity. Indeed, members of this team belong to several evaluation committees (notably INSERM CSS1 and CNRS section 30).

- Evaluation of the project:

For the future, they plan to continue using the methodology they know well to improve therapeutical approaches for HD and PD. In particular for PD they plan to use dopamine replenishment therapy using new AAV vectors and for Huntington, they will use lentiviral vectors for local and long-term delivery of CNTF and will knock-down the Huntiningtin gene in primates by siRNA. For this last project in primates, they started from the idea to treat polyglutamine pathogenesis by reducing the expression of the protein carrying poly Q sequences, as already they have obtained in mouse models for HD and Machado Joseph.

Furthermore, consistently with their previous activity, they also plan to enlarge their subject of research including Alzheimer (AD) disease and fronto-temporal dementia (FTD) in their analyses. Indeed, they plan to investigate the physiopathology of familiar forms of AD and FTD using lentiviral vectors overexpressing wild type or mutated version of APP and tau proteins in different brain regions of M. mulatta. The animal models generated by this method will be studied combining behavioural tests and brain imaging techniques.

The projects are well presented. The approach is original and feasible considering the know-how of the team, the platforms they can use in their institute and the financial resources available. For these reasons, this committee envisages that they will make an outstanding contribution to the advance of research in the field.

Furthermore, continuing on the same track, they also propose to develop new methods for in vivo validation of PET tracers that impact therapeutic treatments in pre-clinical studies, in collaboration with other teams of URA2210 and I2BM

- Overall opinion:

Outstanding team with long and unique experience

- Points to Improve:

No weak points have been identified.

- Recommendations:

Even if the team has a solid experience, the recruitment of a researcher with experience in AD and/or FTD would positively contribute to the rapid advance of the project.

Team 3: Preclinical Brain Imaging

Team leader: Mr. Vincent LEBON

- Staffing levels

	Dans le bilan	Dans le projet
N1 : Nombre d'enseignants-chercheurs (cf. Formulaire 2.1 du dossier de l'unité)	0	0
N2 : Nombre de chercheurs des EPST ou EPIC (cf. Formulaire 2.3 du dossier de l'unité)	4	5
N3 : Nombre d'autres enseignants-chercheurs et chercheurs (cf. Formulaire 2.2 et 2.4 du dossier de l'unité)	0	0
N4 : Nombre d'ingénieurs, techniciens et de personnels administratifs titulaires (cf. Formulaire 2.5 du dossier de l'unité)	1	2
N5 : Nombre d'ingénieurs, techniciens et de personnels administratifs non titulaires (cf. Formulaire 2.6 du dossier de l'unité)	0	0
N6 : Nombre de doctorants (cf. Formulaire 2.7 du dossier de l'unité)	6	5
N7 : Nombre de personnes habilitées à diriger des recherches ou assimilées	2	2

- Scientific quality and quantity of the production:

The number of publications is good even though it it a little behind the mean for the service as a whole. The methodological effort associated with the installation of the 7T MRI system explains completely the bell shaped temporal distribution of the publications. The two types of publications produced, by nature methodological and by nature more applied in journals with a high impact factor are explained perfectly by the efforts needed for implementation by the team.

- Influence, attractiveness and integration of the team and the project in its environment:

The effort associated with the development of post mortem imagery has permitted incontestably an international recognition of the team, which could have been brought out more explicitly in the evaluation document. The past division of the team into two distinct poles of service with the same scientific objectives in understandable given that there exists a continuum between in vivo imaging and in vitro imaging and that the dynamics of the team rests in part on the exchanges between these two groups. The team is perfectly integrated into the service. It is a link of the programme of the service.

- Strategy and management:

The committee appreciated the effort directed towards teaching. The team undertook a considerable risk in installing the imaging system in the A2/A3 situation. Finally, this risk was well managed. There will be shortly in the year to come a similar risk in installing 2 perhaps 3 PET systems in a similar environment, Past experience suggests that this installation will be equally a success even if the total installation in not as yet an actuality.

- Evaluation of the project:

The project is centered in a very pertinent manner along three comnplementary constituents, MRI, linking MRI and PET and post mortem imaging. The portage of three projects of which two are immediately operations

- Conclusion:

  - Overall opinion:

The overall opinion on this team is very positive. This is an essential team within the service, perfectly integrated within the Institute and with strong interactions with SHFJ and NeuroSpin.

  - Strong points and opportunities:

The "post-mortem programme" is an opportunity for further development. The links with the in vivo work are very promising.

  - Points to improve and risks:

The PET project requires more personnel than currently available.

  - Recommendations:

Maintain a significant aid by the management of the Institute to accelerate the PET project and in particular the aspects of the availability of radioisotopes by the supplier (SHFJ). In particular, it seems to be imperative to establish as quickly as possible one or two new posts dedicated to the PET sector which cannot take off within the current state of the available resources within the team.

Team 4 : Imagerie cérébrale clinique pour les maladies neurodégénératives

Team leader : Mr. Philippe REMY

- Staffing levels

	Dans le bilan	Dans le projet
N1 : Nombre d'enseignants-chercheurs (cf. Formulaire 2.1 du dossier de l'unité)	2	1
N2 : Nombre de chercheurs des EPST ou EPIC (cf. Formulaire 2.3 du dossier de l'unité)	0	0
N3 : Nombre d'autres enseignants-chercheurs et chercheurs (cf. Formulaire 2.2 et 2.4 du dossier de l'unité)	4	4
N4 : Nombre d'ingénieurs, techniciens et de personnels administratifs titulaires (cf. Formulaire 2.5 du dossier de l'unité)	1	2
N5 : Nombre d'ingénieurs, techniciens et de personnels administratifs non titulaires (cf. Formulaire 2.6 du dossier de l'unité)	1	1
N6 : Nombre de doctorants (cf. Formulaire 2.7 du dossier de l'unité)	1	1
N7 : Nombre de personnes habilitées à diriger des recherches ou assimilées	2	1

- Scientific quality and production :

Research has been focused on two complementary strategies: use of functional imaging to identify biomarkers of neurodegenerative diseases, and use of imaging tools to evaluate new treatments in these diseases. The committee considers this research carried out by Team 4 as an essential part of the MIRCEN/URA2210 research activities: this

translational clinical activity of MIRCEN requires the involvement of these clinical studies. Despite a lack of manpower (3.1 EFT), the scientific output is considered as excellent, with 34 publications over the last 4 years, most of them being published in international high standard journals.

- Evaluation of impact, attractivity and integration of the team to its environment :

The clinical team of MIRCEN/URA2210 is well recognized internationally as the team leader is invited as chair of sessions in international meetings, and is participating to international networks (European funded projects). The impact is therefore considered as very good. However, the committee also considers that the ability to recruit external researchers was rather limited.

- Evaluation of strategy and governance :

Overall, the committee considers that this segment of activity is an essential part of the translational activity of MIRCEN.. However, the committee believed that there should be more effort to mobilize manpower for research activities, with special attention to the MR clinical studies. As such, the strategy looks rather short focused.

- Evaluation of the project:

Overall the project was considered as very good, but the enthusiasm was mixed, depending on the sub-projects. One the one hand, it brings a lot of enthusiasm for the biomarkers part of the project, although the MRI part could be hampered by the need for a MR team in SHFJ that should be more involved in the project. The gene therapy part and neuroprotection evaluation in Parkinson disease were also considered as very important translational clinical studies. On the other hand, the other parts of the project linked to the evaluation of treatments were considered as not mature enough or described in sufficient detail in the documents to be considered for impacting the field. Considering the present human resources, the lack of focus could hamper the overall translational studies. There is a need to adapt ambition and means, or means to the ambition.

- Conclusion :

  - Overall

The research orientation led by the group 4 is an essential part of MIRCEN activities and of I2BM. I2BM and MIRCEN constitute a unique environment to carry out this cutting-edge research in the field of neurodegenerative diseases.

  - Strengths and opportunities :

- MIRCEN environment: at the end of an outstanding line of research in neurodegenerative research;

- Well recognized expertise of the team leader.

  - Weaknesses :

- Limited manpower and resources to embrace all research projects.

- Concerns about the clinical MR studies to be done. The committee identifies a lack of manpower, expertise and up-to-date MR instrumentation in SHFJ where the clinical studies could be carried out. The arrival of the CIERM group is unlikely to provide an adequate support for the investigations of the team 4 (due to different research orientation).

- Recommendations :

- Focus effort on the accessibility of patients for projects to up-to-date MRI and MR experts is an important issue. This could be solved either by solving accessibility issues to Neurospin facilities (staff requirements: nurses, MD plus agreement of regulation agencies) or upgrading MR system at SHFJ and bringing MR expert in the team.

5 • Appreciation on the Neurospin Center

- History and geographic localisation of the service and a synthetic description of the domain of its activities :

Neurospin opened January 1st, 2007, in Saclay, about 25 km south of Paris. The NeuroSpin platform has nearly 11000 m² of laboratories, offices, technical facilities, and seminar space. It includes both a clinical facility (8 beds) for hosting normal human participants and patients and a preclinical facility for small animals (several hundreds of mice and rats) and primates (30 animals, including trained primates). NeuroSpin has been developed specifically with the idea of being a platform dedicated to research in Neurosciences using high and ultra high magnetic field magnetic resonance imaging.

- Management Team:

Neurospin is headed by Denis Le Bihan, a member of the French Academy of Sciences, and includes 5 labs, each headed by a specific chief : NMR methodological research for imaging and spectroscopy (LRMN, Chief D. Le Bihan interim, new chief to be appointed in 2010)), Neurocomputing (LNAO, Chief Jean-François Mangin), Clinical research (LBIOM, Chief Lucie Hertz-Pannier), Cognitive neuroimaging (LCOGN, Chief Stanislas Dehaene, also a Member of the Academy of Sciences) and Preclinical research (LBI, interim Chief Marc Dhenain, new chief to be appointed in 2010).

- Staff members:

	Dans le bilan	Dans le projet
N1 : Nombre d'enseignants-chercheurs (cf. Formulaire 2.1 du dossier de l'unité)	1	1.10
N2 : Nombre de chercheurs des EPST ou EPIC (cf. Formulaire 2.3 du dossier de l'unité)	13,30	16,6
N3 : Nombre d'autres enseignants-chercheurs et chercheurs (cf. Formulaire 2.2 et 2.4 du dossier de l'unité)	0,2	0,2
N4 : Nombre d'ingénieurs, techniciens et de personnels administratifs titulaires (cf. Formulaire 2.5 du dossier de l'unité)	27,50	27.9
N5 : Nombre d'ingénieurs, techniciens et de personnels administratifs non titulaires (cf. Formulaire 2.6 du dossier de l'unité)	10	7
N6 : Nombre de doctorants (cf. Formulaire 2.7 du dossier de l'unité)	21	22
N7 : Nombre de personnes habilitées à diriger des recherches ou assimilées	9	11

5.1 • Overall appreciation on the research unit

- Global Opinion:

The Neurospin Center is an outstanding and unique facility dedicated to research in Neurosciences using high (HMF) and ultra high magnetic field (UHMF) magnetic resonance imaging. Given its recent installation (2007), it is not fully equiped yet (delay in the installation of the UHMF scanners) and only 3 out of the 5 Neurospin labs have established research projects, in addition to the platform activity.

The research projects currently run at Neurospin are highly original, even risky, and can be considered as leading edge research. The leaders of the projects have international recognition. Lack of human resources however limits the full exploitation of the current facilities, and threatens the balance between research activity and platform activity. A number of logistical aspects will have to be improved to fully establish Neurospin as a leading UHMF research center in the world.

- Strong points and opportunities:

- Unique and fully equiped HMF and UHMF magnetic resonance imaging platform in France and even in the world, including teams of excellence in both hardware (instrumentation) and software (data processing).

- Joint preclinical and clinical research facilities facilitating translational research.

- International recognition of most of the research staff.

- High attractivity due to the uniqueness of the imaging platform. Bright young and skilled researchers recently joined Neurospin to develop their own research projects.

- Depending on the outcome of the current research in instrumentation performed at CEA and Neurospin, Neurospin might really become a worldwide leader in UHMF imaging.

- The « Plan Campus » project might bring new opportunities for the development of Neurospin.

- Points to improve and risks :

- Insufficient human resources to make the most of the available imaging facilities, with no clear plan to attract the required additional resources and funding.

- Limited connexion with large hospitals, reducing the opportunity to successfully conduct large scale clinical studies due to insufficient recruitment.

- Lack of clear vision about the future insertion in the Plan Campus project.

- Lack of clear plan about the financial sustainability of Neurospin as a whole, and about the appropriate balance between research and platform activities.

- Chief positions to be urgently filled not to jeopardize a number of projects.

- Balance between platform activities and research activity should be carefully controlled, so that the staff hired for research does not spend more than 30% of their time to the platform activity, as initially planed.

- External projects run in Neurospin should go through a thorough review process before accepted.

- The primate surgical facilities (including operating theater) are below state-of-the-art installations. They may quickly become obsolete and not pass future authorization clearance procedures.

- Recommendations to the director of the Service:

- The leadership position of Neurospin will only be maintained if sufficient human and financial resources can be found to fully exploit the current facilities and successfully complete the on-going installation and establishment of research projects. An aggressive strategy is encouraged to further attract funding and skilled collaborators.

- A Scientific Advisory Board should be convened rapidly to help in the definition of mid-long term development research and funding strategies.

- The balance between platform activity and research activity should be carefully controled, at the level of Neurospin and also at the level of every member of the staff, so that it remains conform to the initial commitments.

- Recruitment strategy should not overlook the strong need in technicians and non-PhD engineers to take care of platform activities and also contribute to research activities.

- More regular information meetings related to Neurospin scientific strategy and development policy might be beneficial.

- Staffing levels and production

A1 : Nombre de produisants parmi les chercheurs et enseignants chercheurs référencés en N1 et N2 dans la colonne projet	17,70
A2 : Nombre de produisants parmi les autres personnels référencés en N3, N4 et N5 dans la colonne projet	0
A3 : Taux de produisants de l'unité [A1/(N1+N2)]	100%
A4: Nombre d'HDR soutenues	9
A5: Nombre de thèses soutenues	14

5.2 • Specific comments

- Appreciation on the results

Research conducted at Neurospin, be it related to instrumentation or data processing, is highly original and extremely relevant.

Research results are published in high impact factor journals, with a mean impact factor of 5.7 for publications between 2005 and 2009. The published articles are also cited frequently (average of 15 citations per article between 2005 and 2009), suggesting a good impact of the research results.

It was impossible to distinguish between pure Neurospin publications and publications associated with previous research in the documents made available to the experts, which included publications from 2005 to 2009 (Neurospin was created in 2007). However, overall, the publication records of Neurospin research staff is very good and even excellent for some teams (11.6 articles / FTE between 2005 and 2009)

Neurospin benefits from a large number of contracts with a broad variety of funding agencies (14 ANR contracts between 2005 and 2009, but also INCA, PHRC, aso) and companies (Guerbet, Bruker, Siemens, Servier), and is also involved in 7 European contracts. The part of external funding (salaries excluded) decreased however from 61% in 2007 to 42% in 2008.

- Appreciation on the impact, the attractiveness of the research unit and of the quality of its links with international, national and local partners

Since 2007, members of the Neurospin staff have been invited to give 58 conferences (23 at national and 35 at international meetings), and have been awarded 8 prizes (among which 3 international prizes). This reflects an outstanding visibility of the Neurospin staff.

The number of permanent researchers has increased from 19 in 2007 to 23 in 2009, corresponding to 10.7 FTE in 2007 and 14.5 in 2009 illustrating the attractivity of Neurospin and the ability to recruit new researchers. The proportion of foreign researchers has not been specified, but at least 2 skilled foreign researchers joined Neurospin to establish their own research projects.

The proportion of external funding (salary excluded) was 61% in 2007 and 42% in 2008. This corresponds to a large number of contracts with funding agencies (14 ANR contracts between 2005 and 2009, but also INCA, PHRC, aso) and companies (Guerbet, Bruker, Siemens, Servier). Neurospin is also involved in 7 European contracts. Neurospin is also part of MEDICEN, the Paris Region Competitivity Cluster.

Neurospin has a major collaboration contract with Germany, through the ISEULT program (215 M€ involving companies, academia, and public funding agencies such as Oséo in France and BMBF in Germany).

Collaboration agreements with exchange of researchers have also been signed with the University of Kyoto and Tokyo, the National Yang-Ming University of Taiwan, the Julich Research Center in Germany and the National Research Council of Canada. Several other agreements are pending. NeuroSpin is also a founding member of EATRIS, a European network of Infrastructures within EU ESFRI framework.

Nationally, NeuroSpin is also part of several networks (Federative Research Institute on Neuroimaging, IFR 49, advanced research networks such as FONDamental (psychiatric disorders), Sensorial Handicap.

This network of collaborations clearly demonstrate the involvment of Neurospin in a broad range of national and international research programs.

In addition to getting an international recognition through high level publications, Neurospin has also a proactive promotion strategy aiming at increasing the national and international visibility of the facility. This includes a major involvement in the organization of training courses in neuroimaging in France, open-doors events, organization of artistic shows, organization of general public conferences (CYCLOP, UTLS, TV, radio).

- Appreciation on the strategy, management and life of the research unit

Neurospin organization is well structured, with 5 well identified laboratories (2 of which having only platform activities at the moment), and 6 research programs, most of which involving several laboratories. Two labs have open chief position however, with interim chiefs at the moment.

The management is of top-down type, and felt as such by the staff. In addition to the large number of scientific seminars organized in Neurospin, more regular information meetings related to Neurospin strategy and policy involving the staff could be encouraged. This could be an opportunity to regularly check with the staff the balance between research activity and platform activity, and identify early what might become a source of frustration for part of the staff (involved in too much platform activity at the expense of research activity, limited access to the imaging instruments and reserch facilities due to the opening hours of Neurospin).

A Scientific Advisory Board should be convened regularly to help in the definition of mid-long term development research and funding strategies.

Internal communication is appropriate. Sufficient internal communication opportunities to discuss severe issues that might be encountered by the staff. However, a number of technical issues (like access to one's PC from outside Neurospin) have been raised, for which solutions seem to exist but are not widely shared between the staff.

Neurospin is also affected by a number of administrative constraints related to CEA, which are felt counterproductive by the staff. Among these constraints, one can quote the closing hours that limit the access to research facilities (especially penalizing for Master and PhD students), lack of access to Neurospin computers from oustide, lack of visibility in the recruitment process for non-permanent researchers hired on contracts, and non-permanent positions limited in time, which makes it impossible for a PhD to pursue his/her research in Neurospin as a post-doc.

The composition of the staff shows a extremely large proportion of highly qualified staff (PhD) but few lower level engineers without a PhD and technicians (the exact figures cannot be derived from the data provided to the experts though). Due to this situation, tasks that should be performed by technicians or lower level engineers are actually often performed by highly qualified staff. Rethinking the optimal distribution of the qualification of the staff might be worthwhile.

Communication between the other I2BM centers (MIRCEN and SHFJ) could be enhanced, for the sake of consistency of I2BM as a whole.

External communication to general public is excellent, with a large number of events dedicated to disseminating knowledge related to Neurospin activities.

The Neurospin staff is extremely satisfied by the large number of opportunities they have to meet worldwide experts in the field of neuroimaging through high quality seminars organized weekly. The scientific animation is relevant and of high quality, and contributes to the efficient dissemination of knowledge through the broad variety of specialties existing in Neurospin.

Undertaking risky projects is an integral part of Neurospin and is probably its major asset. Given the outstanding expertise of the staff and of the CEA expertise in magnet technology, it is almost certain that these projects will significantly contribute to advances in the domain of HMF MR and UHMF MR.

The Neurospin staff is involved in training and education activities at the national level (courses in Neuromaing) and at the European level (European Master in Molecular Imaging). Efforts are made to contribute to the structuration of research in imaging for Neuroscience at the regional level (for instance, through the leadership of IFR49), and at the national level (for instance, CATI project – Centre d'Acquisition et de Traitement d'Images).

- Appreciation on the project

Pushing the limits of MR imaging, which is the core project of Neurospin, is of high relevance from a fundamental physics point of view. The Neurospin facilities have been designed appropriately to help push these limits.

The feasibility of the scientific project includes 2 aspects, which are discussed separately here. The first aspect is the technical feasibility, as building and running successfully a 11.7 T human MR remains a extremely tough challenge, as well as running a 17.2 T for preclinical studies. However, the CEA expertise (beyond Neurospin) makes it reasonable to bet that at least significant advances will be made.

The second aspect concerns the financial feasibility of the scientific projects. This mid-long term feasibility will strongly depend on the success in recruiting the staff needed to make the most of the current and future imaging facilities. The lack of clear plans concerning an aggressive strategy to attract fundings on the mid-long run is definetly a weakness. The management is clearly well aware that Neurospin cannot be supported on the long run by CEA on its own, or by a unique funding entity, but that an agreement of some sort has to be found between several academic, public or private partners to sustain Neurospin. However, clear plans regarding the actual annual cost of Neurospin, and associated funding solutions are lacking.

A number of needs have been identified, especially regarding lacking human resources. However the policy which will be undertaken to meet the needs is unclear. In addition, the priority with which the different needs will be satisfied has not been presented.

A Scientific Advisory Board might be helpful in orienting this policy of affectation of human and financial resources.

The originality of the research activity performed in Neurospin is outstanding. Highly risky projects are on-going, using leading edge technology. This is defintely the strongest asset of Neurospin, which can certainly be viewed as the most innovative medical imaging project in France.

5.3 • Appreciation team by team

Team 1: Laboratoire d'imagerie et de spectroscopie (LRMN)

Team leader: Mr. Denis LE BIHAN

- Staffing levels

	Dans le bilan	Dans le projet
N1 : Nombre d'enseignants-chercheurs (cf. Formulaire 2.1 du dossier de l'unité)	0	0
N2 : Nombre de chercheurs des EPST ou EPIC (cf. Formulaire 2.3 du dossier de l'unité)	4.3	5
N3 : Nombre d'autres enseignants-chercheurs et chercheurs (cf. Formulaire 2.2 et 2.4 du dossier de l'unité)	0,2	0,2
N4 : Nombre d'ingénieurs, techniciens et de personnels administratifs titulaires (cf. Formulaire 2.5 du dossier de l'unité)	5,4	5.8
N5 : Nombre d'ingénieurs, techniciens et de personnels administratifs non titulaires (cf. Formulaire 2.6 du dossier de l'unité)	2	1
N6 : Nombre de doctorants (cf. Formulaire 2.7 du dossier de l'unité)	5	7
N7 : Nombre de personnes habilitées à diriger des recherches ou assimilées	1	1

- Appreciation on the results

The team is an international leader in its field. The methodologies of NMR instrumentation and signal acquisition developed in this group are among the best in the world; especially in the domain of high field MRI in general and in the domain of Neuroimaging in particular. As the team creation is new (2007), the assessment of its proper scientific production as a team is rather difficult to establish. However, the scientific production of the past team members and of the scientists who joined the group more recently is excellent. As a whole, this research group has published more than 80 papers in peer reviewed publications between 2005 and 2009, most of them in journal with very high visibility, such as Proceedings of National Academy of Sciences, Nature, Neuroimage, Human Brain Mapping, Cerebral cortex, Radiology, Magnetic Resonance in Medicine, Journal of Cerebral Blood Flow and Metabolism. Team members have also participated to 95 international conferences between 2005 and 2009.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

This group has been very successful in generating funding. LRMN has obtained several international, national and regional contracts with participation of academia, industries, and public agencies. This funding will allow the building of the first whole-body 11.7T MRI scanner in the world.

The exceptional environment and the research quality of the team have led to an exceptional attractiveness: numerous foreigner students, post-docs as well as researchers have joined the team since its creation.

LRMN has also established several international collaborations with the University of Kyoto and Tokyo, the National Yang-Ming University of Taiwan, the Julich Research Center in Germany and the National Research Council of Canada. The team is also part of European, National and Regional networks. Team members have been invited speakers 77 times during the last four years.

- Appreciation on the strategy, management and life of the team

The group is seeking a team leader as the actual leader is also heading Neurospin. The two groups named 'Brain plasticity (rodents, primate, humans)' and 'Translational and cognitive neuroscience (from monkey brain to patient brain)' are part of the LRMN although their topics are not properly fitting the LRMN scientific orientation which is rather dedicated to instrumentation and NMR signal acquisition.

Concerning communication policy, the lack of strategic meeting inside the LRMN seems to lead to unilateral decisions (top-down) in term of team strategy.

Team members are not participating to teaching and only one member has got an 'HDR'.

- Appreciation on the project

Most of the projects proposed by this team are of outstanding interest and originality. The high risks taken by especially regarding the UHF MRI developments (particularly the 11.7T project) could have the highest impact in the domain in case of success. Projects concerning NMR signal acquisition methodologies, for instance in the domain of real time MRI, microscopic imaging, functional and diffusion MRI are also particularly remarkable. The team has the skills to perform these ambitious projects. However, the current lack of sufficient human resources (technicians, nurses, MD) might jeopardize the feasibility of the project.

- Conclusion:

- Summary

The exceptional MR platform of Neurospin and the quality of researchers in the LRMN team lead to an excellent research activity in the domain of instrumentation and MR signal acquisition at high and ultra high fields. LRMN is one of the world leaders in the domain.

- Strengths and opportunities

The facilities of Neurospin and the high risk cutting-edge projects of the LRMN could bring very original results with potential outstanding impact.

- Weaknesses and threats

The strategic organisation of the LRMN is not yet completed. In particular, the logistics (mechanics workshop, electronics, but also nurses and MD) to be associated with the research activities is not fully operational yet, mostly due to lack of staff. Lack of additional human task force might jeopardize the feasibility of a number of preclinical and clinical studies and reduce the competitiveness of LRMN with respect to that of other ultra high field international centers.

The involvement of the team members in teaching is weak.

- Recommendations

- A leader for the LRMN lab has to be identified.

- The organisation and the communication policy could be improved to better involve the staff into the scientific life of the LRMN and increase the cohesion of the group.

- Taking into account the quality of the researchers, one can encourage them to be more involved in teaching.

- More HDR in the LRMN is also needed to facilitate the supervision of the students working at the LRMN.

- The 'Brain plasticity' and 'Translational and cognitive neuroscience' groups should grow and become independent from the LRMN in the future.

- Additional staff should be attracted to ensure the technical feasibility of the developments that will be needed to make the 17T rodent imaging and 11.7 T human imaging become a reality.

Team 2 : Laboratoire de Neuro-imagerie Assistée par Ordinateur (LNAO)

Team leader : Mr. Jean-François MANGIN

- Staff members

	Dans le bilan	Dans le projet
N1 : Nombre d'enseignants-chercheurs (cf. Formulaire 2.1 du dossier de l'unité)	0	0
N2 : Nombre de chercheurs des EPST ou EPIC (cf. Formulaire 2.3 du dossier de l'unité)	5,2	7,6
N3 : Nombre d'autres enseignants-chercheurs et chercheurs (cf. Formulaire 2.2 et 2.4 du dossier de l'unité)	0	0
N4 : Nombre d'ingénieurs, techniciens et de personnels administratifs titulaires (cf. Formulaire 2.5 du dossier de l'unité)	5,8	5,5
N5 : Nombre d'ingénieurs, techniciens et de personnels administratifs non titulaires (cf. Formulaire 2.6 du dossier de l'unité)	5	4
N6 : Nombre de doctorants (cf. Formulaire 2.7 du dossier de l'unité)	12	12
N7 : Nombre de personnes habilitées à diriger des recherches ou assimilées	4	6

- Appreciation on the results

The scientific production of the LNAO team is of international level. E.g. the work on Diffusion Tensor Imaging, as well as the development of new statistical tests for fMRI data, is clearly state-of-the-art. Moreover, the cerebral structural analysis based on the sulci is totally original and has no equivalent worldwide.

There are two main types of publications: either "methodological" publications in the best journals (HBM, NeuroImage) and conferences (MICCAI, IPMI), or "applicative" publications, co-authored with other groups, some of them being in the very best journals (Science, …).

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

Throughout "BrainVisa", the LNAO team offers unique means to integrate methodological results and tools into a single software platform, which facilitates and enforces the collaborations between the I2BM teams. The LNAO team recently made efforts to increase the international spread and recognition of BrainVisa (for instance by organizing BrainVisa training at the national level), which should further enhance the visibility for the team.

The team has won best paper awards at the two main methodological conferences (IPMI and MICCAI). It also has organized some international meetings (e.g. satellite workshop of MICCAI on white fiber tractography evaluation).

The team succeeds in attracting foreign PhD students, who are clearly aware of working in a high standard research environment. The team also participates in a quite large number of national (e.g. ANR) or international (e.g. Iseut) contracts, but unfortunately, the current information available at the time of the review could not clearly give objective figures of this.

- Appreciation on the strategy, management and life of the team

LNAO has both a long-term research strategy (e.g. the sulci-based analysis, or development of BrainVisa that aims at gathering and spreading the methodological results of the team) and the ability to launch new research topics (e.g. genomic-based image analysis). This allows publishing at the top international level.

To increase the team visibility, an active policy has been set-up with a large increase in conference publications, as well as a significant involvment in the organization of international meetings.

These actions enable the team to be considered as a major player in the field of data processing for neuro-imaging at the international level.

- Appreciation on the project

The LNAO scientific project has several goals that can be classified according different types.

Some of them follow a long-term strategy, as the sulci-based structural and functional analysis of the brain. This is an original research topic that has no equivalent worldwide. Major breakthroughs and findings can be achieved using such an original approach.

Some of them aim at proposing high-quality tools for the neuroscientist end-users: it goes from segmentation tools to the development of new (and original) statistical methods that offer an alternative to the well-known SPM software. However, such tools can only gain acceptance throughout a massive use by neuroscientists. The diffusion policy maintenance services associated with BrainVisa will be determinant factors to establish the role BrainVisa will play at the international level in the future.

Some of them aim at introducing new research topics, as identifying relationships between genes and anatomical/functional characteristics. This is a new research topic, which might lead to major discoveries.

- Conclusion :

- Summary

This is a strong research group that publishes in the best journals and conferences in the field of data processing in neuroimaging. It is clearly among the top ten percent best research teams in that field.

- Strengths and opportunities

It is embedded in Neurospin, so has strong connections with the LRMN group, hence can have access in advance to data generated with the top-of-the-art MR sequences, which gives a definite advantage. In addition, collaboration/discussion with end-users of MR scanners (neuroscientists) helps in defining an efficient scientific strategy. Last but not least, it has a potential access to the data generated in NeuroSpin, which makes large group studies possible.

- Weaknesses and threats

The group is also involved in the processing of the data generated by the neuroscience studies taking place in Neurospin (platform activity), which is a source of contractual incomes. Up to now, this activity seems balanced with the research activity, but an uncontrolled increase of the platform activity might lead the team to be considered only as “image processing technicians”.

The policy associated with the diffusion and maintenance of the BrainVisa software is quite unclear.

The positioning of LNAO with respect to other excellent competitive teams working in the same field in France should be clarified (e.g. INSERM and CNRS from Paris and abroad).

- Recommendations

- Define a clear policy for the BrainVisa software regarding its diffusion, maintenance, and user support.

- Be proactive at selecting the external projects that are run in Neurospin and can be demanding in terms of post-processing developments so as to control the balance between development activities induced by the platform services and research activities corresponding to a scientific strategy.

- Clearly define the positioning of LNAO with respect to other teams of excellence working in the same field in France, in order to make the most of the limited resources and share expertise.

6 • Appreciation on the Service Hospitalier Frédéric Joliot

- History and geographic localisation of the service and a synthetic description of the domain of its activities :

This service aims to invent, to develop and to valorise imaging methods for improving the management and treatment of diseases. It has expertise in several domains of health:

- Neurology, including neurodegenerative and neuroinflammatory diseases in particular,

- Psychiatry, including schizophrenia, addiction, mood disorders and autism in particular,

- Oncology, including neurological cancers, hormone-dependent cancers, neuroendocrine tumours and lung cancers in particular,

- Vascular diseases (atheroma, ischemia), metabolic diseases (diabetes) and systemic,

- Inflammatory diseases.

The SHFJ will also valorise and develop its expertise by undertaking “platform” activities, making its resources available to internal and external partners. This reorientation is currently underway and the SHFJ in its new form should gradually become operational over the course of 2010 and 2011.

The SHFJ also includes a clinical nuclear medicine unit serving as a diagnostic centre, in accordance with the national cancer research plan.

- Direction :

The Service Hospitalier Frédéric Joliot (SHFJ) includes the U1000, U1023, U663 and the Cierm. The head of the service is Mr. Pascal Merlet.

- Staffing levels:

	Dans le bilan ETP 30/06/09	Dans le projet ETP 01/01/11
N1 : Nombre d'enseignants-chercheurs (cf. Formulaire 2.1 du dossier de l'unité)	0,90	2,4
N2 : Nombre de chercheurs des EPST ou EPIC (cf. Formulaire 2.3 du dossier de l'unité)	18,8	19,90
N3 : Nombre d'autres enseignants-chercheurs et chercheurs (cf. Formulaire 2.2 et 2.4 du dossier de l'unité)	3,5	2
N4 : Nombre d'ingénieurs, techniciens et de personnels administratifs titulaires (cf. Formulaire 2.5 du dossier de l'unité)	37,3	40,10
N5 : Nombre d'ingénieurs, techniciens et de personnels administratifs non titulaires (cf. Formulaire 2.6 du dossier de l'unité)	8	
N6 : Nombre de doctorants (cf. Formulaire 2.7 du dossier de l'unité)	8	13
N7 : Nombre de personnes habilitées à diriger des recherches ou assimilées	13	18

6.1 • Overall appreciation on the Service

The Committee was only asked to review three teams in detail. The committee received the document « AERES EVALUATION » (DOC DEF.REPRO SHFJ 140110.pdf) which dedicates 47 of 117 pages to an overview of the SHFJ and the three laboratories that were evaluated in detail ; i.e. the committee did have access to information on the other constituents of the SHFJ (pages 48-117). In addition, the SHFJ was presented by its head during one hour on the 11th of February, and the slides were made available electronically ; posters were presented ; and in addition to 45-minute presentations by the Group Heads of the three teams evaluated in detail, short (20 min) presentations were given by the Genetic/Imaging group (U803 = U 1023 ; previously evaluated) ; the Epilepsy and Brain Plasticity group (U663 ; previously evaluated) ; and the Psychiatry Imaging group (U797 = U 1000 ; previously evaluated). The CIERM was briefly presented during discussions, and the Nuclear Medicine Laboratory more briefly still. Finally, Committee members met separately with PhD students / postdoctoral fellows ; engineering / technical / administrative staff ; and permanent research staff.

- Global Opinion:

As was clear from the report and mentioned several times during the presentations, the SHFJ has undergone major changes with the departure of several groups in their entirety ; regulatory issues leading to a cessation of clinical radiochemistry production activity for nearly two years ; the coming into existence of Neurospin and Mircen as the other constituents of the I2BM ; the planned arrival of an entirely new team (CIERM) together with its infrastructure ; as well as major changes in composition of its Nuclear Medicine Laboratory. The SHFJ, also known as « Orsay » for short, is one of the very well respected neuroscientific PET centres in the world, with an enviable track record of innovation in radiochemistry, tracer development / evaluation, progress in instrumentation / reconstruction, and clinical studies mainly in the neurosciences and neurology. The committee saw plenty of evidence

of such excellence continuing (see evaluations of individual groups) and notes that those of SHFJ's teams evaluated prior to this visit did all achieved « A » ranking, in line with the internationally competitive standing of the SHFJ.

The committee had some concerns regarding overall strategy, internal communication, and governance. One particular point that caught the committee's attention is the role of the Nuclear Medicine Laboratory which seems ill defined, at odds with previous strategy, and its new aims difficult to achieve with the means allocated.

The SHFJ has a long and strong history in quantitative (nearly exclusively neurological) ligand PET and can build on the strong « Orsay brand ». The SHFJ disposes of a complete gamut of techniques and laboratories around quantitative ligand PET, set up to work from target identification, optimisation, production, pharmacological and preclinical biological evaluation (including rodents and non-human primates), first in man studies including regulatory know-how, to patient studies. It also has public transport on rails nearby, in contrast to the other I2BM structures, which should be a major bonus in particular for patient studies.

- Points to improve and risks:

There was an impression of lack of focus during the major reorganisation following the departure of the MIRCEN and Neurospin teams. The integration of the CIERM team may work but is not perceived as a natural addition to SHFJ's resources. Finally, it never became quite clear how the new planned focus of the Nuclear Medicine Group on oncology and cardiology will be integrated and achieved – hardly any of the groups evaluated or presented seemed to have any particular interest in either field, and no new resources seemed to be strategically allocated.

There is a risk of resources being redirected to Neurospin in particular, for example in terms of radiography staff allocation, and MRI support. For example, the budget is increasing minimally, in contrast with large increases for the other constituents of the institute.

The committee felt that there may not be enough communication of overall strategy and not enough mid-level discussion with the heads of the individual groups (rather than between the institute's director and the three directors of the « services »). In addition, staff seemed somewhat disengaged from the overall strategy and may need better communication strategy. In a similar vein, Human Resources seemed to be underused, and the committee did not get the impression that staff with concerns had easy communication channels at their disposal. Finally, the Committee had found it relatively difficult to extract overall direction from the written report; some more « executive summaries » would have been in order. A minor point, but easy to improve, is the excessive use of unexplained abbreviations.

A scientific advisory board with a clearly defined role would be as useful for the SHFJ as for the I2BM as a whole.

While there is quite a large proportion of foreign doctoral students and postdocs within I2BM (25%), there was little English spoken, and a large proportion of staff felt their English could be improved. English lessons are available; it may be possible to restructure the offers or hold certain meetings in English to improve language made overall.

- Recommendations to the director of the service:

The SHFJ is a centre of international standing and well able to compete on the international stage in its core competences. Concentrating on these, investing wisely to keep facilities, equipment and human resources in top form, and further integrating with the other constituents of the I2BM should enable SHFJ to flourish despite the major upheaval of the recent years.

If expansion into a new oncology/cardiology programme is strategically desired (and the Committee was not convinced such a desire was shared by all involved rather than being a by-product of regulatory pressure for a large number of studies per machine), then firstly some external input or review should be sought (e.g. by having the Nuclear Medicine Laboratory and its research plan evaluated by the AERES; by discussing matters with a Scientific Advisory Board) and secondly the SHFJ and I2BM need to consider which resources need to be made available to the Nuclear Medicine Laboratory itself and to the upstream / downstream laboratories in order for the expansion to succeed.

	ETP
A1 : Nombre de produisants parmi les chercheurs et enseignants chercheurs référencés en N1 et N2 dans la colonne projet	22.30
A2 : Nombre de produisants parmi les autres personnels référencés en N3, N4 et N5 dans la colonne projet	2
A3 : Taux de produisants de l'unité [A1/(N1+N2)]	100%
A4: Nombre d'HDR soutenues	13
A5 : Nombre de thèses soutenues	17

6.2 • Specific comments

- Appreciation on the results

The SHFJ teams undertake original and relevant research, centred on brain PET. The centre and its groups are very well respected and have « exported » knowledge in the form of many trained researchers, software, know-how and methods, and entire new groups or even institutions. The quality of publications is generally good and naturally very variable in terms of journal and subject. The committee notes a reasonable number of publications in top clinical or methodological journals (e.g. Brain, Lancet Neurology, J Nucl Med, PNAS, Am J Psychiatry,..). The (not terribly relevant) journal impact factor for chemistry or signal processing journals is lower than that of clinical journals, but the Committee notes that the SHFJ has achieved numerous citations for non-clinical, non-biological papers in chemistry journals too (e.g. Bioconjugate Chemistry 2005). There were 12 patents over the evaluation period which is very good and bears witness to originality.

With 24.3 full time equivalent (FTE) researchers, SHFJ has produced 256 peer-reviewed articles during the review period as stated in the slide show, or more than two per FTE researcher per year, which is reasonable. As a group, SHFJ researchers achieved an h index of 22 over this time which is good.

Productivity varies widely between individuals, perhaps more so than in other centres, but overall it is clearly internationally competitive.

The various teams have contributed to software packages (e.g. BrainVisa; reconstructions in collaboration with Siemens which contributed to Siemens' latest commercial reconstruction software; new partial volume effect corrections and basal ganglia automated segmentations); the Radiochemistry group regularly teaches internationally and has helped to set up radiosyntheses elsewhere in France and abroad. As mentioned above, 12 patents have been filed over the evaluation period.

- Appreciation on the impact, the attractiveness of the research unit and of the quality of its links with international, national and local partners

The SHFJ is very well established on the international scene, having been at the forefront of quantitative (brain) PET for a long time. About 1.6 M€ of industry grants were won in 2009 alone. The overall non-CEA funding (i.e. industry plus academic grants) was proportionally stable at about 75% between 2007 and 2008, but increased in absolute terms from about 3.5 M € to about 4.5 M €. While it is difficult to project permanence of research contracts into the future, we feel it is safe to assume that past history should be an indicator of future performance.

Approximate 2008 external funding was: from government agencies (0.5M€), industry (1.2M€), "health care funding" (1.25M€, up more than fivefold during the review period) and EU research grants (0.45M€), i.e. about 3.5M€ in total does not quite seem to add up to the about 4.5M€ of external funding. The committee assumes that "health care funding" corresponds to revenue from clinical nuclear medicine investigations; the director's office has most probably considered the likely future development of this income stream.

- Appreciation on the strategy, management and life of the research unit

There were five prizes listed, 24 "invited lectures" (assumed to be given at international conferences), and there are other measures of esteem like frequent invitations to review, eight editorial board memberships, membership of European networks, memberships of academic self-administration bodies, review committees and grant reviewerships. In addition, 13 meetings were organised of which about half international. We also note international teaching and developmental activities.

17 students finished their PhDs, but no data were available on the success rate or time taken. These indicators are commensurate with the internationally competitive status of the SHFJ.

For a centre of SHFJ's standing, it should be no problem to attract high-calibre staff, including non-French. According to the overview I2BM presentation, 25% of I2BM's postdoctoral researchers and PhD students are non-French which may indicate sufficient attractivity but is probably on the low side internationally. In addition, most and possibly all of SHFJ's team leaders are French which appears somewhat unusual. In discussions, the committee formed the opinion that CEA's recruitment mechanics may possibly be unfavourable to international mobility, as this often requires great flexibility and speed in decision-making.

See paragraph above on "relations contractuelles". The committee was pleased to see that over 40% of total spending (about three quarters excluding salaries) was through external funding in 2007/8 (slide 12), and that the SHFJ has been able to increase its funding from government agencies, industry and EU grants over the review period.

There are several international collaborations (see notably detailed evaluations of the three individual teams) even if many collaborations are internal (SFHJ, I2BM), local (Paris universities and hospitals) or regional (Ile de France). Participation in international programs is good, with several EU grants for example, and the outreach through SHFJ's production (see above).

The SHFJ has obtained twelve patents over the review period. No information on the associated income from these was available. Cultural output (e.g. popularisation of science books) is naturally lower than that of e.g. Neurospin with more cognitive research, if this is what is meant by the question.

There is a lack of clarity of the role of the teams in overall strategy and the clinical part of the activities (i.e. "platform" versus research activities).

The committee felt that there may not be enough mid-level discussion with the heads of the individual groups (in addition to the regular meetings between the institute's overall director and the three directors of the « services »/institutes). In addition, staff seemed somewhat disengaged from the overall strategy and may need better communication of common aims. In a similar vein, Human Resources seemed to be underused, and the committee did not get the impression staff with concerns had easy communication channels at their disposal. Finally, the Committee had found it relatively difficult to extract overall direction from the written report; some more « executive summaries » would have been in order.

The governance strategy was not entirely clear to the Committee. An example was the lack of clarity around the decision-making about the planned major change in scientific focus (from brain PET to cardiological and oncological PET). Another striking example is the apparent near complete lack of yearly appraisals as an instrument of people management. High attrition rates in some teams may conceivably be related to (lack of) feedback mechanisms which the committee felt to be undeveloped.

External communication leaves much to be desired. For example, the AERES document for the SHFJ displays lack of overall high-level explanation of the SHFJ, complete lack of information on team membership for several teams and unclear attributions in other cases, lack of requested performance statistics like grant income or papers per FTE researchers except for P Remy's team, confusing nomenclature (e.g. two groups have changed their number, LRR / LPAI / LINP are referred to by their abbreviations in the text but not the table of contents) etc. The web page is a nearly unmanageable maze. As a small example of where confusion arises, it shows a different organisation to the

AERES document (e.g. Psychiatric Imaging is shown as part of Nuclear Medicine on the web page, but both appear at the same hierarchical level (D. & E.) in the AERES document – and Psychiatric Imaging is listed as a part of the Clinical Investigations Laboratory on slide 34 of the presentation. The English version of the web site exists only in fragmentary form; the English itself needs urgent revision (for example, http://www-dsv.cea.fr/en/instituts/institut-d-imagerie-biomedicale-i2bm/presentation contains an involuntary rude joke – such errors may be enough to put potential students off). Research teams are usually not accessible via the search function on the main (CEA) web site, neither with their code (e.g. U 797, U 1023) nor via their abbreviation (e.g. LINP). It is not clear to the committee to what extent the SHFJ has control over its own web appearance.

There seems to be good internal scientific animation with yearly "PhD days" and fortnightly seminars plus occasional invited speakers. The committee omitted to ask whether PhD students are systematically encouraged to present even work in progress, and to present in English.

The SHFJ has a good presence at international conferences.

In reviewing the three individual groups, the committee noted a rather conservative attitude with respect to risk taking. Some of this will be due to the nature of the research in those groups that need to coordinate PET tracer development between the other SHFJ teams.

All of SHFJ seems to be very implicated in teaching in the region, with teaching activities mainly in the various Paris universities. The SHFJ currently plays a major role in structuring imaging research in the Paris region, and is the essential platform for brain PET in Paris, itself a major neuroscience hub in Europe.

Overall the committee felt the teaching and outreach activities were very good.

- Appreciation of the project:

There was an overall feeling of lack of direction, probably related to the ongoing major restructuring efforts as mentioned earlier. The individual groups do have realistic, reasonable, feasible and often excellent four-to-five-year projects; it is less clear what the strategic vision for SHFJ's position five years into the future will be.

Some concrete examples have been mentioned earlier. They include e.g. the future role of the nuclear medicine team where the Committee notes an apparent absence of links for the planned programs. To take the example of Oncology, slide 41 lists the "University Hospital Network Oncology". The committee is very concerned indeed that for the seven named collaborators from four institutions, there are only two peer-reviewed papers out of the SHFJ in five years where any one of them (Lievre) is a co-author (middle author). There seems to be no track record whatsoever on which to build a new programme.

Another example is the hosting of CIERM – in itself an excellent team, but the hosting seems to be happenstance rather than driven by strategic logic, and the SHFJ might at best benefit from technical competence in maintaining its MRI imaging capabilities.

This is a slightly less acute problem for the SHFJ with a budget that is relatively stable compared to Mircen or Neurospin. Nonetheless, the Committee felt that there was little strategic thinking about resource allocation - for example, we noted the lack of plans regarding MRI support and long-term equipment replacement.

Some of this may be culturally specific to SHFJ's situation, with a long and distinguished history, a large part of the scientific workforce on permanent contracts, and groups adjusting their funding to their needs via external funding.

There also seemed to be no provision for the planned expansion for oncology and cardiology.

Many individual projects are original and linked to some risk. The "core business" of the SHFJ, as a high-level technological platform, is less amenable to risk taking as many groups have to maintain a high level of research excellence for providing services.

6.3 • Appreciation team by team

Team 1: Radiochimie et radiopharmacie

Team leader: Mr. Frédéric DOLLE

- Staffing levels:

	Dans le bilan	Dans le projet
N1 : Nombre d'enseignants-chercheurs (cf. Formulaire 2.1 du dossier de l'unité)		
N2 : Nombre de chercheurs des EPST ou EPIC (cf. Formulaire 2.3 du dossier de l'unité)	3,4	3,4
N3 : Nombre d'autres enseignants-chercheurs et chercheurs (cf. Formulaire 2.2 et 2.4 du dossier de l'unité)		
N4 : Nombre d'ingénieurs, techniciens et de personnels administratifs titulaires (cf. Formulaire 2.5 du dossier de l'unité)	9,6	9,6
N5 : Nombre d'ingénieurs, techniciens et de personnels administratifs non titulaires (cf. Formulaire 2.6 du dossier de l'unité)		
N6 : Nombre de doctorants (cf. Formulaire 2.7 du dossier de l'unité)	3	2
N7 : Nombre de personnes habilitées à diriger des recherches ou assimilées	2	2

- Appreciation on the results

The laboratory has a strong platform activity and a large part of the research projects conducted at I2BM depend on it for the access to carbon-11 and fluorine-18 labeled PET tracers. As a result, the laboratory is a key laboratory for I2BM and a real asset. The laboratory is organized around three activities: research on radiolabeling techniques; development of new labeled tracers; and production of labeled tracers for preclinical and clinical research. The level of expertise is excellent and the team is internationally recognized as one of the leading groups in this particular field.

The laboratory has an important production, both quantitatively (60 for 2005-2009) and qualitatively. The publications are of two types: papers dealing with radiochemistry and radiopharmacy, specific productions of the laboratory, difficult to publish in high ranking journals; and papers that result from collaboration (to a large extent with other laboratories of the I2BM) describing the biological properties of the radiotracers. Both kinds of publications have a real impact in terms of number of citations and many are published in the best specialty journals. The laboratory also produces patents.

The laboratory participates in a series of scientific collaborations with academic (including European networks of excellence) and industrial partners (including large pharmaceutical companies). A contract being by definition limited in time, the committee did not understand the question about continuity of contract relationships.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

The laboratory is composed of young scientists, engineers and technicians. However, its leader has been invited to give many lectures (31) including 10 in international meetings during the years 2005-2009.

The laboratory has an internationally recognized know-how that attracts foreign visitors and students.

The laboratory has good connections with industry, both radiopharmaceutical companies and major pharmaceutical companies.

The laboratory is involved in collaborations with French academic laboratories and with academic laboratories in Scotland and Australia. It is also part of the EMIL network of excellence.

This is another strength of the laboratory. Tracers developed in the laboratory as part of its research activity are produced for use in research at I2BM as part of the platform activity of the laboratory. In the past, production for clinical investigations was an important part of the group's activity, which should resume in the next few months after the renovation of the production laboratory.

The laboratory transfers its know-how to other institutions (Bejing Union Medical College Hospital, GIP CYROI platform (CYclotron Réunion Océan Indien), La Réunion, France)

- Appreciation on the strategy, management and life of the team

The laboratory is very well organized to maintain, within the same environment, the platform activity (production of radiolabelled tracers for preclinical and clinical research) and the research activity. Both are well connected and clearly identified.

The laboratory is involved in the organization of meetings, both national and international, and participates in several scientific networks and scientific societies, both at the national and international levels.

The role of the laboratory in I2BM's research has already been mentioned. Members of the laboratory are very active in teaching, both at the national level (masters) and at the international level (courses organized by European NoE and INSTN).

- Appreciation on the project

The project for the next few years is clearly defined with, in particular, the development of [18F]fluorinated "click" reagents and the development of tracers targeting the peripheral benzodiazepine receptor (PBR). The development of the Fluor-C project, a platform for the GMP production of radiopharmaceuticals, is another important project for the I2BM.

The strategy for the allocation of resources should be assessed at the SHFJ and the I2BM level.

Only a few groups in the world have developed the know-how for the discovery and production of new carbon-11 or fluor-18 labelled tracers and it is important that this know-how is maintained and expanded. Although the laboratory has a clear objective of developing new techniques, the projects remain within the limits of the transposition to this field of approaches that have proven their feasibility. Risk taking in the definition of research projects could be increased.

- Conclusion :

  - Summary

Once the GMP facility will be in operation, the platform will be one of the most productive in the world for preclinical and clinical research. The know-how that made the reputation of the SHFJ for the application of short-lived radionuclides to PET imaging is maintained and expanded.

- Strengths and opportunities

Only a very small number of laboratories have the ability to produce the kind of radiotracers that are needed for PET imaging research within the I2BM and this laboratory has achieved excellence in this field. Complementarity between the laboratory and the groups involved in biological applications of the tracers is a great opportunity.

- Weaknesses and threats

The laboratory has faced a great risk: the regulatory risk, which is outstanding in radiopharmacy. The fluor-C project is the right response to this risk. Beyond that, one risk is the fact that the biological evaluation of the tracers (metabolism, pharmacokinetics, imaging properties) depends on other groups of I2BM and outside collaborations, but it is difficult to think of a different organization and there is an excellent track record of the different groups within the SHFJ working together on these tasks.

- Recommendations

The committee encourages the laboratory to continue its activity with the same enthusiasm and competence, to look for new applications of radionuclide imaging and maintain creativity.

Team 2 : Imagerie Neurologique et Pharmacologique (LINP)

Team leader: Mr. Michel BOTTLAENDER

- Staff members

	Dans le bilan* ETP	Dans le projet ETP
N1 : Nombre d'enseignants-chercheurs (cf. Formulaire 2.1 du dossier de l'unité)	0,10	0,10
N2 : Nombre de chercheurs des EPST ou EPIC (cf. Formulaire 2.3 du dossier de l'unité)	3,1	2,6
N3 : Nombre d'autres enseignants-chercheurs et chercheurs (cf. Formulaire 2.2 et 2.4 du dossier de l'unité)	0,5	0,5
N4 : Nombre d'ingénieurs, techniciens et de personnels administratifs titulaires (cf. Formulaire 2.5 du dossier de l'unité)	1,2	1,2
N5 : Nombre d'ingénieurs, techniciens et de personnels administratifs non titulaires (cf. Formulaire 2.6 du dossier de l'unité)	0	0
N6 : Nombre de doctorants (cf. Formulaire 2.7 du dossier de l'unité)	0	0
N7 : Nombre de personnes habilitées à diriger des recherches ou assimilées	1	2

* périmètre reconstitué

- Appreciation on the results

The team pursues research in neurological Imaging and pharmacology, centred on the evaluation of novel ligands that are produced in Team 1 (F. Dollé) and based on the needs of the Service (SHFJ) and associated programs. The team enables translation of new tracers and quantification methods from animals to humans and hence fulfils a function that is indispensable for the successful operation of the SFHJ. The implementation of sophisticated modelling

methods for PET time series has, for example, enabled the original description of a change of affinity but not number of nicotinergic acetylcholine receptors in baboons chronically exposed to nicotine.

With 3.7 full-time equivalents (FTEs) of researcher time, the team has produced about 34 peer-reviewed papers during the period under review, which have attracted 14 citations on average. The group's impact has been maximal in a consensus paper on modelling and in the workup of a new ligand for nicotinergic acetylcholine receptors. We note the group's importance for clinical studies, reflected in senior authorship of a high-impact clinical paper for the group head (Picard F et al. Brain 2006). This output is complemented by about two yearly conference appearances per FTE, and a total of 18 invitations to speak at conferences. Other measures of esteem include membership of a scientific advisory board, provision of expertise, membership in an Ethics committee, and peer review activities for a number of journals. The scientific output is doubtlessly internationally competitive.

A senior team member with permission to be principal investigator (habilitation à diriger des recherches, HDR) has just left due to retirement, but two members of the team have planned to obtain HDRs in 2010. This will be important in order to accommodate students and continue the essential role of forming future experts in PET data modelling, a recognized bottleneck in the expansion and future success of PET.

The team has been consistently successful in attracting grants, not surprisingly from both industry and academia; again the volume, diversity and interest of these contracts is internationally competitive.

As an aside, some researchers should pay attention for his/her name always to appear identical in publications. No fewer than six variants, in no apparent chronological order could be counted.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

The committee was pleased with the number of invitations to speak at conferences, reflecting the internationally competitive standing of the group. Two of the four current students are non-French, and at least one is funded from outside the CEA.

The total amount of outside funding attracted, and the number of contracts, is impressive. Most of them are naturally in collaboration with other preclinical and clinical groups; there is a good mix of preclinical versus clinical and academic versus commercial studies. There are extensive networks of collaboration; the committee notes that these are largely local (I2BM/CEA; Ile de France) with one collaboration elsewhere in France and three listed collaborations in the USA and Australia (the latter including an exchange of researchers); the group could consider whether a stronger involvement in European networks would be useful.

The group's methods, notably the partial saturation method, have been taken up by several groups in the past. New methods, e.g. for the quantification of [18F]A85380, are also being taken up outside the group. In addition, the group is heavily involved in the preclinical workup of the large number of PET tracers, with four publications where group members are both first and last authors since 2007, and fully taking advantage of its privileged position being able to use nonhuman primates for evaluation. Whenever one of the many new tracers from the SHFJ will be taken up widely, these papers will become widely cited. There is an increase in first/last author publications in the last years.

The publication impact is fully in line with the group's internationally competitive standing.

Appreciation on the strategy, management and life of the team

Team members do a very reasonable amount of teaching per year, >25h/y, particularly considering the highly specialised nature of much of their work. Teaching includes local teaching in Masters courses in Paris universities and university diplomas.

The internal communication seemed good, with consensual discussion of projects. The external communication is excellent insofar as teaching and conference activities are concerned. However, the web page needs improving – for example, there does not seem to be an English version, and no current work or publications are shown. The committee is aware that this aspect may have to be seen in conjunction with the overall SHFJ/I2BM communication strategy and may not depend entirely on the group itself.

The possibilities for risk taking are limited in a group that does essential and high-quality work at the interface between radiochemistry and imaging, and the committee was not surprised that many projects were designed in demand to the needs of these translational aspects.

The committee notes the creative application of existing and well-validated tracers to novel uses, e.g. flumazenil and PIB in multiple sclerosis, or A-85380 in Alzheimer's disease; many of these projects are internationally competitive.

- Appreciation on the project

The team presented four research axes, all of which appear realistic and achievable in the time frame.

Axis 1: Characterising metabolism is important; it is more difficult to predict whether it can be influenced in human studies for the tracers under study, but the enterprise is worthwhile as one such strategy has worked for an existing PET tracer (F-Dopa).

Axis 2: The blood-brain barrier (BBB) work is done in collaboration with an expert in drug transporters and the BBB. We were shown a poster with first, encouraging, results in vitro. The committee recommends that the group make contact with EURIPIDES, a large FP7-funded consortium already developing radiotracers for PGP or BCRP. We note that there may be commercial sensitivities and that we have not seen the strategic data for the development of such tracers by F Dollé's group; hence it is difficult to comment on this research axis. The general theme is, however, of great interest.

Axis 3: Morphometry work will be conducted both within the lab and in collaboration with other I2BM partners (LPAI, Neurospin). The methods that the team plans to use are internationally competitive; the group's own role will remain to be defined as the research unfolds.

Axis 4: In modelling, the team aims to expand their repeated injection protocols for the determination of receptor occupancy to humans and to neurotransmitter systems other than nicotinic acetylcholine receptors. This is likely to be successful, provided tracers with large k2 rate constants are used. Similar work is already possible with dual scans paradigms or bolus/infusion protocols; the group may develop a niche for itself using a presumably small number of mainly 18F tracers suitable for the purpose.

The committee has no doubt that the group will be able to deliver high-quality work on the above themes.

The question on resource commitment would probably best be answered at the institute ("service") level. We note that there are no plans to work on cardiological or oncological tracers; expanding work in these areas on the institute level would presumable require increasing resources.

- Conclusion:

  - Summary

This is a strong group, making its marks internationally in PET modelling in the wider sense, a field that is both difficult and often underappreciated. It fulfils an essential role within the SHFJ and, through training, in the wider community.

  - Strengths and opportunities

The integration within the I2BM in general but particularly in the SHFJ seems excellent, with seamless integration between the previous stage in ligand development (team 1), access to both clinical and preclinal imaging facilities and (collaborators') data, collaboration with team 3 e.g. on morphometry, collaboration with MIRCEN groups on animal models, and Neurospin.

There should be opportunities for further integration and interaction at the European level.

  - Weaknesses and threats

Quantification of PET data relies on the availability of state-of-the-art structural neuroimaging to be used in conjunction with the more functional PET imaging, notably for the proposed axes 3&4 in the project. There is a risk, with the massive investment in Neurospin, that MRI could be neglected at SHFJ. The committee heard concerns about the existing 1.5T MRI scanner ageing and the level of support having dropped since the opening of Neurospin.

While it cannot be guaranteed that the team's investigations of metabolism in different species will generalize to other tracers studied in the future, attempting a unifying prediction tool would be one example of where the committee would encourage the team to "think outside the box" and take greater risks on occasion.

- Recommendations:

The committee encourages the team to continue its activity with the same enthusiasm and competence, to look for new applications of their expertise in PET modelling, and maintain and enhance creativity.

Team 3: Laboratoire dePhysique et Analyse d'Images (LPAIM)

Team leader: Ms. Regine TREBOSSEN

- Staffs members:

	Dans le bilan* ETP	Dans le projet ETP
N1 : Nombre d'enseignants-chercheurs (cf. Formulaire 2.1 du dossier de l'unité)		
N2 : Nombre de chercheurs des EPST ou EPIC (cf. Formulaire 2.3 du dossier de l'unité)	2,20	2,20
N3 : Nombre d'autres enseignants-chercheurs et chercheurs (cf. Formulaire 2.2 et 2.4 du dossier de l'unité)		
N4 : Nombre d'ingénieurs, techniciens et de personnels administratifs titulaires (cf. Formulaire 2.5 du dossier de l'unité)	4,8	4,8
N5 : Nombre d'ingénieurs, techniciens et de personnels administratifs non titulaires (cf. Formulaire 2.6 du dossier de l'unité)		
N6 : Nombre de doctorants (cf. Formulaire 2.7 du dossier de l'unité)	3	4
N7 : Nombre de personnes habilitées à diriger des recherches ou assimilées		2

- Appreciation on the results

Peer reviewed publications appears to be 2 (2005), 2(2006) 11 (2007), 5 (2008), 6 (2009) as stated in the SHFJ document. The quality of publications is good in general and rather varies in terms of journal and subject. There are a reasonable number of publications in very relevant journals such as IEEE Trans Nucl. Sci, IEEE Trans Med. Imag., J. Nucl. Med., which for this discipline have excellent impact factors. The group is established as having an output of good scientific quality and originality. They state the overall impact factor to be just above 5 which is very good. They have also 2 patents.

The output in terms of number of peer reviewed publications is therefore about 2 per FTE which is acceptable. They claim 3 invited 'plenary' conference presentations. They are very involved with the GATE consortium and the BrainVisa software package. They have provided software for reconstruction to Siemens which it appears assisted the Siemens development of one of their current reconstruction packages. There is additional output in terms of software for automated segmentation and Partial Volume Correction.

They are a well established group and have been functioning for a long period. They are well integrated within the SHFJ, and appear to have good links to other groups within the CEA including engineering and instrumentation.

- Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners

The group has a good international reputation and has attracted at least one significant visitor and are in principle attractive to the outside world. Apart from the invited lectures mentioned previously (3), no prizes are indicated. Their ability to recruit should be excellent but the numbers cited in the document seem to be rather on the low side. They have obtained external funding cited Euros 600k in the period 2005-2009 which is satisfactory but not exceptional. They are an important component of the GATE consortium. No other major collaborations are mentioned. There is some technology transfer (c.f. Siemens) but overall this appears to be on the low side.

- Appreciation on the strategy, management and life of the team

In general this appears to be very good with good internal communications and planning. The links in this respect to other teams within the SHFJ service are less apparent in the respect of strategy. The team shows excellent internal communication, but some weaknesses with respect to external communications. The team shows good internal scientific animation, but rather conservative with respect to risk taking. The team shows good involvement of the members of the team with respect to teaching for example INSTN, but less so with respect to universities and MScs. Total number of hours of teaching low but fairly typical.

- Appreciation on the project

The project is correctly specified, certainly feasible, and pertinent. It is rather conservative and appears to be a continuation of current research projects, both with respect to middle and long term objectives.

With respect to the team itself, there is no evidence of any problem with respect to allocation of resources. This is unclear with respect to strategy for the SHFJ as a whole.

The originality and the associated risk taking could be improved. In particular while the group are excellent and well placed with respect to simulation and reconstruction, the impact of their work with respect to instrumentation development presumably for external groups is rather unclear.

- Conclusion :

  - Summary

Scientifically a strong and well respected group both nationally and internationally. They appear to be somewhat isolated from other groups with whom collaborations with respect to instrumentation in particular is important and possibly other groups within the SHFJ. Some brainstorming about middle and long term strategy is advisable, to refocus their research objectives. The current resources in terms of staff, space and equipment seem to be appropriate.

  - Strengths and opportunities

This is a well-established group with very good scientific output. There is an opportunity for increased collaboration with other external groups in particular industry. There is an excellent opportunity for better links to the university groups based at Orsay (Plan Campus) and in particular those involved in (PET +) proton and hadron-therapy.

  - Weaknesses and threats

Provided that resources can be identified and allocated, a higher risk strategy in particular with respect to instrument would be appropriate. The links between this group and other related physics groups both within the Paris region and further away nationally and internationally need to be considered. Obtaining of substantial grant income could be improved.

- Recommendations

A good group which is very well worth supporting. Some refocussing of objectives would be desirable.

Nom de l'unité : I2BM - MIRCEN - URA 2210

Note de l'unité	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A	B	A

Nom de l'équipe : INTERACTION CELLULAIRE DANS LA DÉGÉNÉRESCENCE NEURONALE ET GLIALE

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A+	A	A

Nom de l'équipe : THÉRAPIES PRÉCLINIQUES POUR LES MALADIES NEURO DÉGÉNÉRATIVES

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	A+	A+	A+	A+

Nom de l'équipe : IMAGERIE PRÉCLINIQUES POUR LES MALADIES NEURO DÉGÉNÉRATIVES

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	B	A	A	A

Nom de l'équipe : IMAGERIE CLINIQUE POUR LES MALADIES NEURO DÉGÉNÉRATIVES

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
B	A	A	B	B

Nom de l'unité : I2BM - NEUROSPIN

Note de l'unité	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	A+	A+	B	A+

Nom de l'équipe : LABORATOIRE D'IMAGERIE ET DE SPECTROSCOPIE

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	A+	A+	B	A+

Nom de l'équipe : LABORATOIRE DE NEUROIMAGERIE ASSISTÉE PAR ORDINATEUR

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A+	A	A+

Nom de l'unité : I2BM - SERVICE HOSPITALIER FRÉDÉRIC JOLIOT

Note de l'unité	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A	B	B

Nom de l'équipe : LABORATOIRE RADIOCHIMIE ET RADIOPHARMACIE

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A+	A	B

Nom de l'équipe : LABORATOIRE D'IMAGERIE NEUROLOGIQUE ET PHARMACOLOGIQUE

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A	B	B

Nom de l'équipe : LABORATOIRE DE PHYSIQUE ET D'ANALYSE QUANTITATIVE EN IMAGERIE MOLÉCULAIRELABORATOIRE D'IMAGERIE NEUROLOGIQUE ET PHARMACOLOGIQUE

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
B	A	B	B	B

energie atomique • energies alternatives

L'Administrateur Général

Monsieur Pierre GLORIEUX
Directeur de la section des Unités de recherche

AERES
20, rue Vivienne
75002 PARIS

Saclay, le 07 mai 2010

N/Réf. : DPg/AN/np/2010-128

Objet : Observations du CEA sur le rapport d'évaluation de l' « Institut d'Imagerie Biomédicale » (I2BM)

Monsieur le Directeur, Cher Pierre,

Je remercie tout d'abord l'AERES pour la qualité du rapport d'évaluation sur l'activité de l' « Institut d'Imagerie Biomédicale » et pour la pertinence des recommandations qui ont été faites.

En tant qu'Administrateur Général de l'Etablissement CEA, ce rapport n'appelle pas de commentaires particuliers de ma part. Je puis vous assurer que je prêterai la plus grande attention à la mise en œuvre des actions qui permettront de répondre aux recommandations formulées par l'Agence.

Veuillez agréer, Monsieur le Directeur, l'expression de mes cordiales salutations.

Bien cordialement,

Bernard BIGOT

Commissariat à l'énergie atomique et aux énergies alternatives
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Observations sur l'évaluation globale de l'i2BM

Nous remercions l'AERES pour l'évaluation approfondie et constructive du fonctionnement et des choix stratégiques des trois services de l'i2BM qui étaient en évaluation cette année. L'appréciation très positive de l'activité scientifique en imagerie et neurosciences complète les évaluations des unités mixtes réalisées l'an dernier[1] et est un puissant encouragement à poursuivre le développement innovant des plateformes dans une perspective d'excellence scientifique et d'ouverture plus large vers la communauté scientifique nationale et internationale. Des informations plus approfondies concernant l'URA 2210 (dans MIRCen) et le SHFJ sont données en annexe pour répondre aux interrogations du comité.

Il faut également rappeler que l'organisation qui a été évaluée cette année est récente, NeuroSpin et MIRCen, mises en place respectivement début 2007 et début 2009, sont issues du développement des activités du SHFJ. En parallèle, ceci implique une évolution des activités propres du SHFJ qui passe par la rénovation de ses installations afin d'accueillir de nouvelles équipes scientifiques, notamment en recherche clinique.

La création de l'institut en 2007 vise à gérer cette évolution majeure en imagerie fonctionnelle centrée sur le couplage de la recherche technologique bénéficiant des compétences du CEA et de la recherche préclinique et clinique avec des collaborations tant académiques qu'industrielles et institutionnelles (AP-HP).

Il est cependant difficile de reconnaître l'institut dans la présentation qui en est faite. Nous considérons en effet que ce rapport fait l'impasse sur :

(i) la qualité du travail de l'équipe support sur laquelle repose la totalité de la gestion RH et financière (dont le montage des projets) d'un institut de près de 500 personnes (tous statuts et organismes confondus) au budget consolidé de 36,7 M€,

(ii) la coordination et la mutualisation des efforts très importants consacrés aux développements technologiques pour l'imagerie biomédicale. Il s'agit là d'un objectif primordial de l'i2BM, pour lequel il dispose d'une expertise reconnue, peu ou pas abordée dans le rapport,

(iii) L'importance, la qualité du matériel et le soutien logistique mis à disposition des équipes de la communauté scientifique et industrielle,

(iv) L'animation de la communication au niveau de l'institut (journées de réflexion stratégique, journée thésards, rapport annuel, assemblée générale, réunion mensuelle des chefs de service…) malgré la dispersion géographique des différents services.

Nous souhaitons souligner par ailleurs deux points concernant l'évaluation globale de l'institut :

- des plateformes comme NeuroSpin ou MIRCen résultent de la conjonction d'un projet scientifique ambitieux et de l'essaimage d'équipes scientifiques au sein de l'i2BM qui a nécessité un travail de longue haleine réalisé collectivement à partir du SHFJ
- l'i2BM dans son format actuel est une structure récente ; dont les structures de gouvernance doivent bénéficier du retour d'expériences des premières années de fonctionnement des plateformes d'une dimension nouvelle pour les sciences du vivant. Nous sommes réjouis de constater qu'une grande part des recommandations du comité de visite reprend les objectifs que s'est fixée la direction comme l'indique le rapport soumis aux experts.

Malgorzata Tkatchenko
Chef de l'Institut d'Imagerie Biomédicale

[1] Trois unités mixtes CEA-Inserm : U 562, U797 et U803, implantées à Neurospin et au SHFJ

Observations sur l'évaluation détaillée de l'URA 2210

We thank the committee for having emphasized the quality of research activities and research projects conducted at URA2210 on neurodegenerative diseases both at the preclinical (Team 1,2 and 3) and clinical levels (Team 4).

Our comments on the AERES evaluation will focus on Team 4, which, despite a globally very positive report, has been rated with a B score that appears largely unjustified.

The committee emphasized that the clinical research conducted by Team 4 led by Pr Philippe Remy at Henri Mondor Hospital (Creteil) and SHFJ (I2BM, Orsay) is essential for the translational activity of URA2210 and productive (Team 4 "output is considered as excellent"). The committee has recognized the scientific expertise of Pr Philippe Remy. His leadership (international visibility, active involvement in international networks) has also been qualified as "very good". The committee also quotes the quality of the research project indicating "overall the project was considered as very good. […] It brings a lot of enthusiasm for the biomarkers part". PET biomarker studies are the core of the project. PET studies include the development of new radiotracers and their use to better characterize patients (In particular patients with Parkinson's disease secondary to LRRK2 mutation), and evaluation of new therapies (e.g. PET imaging of the parkinsonian patients who take part in the first European gene therapy Phase I clinical trial). Team 4 implication in therapy evaluation programs is part of a long lasting research activity in the context of ambitious multi-center clinical trials. In this network-based national and international activity, Team 4 has played and will continue to play a central role.

We agree with the committee that the team is understaffed at the present time to embrace its ambitious project fully. Raising the manpower of that team will be a priority for the unit. However, this aspect of the evaluation, which is already taken into account by the B score attributed under "strategy and governance", should not have impaired the evaluation of the project itself.

For these reasons, we believe that the "B" score attributed to the Team 4 project is unjustified. The positive evaluation of the team "core" project related to PET brain imaging studies, together with the very good ratings on scientific production and international visibility, should have led to a better global appreciation of that team.

Observations sur l'évaluation détaillée du SHFJ

We thank the visiting committee for this very complete report concerning the SHFJ. We are grateful for advices and opinions expressed in this report, as well as for careful evaluation of each of its three methodological teams.

We also note concerns expressed by the committee on the overall strategy of the SHFJ, which appeared to it insufficiently explicit in the written document and during presentations performed on the site. As stated in the report of the committee, the SHFJ is in a new situation created by the recent departure of two important groups, which widely contributed to its

reputation in the field of neuroscience, namely MIRCen and NeuroSpin. It was besides confronted with a change of direction and with upgrading operations of its installations for regulatory reasons that have considerably hampered its clinical research activities.

The committee underlines the good scientific quality of three teams assessed as well as that of the associated INSERM/CEA units. The committee wishes that these activities are reinforced and even amplified, especially by encouraging risk-taking projects. We are in full agreement with this point.

Concerning the overall strategy, two main points deserve elucidation:

1/The opening of the SHFJ towards the oncology

This new thematic orientation represents a strategic shift based firstly on the innovativeness of SHFJ in radiochemistry, in pharmacology and in signal processing, and secondly on the strong collaboration with leading institutes in research and clinical oncology as the Institute of Hematology (IUH, Saint Louis hospital, Paris, an European leader in the field of onco-haematology). An agreement has been obtained with the "Assistance Publique-Hopitaux de Paris" (AP-HP), Paris 5 and Paris 7 Universities, and industrial partners to concentrate their effort on an oncology project.

The project, which involves the development of specific tracers for new molecular targets, is based on SHFJ skills previously developed for PET both in radiochemistry and in molecular imaging. Researches will be orientated at first on the molecular imaging of apoptosis, neoangiogenesis, metalloproteinases, chemoresistance (such as PGP and BCRP). The SHFJ is currently in close interaction with the Saclay Institute of Biology and the IUH in order to identify proteins and molecular targets of interest. This implies, both at preclinical and clinical stage, a close cooperation between the platforms of SHFJ and St. Louis and the association of industrial partners in radiochemistry. The molecules identified during this process will be proposed to clinical applications both at the SHFJ and at the Saint Louis hospital. Although we are aware of the potential risks of this decision, we think that it constitutes an investment for the future.

In concrete terms for the SHFJ, before the end of this year, 4 FTE will come from the consortium on the site of Orsay to reinforce the capacities in research and development of the radiochemistry laboratory run by Frédéric Dollé. The contribution of the laboratory run by Régine Trébossen will concerns the methods of quantification based on the input function measurements taken on great vessels, simulation methods (GATE) and segmentation methods. All these methods are already available in SHFJ and are applicable to the oncologic field. Finally, Michel Bottlaender has already given his consent to dedicate 30% in his time to help characterise the new tracers in this domain.

This project will be submitted to a peer review process to get supplementary financial support in relation with the 'Plan Campus'. This will enable us to develop the research capacity in radiochemistry (Fluor C project). Works will be developed under the control of a scientific committee constituted by scientists of the AP-HP, CEA, Universities, INSERM and industrial partners.

A similar approach will be used for cardiovascular projects.

2/ The integration of the CIERM team

All potential contributions of cooperation with the CIERM could not be highlighted because this unit was not specifically heard by the visiting committee, unlike other teams of the SHFJ. Projects introduced by the CIERM in the manuscript are those that were favourably

evaluated by a prior AERES evaluation committee. The integration of the CIERM represents for the SHFJ both a practical and a scientific interest. On the one hand, the 1.5T MRI system of the CIERM will become available to researchers of the SHFJ. This answers the question on the renewal of the MRI equipment raised by the visiting committee. On the other hand, the integration of the CIERM will allow further development within the SHFJ of multimodal imaging projects. For example the CIERM is involved in researches on tumoral perfusion since the team of Drs Roche and Nassau from the "Institut Gustave Roussy" (IGR, Villejuif) has recently joined the group. The PET quantification of membrane receptors is dependent on tissue perfusion in heterogeneous structures such as tumours or diseased myocardium. It appears therefore particularly important to use a multimodal approach merging information on perfusion MRI and receptor PET imaging. Moreover, the measurement of vascular compliance parameters is important because of the frequent association between Alzheimer disease and vascular atheroma. We want to assess these relations by comparing for the same patients the PET markers of the neurodegenerative disease with the lesions of the great vessels. Again the contribution of the CIERM will be important to assess the importance of vascular remodelling in those patients. In summary, the CIERM will bring original methods required by biomedical research teams of the SHFJ.

Concerning the question of the internal communications:

We have weekly meetings where practical and scientific subjects are debated with the representatives of all laboratories. Fortnightly meetings exist within every laboratory. The whole staff of the SHFJ is gathered twice a year to discuss the overall strategy of the service. Therefore information circulates within the SHFJ. We are however aware that recent changes in orientation may make some people uncomfortable. Understandable fears for the research groups are a loss of visibility or a decrease in resource allocation. Now that solutions are clearly achievable, the internal communication will be undoubtedly more efficient.

Concerning the group of nuclear medicine:

It seems to us that there is some confusion in the report of the visiting committee between what was previously called the laboratory of nuclear medicine (web site) and the current nuclear medicine group. This group is in charge of the diagnostic procedures as part of the service of nuclear medicine and supports the clinical research activities of the SHFJ. It is also involved in research projects in the oncologic and cardiovascular field. It is part of the laboratory of clinical investigations which includes all clinical applications including psychiatry, neuropediatry and neurology.

We have hired two medical doctors at the beginning of this year and four additional recruitments are planned in the group of nuclear medicine in 2010. There is therefore a real effort of recruitment in this sector to support the new missions and orientations of the SHFJ.