European Cooperation in Science and Technologie
- COST -
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Secretariat

Brussels, 16 December 2010

COST 4192/10

MEMORANDUM OF UNDERSTANDING

Subject :	Memorandum of Understanding for the implementation of a European Concerted Research Action designated as COST Action TD1007: Bimodal PET-MRI molecular imaging technologies and applications for in vivo monitoring of disease and biological processes

Delegations will find attached the Memorandum of Understanding for COST Action TD1007 as approved by the COST Committee of Senior Officials (CSO) at its 180th meeting on 1 December 2010.

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MEMORANDUM OF UNDERSTANDING

For the implementation of a European Concerted Research Action designated as

COST Action TD1007

BIMODAL PET-MRI MOLECULAR IMAGING TECHNOLOGIES AND APPLICATIONS FOR IN VIVO MONITORING OF DISEASE AND BIOLOGICAL PROCESSES

The Parties to this Memorandum of Understanding, declaring their common intention to participate in the concerted Action referred to above and described in the technical Annex to the Memorandum,
have reached the following understanding:

1. The Action will be carried out in accordance with the provisions of document COST 4159/10 "Rules and Procedures for Implementing COST Actions", or in any new document amending or replacing it, the contents of which the Parties are fully aware of.

2. The main objective of the Action is to create a framework in which researchers involved in the development of PET/MRI equipment, PET/MR bimodal probes and related preclinical and clinical applications can share and increase knowledge and information.

3. The economic dimension of the activities carried out under the Action has been estimated, on the basis of information available during the planning of the Action, at EUR 36 million in 2010 prices.

4. The Memorandum of Understanding will take effect on being accepted by at least five Parties.

5. The Memorandum of Understanding will remain in force for a period of 4 years, calculated from the date of the first meeting of the Management Committee, unless the duration of the Action is modified according to the provisions of Chapter V of the document referred to in Point 1 above.

A. ABSTRACT AND KEYWORDS

The rapid growth in genetics and molecular biology combined with the development of techniques for transgenic small animals has lead to an increased interest in vivo preclinical molecular imaging; PET-MRI has gained attention over the past five years due to the complementary advantages of those technologies, including soft tissue contrast and low radiation. Molecular imaging with PET-MRI is an interdisciplinary topic; new instrumentation, data acquisition strategies, image processing and reconstruction algorithms need to be developed, evaluated and optimised. In addition, bimodal contrast agents, including nanoparticles are promising candidates for a number of preclinical and clinical diagnostic and therapeutic applications. Although a number of prototype hybrid systems are being developed, enhancing interaction with end users is still critical. Recently, four prototypes of integrated hybrid PET/MRI scanners were installed at two PET centres in Europe and in the United States. Understanding the emerging biological needs, preclinical and clinical challenges, will provide the directions for the design of efficient bimodal probes and optimized imaging equipment. The Action fulfils the need for European coordinated research in the development and application of peak technologies, aiming to bridge the gap between basic biological research and preclinical application with significant social impact.

Keywords: bimodal contrast agents, magnetic resonance imaging, multimodal molecular imaging, nanoparticles, positron emission tomography

B. BACKGROUND

B.1 General background

Molecular imaging (MI) links the empirical diagnostics and experimentally tried treatment management protocols with the fundamental understanding of the underlying processes that generate the observed results. MI techniques are ideally based on technologies that have an intrinsically high resolution and allow the detection of low concentrations of target bio-molecules involved, such as nuclear medicine imaging (NMI), optical imaging (OI), magnetic resonance imaging (MRI) etc. Multimodality molecular imaging (MMI) provides complementary information, usually by combining anatomical and functional images. Although the combination of Computerized Tomography (CT) with Single Photon Emission Computerized Tomography (SPECT), Positron Emission Tomography (PET) has been explored and has lead to commercial products such as PET/CT and SPECT/CT, there is increased interest in combining PET with MRI. The obvious benefit from merging these technologies is improved spatial resolution and soft tissue contrast, increased sensitivity and low radiation dose. In addition, nanoparticles (NPs) with ferromagnetic core are ideal candidates for several applications including tumour imaging, therapy, blood brain barrier (BBB) studies etc. By radiolabelling those NPs it is possible to provide spatiotemporal information with the appropriate PET/MRI imagers. Finally, responsive or “smart” bimodal PET/MR contrast agents allow quantification of both concentration and relaxivity. Several institutions worldwide are working on the field of detector development for PET/MRI, both for clinical and pre-clinical applications. In addition, a number of groups are designing, developing and exploring the application of bimodal PET/MRI agents in molecular medicine. A number of international and (mainly) European projects are currently being carried out. However, very often research efforts are being duplicated, as a result of the absence of a network that could coordinate research on a European level, bridge the gap between detector, contrast agent developers and end users, and speed up the transfer of basic research to clinical practice.

COST is the most appropriate framework due to the flexible association mechanism that allows to the interested partners to joint the Action during its development. Since advances in PET/MRI are rapid, this flexibility is critical. In addition, COST enables the participation from laboratories outside the COST countries.

This Action will bring together scientists from interdisciplinary fields including physics, instrumentation, chemistry and biology, will improve exchange of information and results and will facilitate their transportation to industry and/or clinical practice. It will also provide the environment for training of early-stage researchers, support Short-Term Scientific Missions and provide interaction with specialists. Although carefully designed and prepared it must be rather flexible in order to determine and follow when necessary advances in the field of PET/MRI and molecular imaging.

B.2 Current state of knowledge

The first simultaneous PET/MRI systems were realized by placing the crystals of the PET system inside the MRI and by using optical fibers to drive light to the PMT. The introduction of Avalanche photodiodes (APDs) and more recently Silicon Photomultipliers (SiPMs) offered alternative detector modules to the standard Photomultipliers (PMTs), which do not interfere with the magnetic field, making the first preclinical and clinical prototypes available. Recently, four prototypes of integrated hybrid PET/MRI scanners, the 3TMR-BrainPET developed by Siemens Medical Solutions for human brain studies, were installed at two PET centres in Europe (Germany) and in the United States each. While the first non-integrated whole-body PET/MRI constructed by Philips are being tested in a few European and North American clinical centres, some prototypes of integrated whole-body PET/MRI constructed by Siemens will become available in the very near future. This consequently generates the need for multimodal imaging agents, incorporating e.g. a paramagnetic or superparamagnetic material and a positron- or gamma-emitting nucleotide attached with a targeting ligand or drug. The advantage of this approach over a simultaneous application of individual PET and MRI imaging agents is in the redundancy for validation due to the differences in the applied concentration and pharmaco-dynamics.

A number of research projects or funded networks in terms of FP6 and FP7 have shown the interest in PET/MRI. Although those efforts have partially addressed different aspects of PET/MRI they have prepared the field for a holistic approach as it is will be in this Action. The Cambridge PET/MR project (FP6) allowed for the first time high resolution PET and MR to acquire simultaneously, using new APDs and SiPMs in the PET detectors. The FP7 HYPERImage (Hybrid PET-MR system for concurrent ultra-sensitive imaging) project drives the development of a brand new system for simultaneous whole-body PET-MR imaging for humans. The FP7 SUBLIMA (SUB nanosecond Leverage In PET/MR ImAging) project aims at truly simultaneous, fully integrated, solid-state PET/MR technology for concurrent functional and anatomical imaging with unsurpassed image quality.

B.3 Reasons for the Action

The Action has a strong scientific/technological advance, since the field of PET/MRI is a peak research direction for industry and academia. The role of PET in treatment planning and assessment of response to therapy has a strong social impact, since cancer is one of the main causes of death worldwide. Optimizations in treatment planning and fast assessment of response to therapy have not only social impact, but also significant economical benefits for individuals, health insurance organizations and national economies. Besides the technological variations and benefits of PET/MRI, the minimized radiation compared to PET/CT is considered as another important benefit, especially for diagnostic examinations. Finally, the important role that PET/MRI is expected to play in preclinical imaging must be highly emphasized. Preclinical small animal imaging provides not only valuable in vivo information, but also dramatically reduces the number of animals that are needed. This is in accordance with European and International legislation and bioethics.
The Action will provide a framework for collaboration between European institutions that have significant experience and research activity in scientific fields that are complementary for PET/MRI research.

Through this Action several important issues are foreseen to be addressed:

1) Bridge the gap between molecular biologists, tracer and detector developers
2) Extensive study of new detector materials and geometries for improving PET/MRI systems
3) Design, develop and evaluate bimodal contrast agents and nanoparticles with attractive biological applications in diagnosis and therapy
4) Work towards the optimization of existing technical and experimental methodologies and decrease in systems cost
5) Explore and promote the deployment of new imaging methods and instrumentation

It is expected that:

1) New PET/MR compatible detectors and imaging prototypes
2) New bimodal tracers
3) New image reconstruction and processing algorithms and software
4) New preclinical and clinical protocols for bimodal imaging will result and will find application with both scientific and social impact.

This will be achieved by:

- maximizing the use of existing infrastructure and resources
- share of knowledge through meetings
- training of young researchers through short scientific missions
- interact with current running projects and prepare and support new ones
- communicate with scientists from complementary disciplines in MI

The Action will merge several technological areas: Nuclear Physics, Instrumentation, Computer Technology, (Bio-) Chemistry and Life Sciences. Finally, members of the network are specialized in different topics and are uniformly distributed in Europe; thus they can act as local centres to spread and promote participation and cooperation of more partners.

B.4 Complementarity with other research programmes

Interaction with the existing PET/MR projects described in B.2 will be sought through the participation of key groups to the Action. Few European projects, as well as networks or collaborations exist, which are mainly focused on MI and include PET/MRI Work Packages, such as clearPET on Small Animal PET System, NeuroPET projects for high performance PET scanners, CrystalClear collaboration for the development of new crystals; openGATE collaboration dedicated to the numerical simulations in medical imaging.
The Action foresees to share information and knowledge with such scientific efforts. The Action will provide additional opportunities for researchers in such programmes to interact with other scientists. Interaction with other COST Actions has been considered.

C. OBJECTIVES AND BENEFITS

C.1 Main/primary objectives

The main objective of the Action is to create a framework in which researchers involved in the development of PET/MRI equipment, bimodal probes and related applications can share and increase knowledge and information.
To achieve this aim the primary objectives of the Action are:

1) To bridge the gap between detector and tracer developers, demonstrate the benefits of novel techniques understand end users needs and gather feedback from them, to improve services.
2) To extensively study new detector materials and optimized geometries that will improve the performance of existing PET/MRI systems and allow the construction of new more efficient.
3) To design, develop and evaluate bimodal contrast agents and nanoparticles with attractive biological applications in diagnosis and therapy.
4) To systems cost, by improving detectors components and overall architecture.
5) To explore new imaging acquisition and processing methods and protocols.
6) To identify how existing technologies are likely to change either in their operating characteristics or in novel ways, the applications in which they are likely to be used, what impact these would have and on what time scale.

C.2 Secondary objectives

Secondary objectives have been set:

1) To assist sharing of knowledge and cooperation among a core of multidisciplinary groups across (and not limited to) Europe, and invite new researchers and topics into the debate. Two annual workshops, two Training Schools and at least one conference will be organized.
2) To interact with early-stage researchers and post graduate students, by taking advantage of Short-Term Scientific Missions (STSM) and to promote the participation of women by establishing a gender balance observatory.
3) To promote the use of efficient low cost systems in all European regions and institutions. A number of low cost prototypes (based on opposite heads) will be implemented and exploited by interested institutions, while the main effort will be put on the development of new integrated systems.
4) To explore the potential benefits and limitations of the clinical application of PET/MRI.
5) To provide a link between academia, SMEs and big industries, thus investigate the possibilities of industrial products with substantial cost decrease and social impact.

C.3 How will the objectives be achieved?

The main objectives will be achieved through the work of five Working Groups (WG) and Research Teams (RT) and will be coordinated and monitored by the Core Management Team (CMT) and Management Committee (MC) of the Action.

Objective 1 will be achieved through continuous interaction with molecular biologists, chemists, engineers and physicians e.g. participation to the Action workshops and other events, participation in events organized by possible end users and dissemination of Actions results through publications. Objectives 2, 3, 4 and 5 will be achieved by extensive review of existing bibliography, exchange of visits and STSMs and continuous interaction between WGs and RTs. Finally, the last objective will be achieved through the coordinative work of the Action, the interaction with end users and industrial partners and dissemination of the results.

The secondary objectives will be achieved through the scientific work of the Working Groups and the Research Teams, as well as by continuous interaction with end users and industry. Continuous dissemination of the results as well as organization of events for scientists as well as non specialists is a critical parameter for the Action success.

C.4 Benefits of the Action

The short term benefits are:

- An open forum for knowledge sharing in the field of PET/MRI technology.
- Existing low cost detectors that will be exploited by smaller affiliated resource groups.
- New efficient PET/MRI detectors, which can find application in research environment.
- New bimodal agents, which will be preclinically evaluated.
- Scientific results from the study of new detector materials and data acquisition methods.

The middle term benefits are:

- New PET/MRI instrumentation for specific clinical examinations.
- Higher level of young researchers with fair European distribution.
- Strengthen the bonds between participants; new collaborations in terms of FP7 and other EU or international programs.
- Interaction with industry and possible setup of spin off companies.
- Interaction with non-EU countries that have significant experience in the field.

The long term benefits are:

- New diagnostic techniques that will find pre-clinical and clinical application.
- Development of new diagnostic and therapeutic pharmaceuticals.

C.5 Target groups/end users

The Action is expected to provide significant benefits to a number of possible end users:

- Academia and researchers: The Action will give the opportunity to members of the academic community and researchers of all levels that work in the field of PET/MRI to share information, identify research needs, exploit new tools and methods, avoid duplicate work and enhance international collaboration. Early-stage researchers will have the opportunity to increase their experience and knowledge, as well as take advantage of STSMs.
- Detector development industry: More efficient, integrated and novel applications will arise and will be candidates for commercialisation.
- Pharmaceutical industry: New pharmaceuticals are expected to be produced, by using advanced PET/MRI scanners and techniques to provide early indicators of trial drug effectiveness.
- National governmental organizations and EU: The results of the Action will provide valuable input for policy makers in health research and applications.
- Society: when novel diagnostic techniques and/or pharmaceuticals are introduced there will be benefits for diagnostic and therapeutic procedures.

D. SCIENTIFIC PROGRAMME

D.1 Scientific focus

PET/MRI using bimodal agents needs several technologies to be combined in order to provide and fully validate complementary diagnostic information. Basic research in this area requires the co-operation of a large number of scientists from various fields. In general PET/MRI research can be split in the following tasks:

- Research for new basic detector materials and mainly SiPMs, silicon detectors, crystals, electronics etc
- Data acquisition, processing, reconstruction and visualization software
- Detector integration and performance evaluation
- Design and evaluation of bimodal contrast agents
- Preclinical and clinical application

The most important research tasks will be:

- *Crystals*: Besides the conventional crystals (NaI, BGO, GSO, LSO) that are used in existing systems, new fast scintillators crystals like LaCl3:Ce and LaBr3:Ce and Lu-based scintillators show promising results and will be studied. Multilayer crystal assemblies, which provide depth of interaction information and are under investigation -mainly in preclinical applications, as well as alternative geometries that best fit to detectors for PET/MRI will be explored.
- *Semiconductor arrays*: Initial PET/MRI systems where based on APDs, which had low gain and require high voltage. SiPMTs have gain comparable to that of the PMTs, require low voltage supply, can form arrays and their cost is continuously reducing; thus they are the technology of choice and will be studied in detail.
- *Data acquisition electronics and acquisition software*: A significant target is the implementation of dedicated compact and low cost electronics that will address the need for specific applications. Field Programmable Gate Arrays (FPGAs) and Application Specific Integrated Circuits (ASICs) provide an efficient way of reducing cost while optimising programmers' flexibility and significantly decrease overall systems cost. In small animal imaging the most important challenge is maximization of sensitivity, since the ultimate goal is 4D imaging. FPGAs provide the opportunity to implement in hardware acquisition and processing strategies. Depending on the application the parameters that will be taken into account are: a) overall cost, b) overall sensitivity, c) number of channels to be processed simultaneously and d) processing algorithms implemented in hardware.
- *Detector integration*: The resultant prototypes will have to be compact and optimised for the specific applications; issues such as mechanical movements, accurate rotation, radiation protection and optimisation of other system components will be addressed. In advanced small animal systems it is important to consider a) animals position, b) inhaled anesthetics, c) hemodynamic monitoring, d) blood sampling and other vital parameters monitoring. In clinical prototypes extra parameters such as patient safety, background radiation shielding and patient comfort will be considered.

- *Reconstruction software*: PET/MRI reconstruction includes optimization of resolution, sensitivity, motion correction, attenuation correction, tracer kinetics and bimodal acquisition. For this reason novel algorithms will be developed and assessed.
- *Bimodal agents*: Molecular targeted iron oxide positron-labelled NPs, and other targeted nanomaterials designed to carry a large payload of paramagnetic gadolinium contrast agents or F-19, will be designed. New chemistry is required to optimise NPs design and manufacture and to optimise the formation of a site-specific stable bioconjugate link between the NPs and the targeting molecules, and between the NPs and the PET radionuclide. New bifunctional chelator designs for Gd (to optimise relaxivity, stability and response to physiological change) and metallic positron emitters are being developed. Non- NP approaches are also being developed in which single targeting molecules can be labelled with both paramagnetic contrast and radionuclides.
- *Performance evaluation* of the developed prototypes requires the design of experimental protocols and procedures, as well as the development of high resolution and sensitivity phantoms.
- *Application of the developed systems* in small animal imaging or in dedicated clinical cases is a rather complicated procedure where scientists from different areas need to collaborate for designing acquisition protocols and assess results.

The general work plan includes the establishment of five working groups (described in D2) that will follow the aforementioned research directions. Initially the state of art will be reviewed as well as other key players, who will be invited to join the Action, during its implementation. In order to achieve Action objectives the existing infrastructure of Action members, their knowhow and manpower will be used. Most groups activated in the field of instrumentation and chemistry for PET/MRI maintain imaging equipment (both commercial and prototypes), laboratories and equipment suitable for instrumentation development, machinery, computer resources (PCs, cluster, Grid), software libraries (commercial and custom made), chemical facilities, animal facilities and clinical facilities. In addition, there is significant access to students of various levels, as well as collaboration with industrial partners and public sectors.

Depending on the scientific results, research needs and achievements on international level the Action will evaluate and update when necessary its scientific focus.

D.2 Scientific work plan – methods and means

In order to achieve these goals five WGs will be set up. The WGs will coordinate research on focused aspects of detector development, evaluation and application and they will be in close collaboration and interaction. Exchange and sharing of equipment has been considered. In addition exchange of personnel (mainly early-stage researchers) will allow continuous interaction, sharing of knowledge and achievement of the Action objectives.

The Working Groups are:

WG1, Hardware group: WG1 will explore novel scintillator materials and geometries; characterization of SiPMs and other semiconductors; theoretical studies; simulation performance of new materials as system components; development and optimisation of electronic circuits and mainly FPGAs and ASICs; optimisation of peripheral detector components, such as motors, rotating tables, gantries and the necessary mechanical and shielding parts. This WG will:

- asses if new materials can be used as detector components
- define how they should be treated
- determine what are their limitations including both performance and cost
- suggest if technology is mature for their application
- integrate hardware components with data acquisition software
- produce low cost imaging systems
- produce innovative multimodal prototypes for animal and clinical application

WG2, Software group: WG2 will develop advanced software for image reconstruction; implement of accurate algorithms for quantification of the results; preforma motion and attenuation correction using MRI data; implement software for efficient visualization of bimodal images. Finally the WG will be responsible for the development of user friendly software for non-specialized end users (biologists, doctors, etc). This WG will:

- provide the software for efficient translation of multimodal information
- understand user needs in order to make easy-to-use the developed systems

WG3, Bimodal agents group: WG3 will design, synthesize and evaluate bimodal contrast agents. Hybrid NPs with a magnetic core, labelled with PET isotopes with both diagnostic and therapeutic applications; other non-iron based NPs carrying Gd payload and PET payload; pretargeted NPs; non-nanoparticulate approaches with Gd and radionuclide e.g. Ga-68, F-18.

This WG will mainly:

- provide probes for new imaging applications besides oncology and brain imaging
- provide bimodal contrast agents as tools for preclinical research
- provide critical input for the design considerations of prototype PET/MRI systems

WG 4, Preclinical application group: WG4 will carry out all evaluation tasks of systems components (e.g. camera heads) in laboratory, develop phantoms, design evaluation protocols for preclinical (small animal) use and evaluate the performance of integrated prototypes. Experience from the evaluation of existing systems will be considered. This WG will:

- provide input about vital signal measurements during imaging process
- develop specific phantoms and design evaluation protocols
- evaluate the performance of integrated prototypes
- optimise application in small animal imaging
- be in close contact with end users and provide feedback to all WGs and Action as a whole.

WG 5, Clinical application group: WG5 will carry out all evaluation tasks to ensure efficient clinical application. Existing systems will be tested and characterized and experiences in first clinical applications obtained with these scanners will be integrated in the COST interaction. This WG will:

- provide input about specific requirements of clinical imaging
- design specific clinical protocols for dedicated organs imaging
- evaluate and ensure quality of the developed systems in clinical imaging
- be in close contact with end users and provide feedback to all WGs and Action as a whole.

E. ORGANISATION

E.1 Coordination and organisation

This COST Action will be coordinated by the Management Committee (MC) that will be created according to the “Rules and procedures for implementing COST Actions”. The MC will be based on the nominations done by the COST National Coordinators of the participating countries. A Chair, Vice-Chair and Working Group Leaders will be elected by the MC members at the Kick-off meeting.

Members of the Core Management Committee will be the Chair and Vice-Chair and the five Working Group Leaders. The role of the Core MC will be mainly to determine the scientific strategy of the Action and to ensure efficient cooperation between Working Groups. Moreover, the Core MC will propose invited speakers and priority areas to Action events that will be approved by the MC. Finally, Core MC will have the responsibility to circulate possible funding schemes and calls to interested participants in the WGs. The small number of members will allow rapid communication and fast decision making.

The Action will be a forum for sharing knowledge between scientists from multidisciplinary fields. One of its major priorities is to make this knowledge accessible to other researchers and mainly early stage researchers and students. Thus, the organization of two Training Schools on "PET/MRI: Instrumentation, Probes and Applications" has been planned (2^{nd} and 4^{th} year of the Action). Speakers in those schools will be researchers from the participating countries, as well as invited speakers from other programs and projects complementary to the Action. Special attention will be given in order have a good gender balance among speakers and participants.

In addition, the Action will support the organization of workshops, aimed in focused audience (physicians, biologists, etc), in order to promote the use and educate scientists on the benefits of PET/MRI.

Short-Term Scientific Missions (STSM) will offer the opportunity to young students to work in laboratories that participate in the Action. Those short time visits, will be approved by the MC. Although the main research effort will be supported by participating countries, STSMs are a flexible tool whose main goals are i) increase know-how and experience for early-stage researchers, ii) facilitate cooperation on the evaluation of innovative ideas that are not supported by funding projects.

A website of the Action activity will be set up after the kick-off meeting. It will work as a database and portal to gather and provide information on related scientific fields, progress, upcoming events in the fields that the Action covers, Training Schools, workshops and funding possibilities.

The Website will support the communication between participants of the Action, since it will include tools such as instant messaging, voice transfer as well as virtual conference. There will be a "members area" where information will be accessible only to members of the Action (e.g. meetings minutes, unpublished data, etc).
Finally, one challenge will be an e-learning service and existence of educational material (Virtual Learning Environment), possibly by the end of the second year.
The major milestones of the Action will be:

- M1: balance between technological partners and tracer developers / end users, by M12
- M2: At least 3 STSM, by M15
- M3: initiation of exchange of low cost equipment between participating groups, by M18
- M4: common publications between Action participants, by M24

E.2 Working Groups

The Action will be organized into five working groups (see D.2); The WG will be responsible for collecting, evaluating and disseminating results in their thematic areas. Taking into account the rapid advances in the field of PET/MRI and MI, the structure of the WGs may be slightly modified during the four years of the Action.

- WG1, Hardware Group
- WG2, Software Groups
- WG3, Bimodal agents Group
- WG4, Preclinical application Group
- WG5, Clinical application Group

The abovementioned WGs have in some cases complementary or partially common activities. Thus, it is suggested to set the following Research Teams, in order to efficiently study specific topics and address practical needs:

- RT1: Radiation and light detectors
- RT2: Electronics
- RT3: Mechanical components
- RT4: Simulation
- RT5: Image Visualization/Quantification
- RT6: Contrast Agents
- RT7: Small Animal Imaging
- RT8: Clinical Team
- RT9: Dosimetry

E.3 Liaison and interaction with other research programmes

There are no COST Actions that cover the field of PET/MRI and bimodal tracers. The currently running COST Actions have been reviewed and two with potential relevance have been identified, although one is expected to end by the date that the Action is realized. Those are: BM0607 "Targeted Radionuclide Therapy (TRNT)"; MP0701 "Composites with Novel Functional and Structural Properties by Nanoscale Materials (Nano Composite Materials-NCM)"; Representative from these Actions can be invited to future Action meetings or workshops.
The Action aims to interact with current EU projects in the field. The Action foresees to benefit from the experience and knowledge that has resulted from ongoing work and will offer to collaborate with existing projects. Other possible programs with countries outside the COST framework will be considered. Organization of workshops or sessions in conferences is another way of joint activity that will strengthen the bonds between the Action and other schemes. Finally, invitation to include review articles is another way of interaction.

E.4 Gender balance and involvement of early-stage researchers

This COST Action will respect an appropriate gender balance in all its activities and the Management Committee will place this as a standard item on all its MC agendas. The Action will also be committed to considerably involve early-stage researchers. This item will also be placed as a standard item on all MC agendas.

Early-stage researchers will be encouraged to participate in workshops and conferences, as well as carry out Short-Term Scientific Missions supported by the Action. During the kick-off meeting a decision will be made upon the establishment of an unofficial Young Researcher Committee with one representative who will participate in MC meetings.

It is suggested to establish two scholarships for young researchers one for the best male and one for the best female. The scholarships will include financial reward as well as training support. They will be annual and approved by the MC, following the suggestion of participants and CORE MC.

There will be high priority in the involvement of young women in the Action activities. Women will also be encouraged to actively participate take one or more critical positions (such as Workgroup Leaders).

F. TIMETABLE

The duration of the Action will be four years.

Year1

Months 0 to 3

- Kick-off Meeting
- Election of the Chair and Vice-Chair, and MC and CORE MC members
- Setting up of WG's and RT's members, working plan
- Setting up the Website
- Information campaign of the launch of approved COST Action

Months 4 to 12

- One representative of each signatory party prepares a document report of current status and working plan of their area for their institution and country
- Each WG's prepares a technical report of status and working plan

- MC actively promotes the COST Action among other and new institutions and scientific communities
- Each WG prepares and holds a workshop within their areas
- Second Action Meeting and workshop (month 6)
- Publication of First Workshop proceedings, WGs reports and first Action's Newsletter
- Third Action Meeting and workshop (month 12)
- Publication of Second Workshop proceedings, WGs reports and second Action's Newsletter
- Review progress on Short-Term Scientific Missions

Year 2

Months 12 to 18

- Each WG prepares and holds a workshop within their areas
- Fourth Action Meeting and workshop (month 18)
- Publication of fourth Workshop proceedings, WGs reports and Action's Newsletter
- Integration of the Action website – portal
- Organization of the first Training School

Months 18 to 24

- Fifth Action Meeting and workshop (month 24)
- Publication of fourth Workshop proceedings, WGs reports and Action's Newsletter
- Publication of Training Schools proceedings
- Review progress on Short-Term Scientific Missions

Year 3

Months 24 to 30

- Each WG prepares and holds a workshop within their areas
- Sixth Action Meeting and workshop (month 30)
- Publication of fifth Workshop proceedings, WGs reports and Action's Newsletter
- Integration of the Action website – portal
- Organization of the second Training School

Months 30 to 36

- Seventh Action Meeting and workshop (month 36)
- Publication of sixth Workshop proceedings, WGs reports and Action's Newsletter.
- Publication of Training Schools proceedings

- Review progress on Short-Term Scientific Missions.
- Educational material available on the website.

Year 4

Months 36 to 42

- Each WG prepares and holds a workshop within their areas
- Eighth Action Meeting and workshop (month 42)
- Publication of seventh Workshop proceedings, WGs reports and Action's Newsletter.
- Integration of the Action website – portal
- Organization of the Action conference (month 42)

Months 42 to 48

- Ninth Action Meeting and workshop (month 48)
- Publication of eighth Workshop proceedings, WGs reports and Action's Newsletter
- Review progress on Short-Term Scientific Missions
- Hold Final Presentation of Action for European Commission and Stakeholders
- Publication of Action Final Report

G. ECONOMIC DIMENSION

The following COST countries have actively participated in the preparation of the Action or otherwise indicated their interest: BE, DE, EL, ES, FR, HU, NL, PL, UK. On the basis of national estimates, the economic dimension of the activities to be carried out under the Action has been estimated at 36 Million € for the total duration of the Action. This estimate is valid under the assumption that all the countries mentioned above but no other countries will participate in the Action. Any departure from this will change the total cost accordingly.
Ukraine and USA have also expressed their interest to participate to the Action.

H. DISSEMINATION PLAN

H.1 Who?

The Action aims in efficiently coordinating teams from different COST countries with different expertise (mainly: physics, engineering, programming, chemistry, medicine and biology). As a consequence a dissemination plan should be well determined and target audience must be categorized according to research activity and/or occupation. Following these criteria the target groups are:

- Academic community.
- Research community.
- Medical community.
- Industry.
- Organizations.
- Society, since it is generally accepted that individuals and especially young people are more informed in scientific outcomes and possible benefits in everyday life.
- Undergraduate students in the fields of physics, engineering, programming, chemistry, medicine and biology. The main benefit for them will be education and involvement in innovative projects and skilled research collectives.
- Post graduate students in the same fields that will benefit from having access to new knowledge and new research possibilities.
- Professors in the same fields that will have the abovementioned benefits as well as possibility to increase their status in national level.
- Researchers, who will be able to use their enthusiasm and manpower in innovative research.
- Senior researchers that will advise and guide frontier research.
- Doctors, not only as end users but also as active involved participants at various stages of R&D. Understanding their needs and gathering their feedback is critical in order to decide the scientific goals of the Action.
- Patients, who will benefit from new diagnostic and therapeutic methods. Their needs and feedback will be highly taken into account.
- Spin off companies, already existent of newly created, with corresponding research and financial benefits.

- Small private companies, which are willing to commercialize innovative products in the field in collaboration with research groups.
- Big industries that can introduce innovative systems and pharmaceuticals in the clinical practice internationally.
- Universities that will have obvious prestige and financial benefits by participating in innovative projects.
- Research institutions that will have similar benefits (e.g. European Molecular Biology Laboratory (EBML) Heidelberg, Societies of Molecular Imaging).
- Hospitals that will be able to offer high quality services and possibly reduce cost.
- Government, which will benefit from participation of governmental-funded institutions in peak research. These benefits may be through increased European resources by EU funded projects, use of new technology in public hospitals, decrease in patient cost as well as side benefits such as organisation of international conferences, honours in scientists that represent public organizations etc. However, it is important to take into consideration the fact that government is responsible for insurance and legal issues that will arise for application of new technologies in science or health.
- European Union organizations, since possible innovations or fields of increased interest may be the subject of new proposal calls in International, European or bilateral level.

H.2 What?

Web site: A portal will be set up as soon as the Action is approved, as described in section E. Mirror sites in signatory institutions including their native languages will be encouraged, in order to provide easy access to non expert local community, end users, young students and researchers.
Publications: Publications that will result from the common activities of members of the Action will be published in peer reviewed several journals and will be presented in international conferences. The Action will be mentioned in all publications, especially in those that are the related to work that has been carried out under STSM. The proceedings of the workshops will be published, preferably in a relative journal. The aim of such scientific publications will be to provide information to specific audience, in order to allow spread of knowledge, enhance new collaborations, and inform possible end users about new technologies.

Other articles with more simplified content will also be published in press and weekly health magazines. Special provision will be taken in order to publish articles in journals of hospitals, ministries and other public organizations; thus create and strengthen the links with decision centres in national levels. Finally, one book is aimed to be prepared and published by the last year of the Action, summarizing the state of the art in the field of PET/MRI technology and applications and the impact of the Action to this.

Events: The organization of events such as conferences, workshops, seminars and Training Schools are an efficient way of bringing people together and disseminating the results of new activities. Besides Actions meetings, smaller events will be organized in national level with the participation of speakers from Action participants. In the latter case funding of these events from other resources (sponsors etc) will be necessary and requested. It should note be neglected that the invitation and participation of members of big governmental organizations can provide a useful link for further dissemination. The organization of the two Training Schools is considered an optimal way to bring new students and researchers close to the peak research topics that the Action is addressing, with obvious benefits for young students. Seminars by individual scientists will be given taking advantage of Short-Term Scientific Missions or other meetings that will take place in COST Action member countries. Two conferences will be organized by the 2nd and the last year of the Action. Finally, all representatives will make maximum effort to use their personal relations to further help dissemination of Action's outcomes.

H.3 How?

This is the initial dissemination plan. The main effort will be put on making the scientific results of the Action accessible to a large community. Interaction with National Contact Points in target fields will be assessed. In some cases this might be critical in order to overcome even language problems or work towards more simplified presentation for newcomers in the field.
The MC will have the responsibility to evaluate the Action progress as well as its impact on European and international level. New dissemination opportunities, e.g new conferences, journals, web applications, other funded programs will be reviewed and the dissemination plan will be modified when necessary.