

a n e u r I S T

Integrated biomedical informatics for the management of cerebral aneurysms

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@neurIST: Integrated Biomedical Informatics for the Management of Cerebral Aneurysms

Towards integrative decision support systems based on multi-scale computational suites for personalised brain aneurysm rupture risk assessment and treatment.

Objectives of the Project

When considered separately from other cardiovascular diseases, stroke ranks third among all causes of death, after heart disease and cancer. Worldwide, 3 million women and 2.5 million men die each year from stroke. Hemorrhagic stroke occurs when a blood vessel, typically an aneurysm, ruptures inside the brain. This often leads to severe disability or death. Despite considerable advances in treatment, rupture is associated with exceptionally high levels of morbidity and mortality (about 33% in each case).

Currently, invasive or minimally invasive treatment is offered to almost all patients because there is insufficient evidence to support a decision of non-intervention.

Project Description

@neurIST is a European initiative within the Sixth Framework Programme Priority 2 of the Information Society Technologies IST. This 4 year multidisciplinary project started on January 1st 2006 and involves 28 public and private institutions (including industrial, medical and academic organisations) from 12 European countries.

«@neurIST will transform the management of cerebral aneurysm»

@neurIST aims to produce a set of integrated software information retrieval, processing and management suites. Demonstration of the benefits of this integrated IT management infrastructure will also provide a platform for the application of this new approach using, complex data fusion, information extraction, processing and inferential deduction to the treatment of other disease processes.

The @neurIST project will:

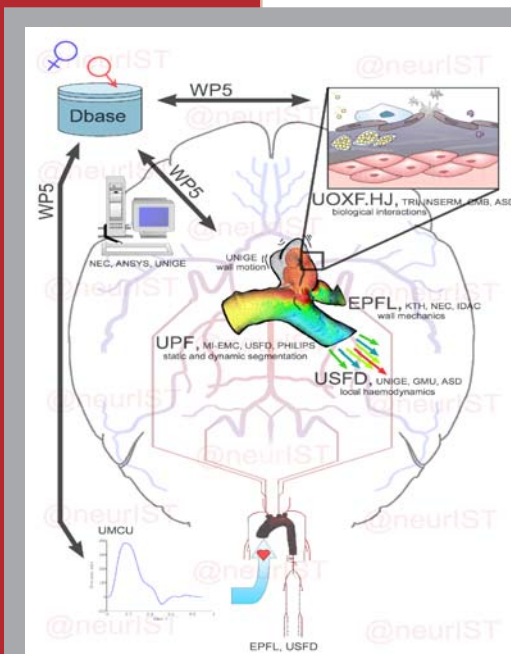
- Develop a new procedure and IT-support system for cerebral aneurysm management.
- Identify and collect all publicly-available, relevant and strategically important data from scientific studies.
- Deliver a rich, multiscale information processing chain that will provide new diagnostic indexes and insight into the process of aneurysm development and rupture.
- Develop a set of scalable and reusable integrative suites and demonstrate their value for revolutionising the understanding and management of cerebral aneurysm.

@neuLink will create an IT environment for the identification of genes associated with the disease and for the integrated analysis of genetic epidemiology (providing a template for future genetic epidemiological studies) and clinical data.

@neuFuse will provide an open source environment to fuse diagnostic and modelling data (using state of the art segmentation techniques, multimodal registration and advanced visualisation techniques) into a coherent representation of the patient's condition.

It is the primary thesis of @neurIST that the process of cerebral aneurysm diagnosis, treatment planning and treatment development is significantly compromised by the fragmentation of relevant data. To address this issue, @neurIST is developing a complete IT infrastructure for the management and processing of heterogeneous data associated with the diagnosis and treatment of cerebral aneurysm and subarachnoid haemorrhage. It will provide seamless access to data spanning the range of scales, from molecular, through cellular, tissue, organ, and patient level, to population level.

@neurIST will transform the management of cerebral aneurysm by providing new insight, personalised risk assessment and methods for the design of improved medical devices and treatment protocols.

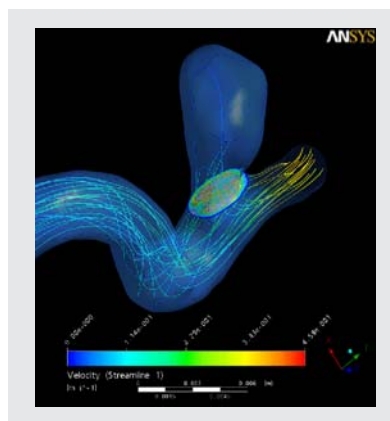


This work was generated in the framework of the **@neurIST Integrated Project**, which is co-financed by the **European Commission** through the contract no. **IST-027703**



Case Study

As a result of a car accident, a 40 year old subject is examined to screen possible lesions and an unrelated and asymptomatic cerebral aneurysm is diagnosed. Subsequent angiography provides improved image data for characterisation of aneurysm morphology. Blood samples are taken and screening for genes that @neurIST has associated, by data mining, with rupture risk is performed. @neuRisk supports the decision that the patient is at risk due to a focused area with unusually high flow impingement and high local tissue strains, to over expression of the eNOS gene, which has been shown to correlate with rupture, to systemic hypertension and to presence of lifestyle risk factors including smoking. The system also points to very recent studies that match the patient profile and may provide additional information. A recent paper suggests an association between the Insertion allele of the ACE gene with ruptured aneurysms. The clinician therefore verifies its presence in the patient by querying the patient's EHR and retrieving the results of her biochip analysis that discloses a positive test. The patient is informed about the risks/benefits of treatment vs. non treatment and that, based on all available information, a personalized treatment guideline has been developed which suggests that endovascular treatment is indicated in this case.



@neuRisk will produce a personalised risk assessment and treatment guidelines by integrating all available information.

@neuEndo will deliver an innovative IT system for supporting the design of implantable devices (such as coils and stents) and, intervention planning by simulation of the structural, haemodynamic and biological response to intervention. This will include advanced numerical-simulation tools to predict the occurrence of device-related thrombosis and drug elution.

- Provide an ICT-system for developing, integrating and sharing biomedical knowledge related to cerebral aneurysm as required by the four integrative suites. The @neurIST infrastructure will not only support computationally demanding tasks such as complex modelling and simulation (@neuCompute) but also enable access to health data distributed in public and protected databases distributed all over the world (@neuInfo).

- Inspire and promote the development of corresponding systems for other disease processes by demonstrating the personal and economic impact of IT-enabled information integration in the context of cerebral aneurysm management.

Expected Results & Impacts

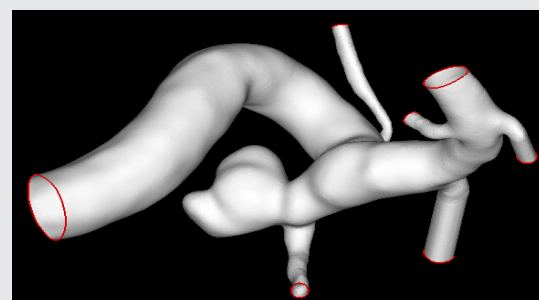
Owing to the increased use and improved resolution of modern imaging technologies, the number of non-symptomatic aneurysms found during clinical examinations will continue to increase. This will result in increasing burden on Healthcare resources.

Integration of multiple clinical data and use of grid-based IST systems provides the platform to tackle this problem. It is anticipated that Healthcare costs can be reduced significantly if the relevant patient population is optimally targeted and unnecessary and potentially risky interventions can be avoided.

The primary aim of @neurIST is to assist the clinical decision-making process by providing an objective measure of risk, based on all available data, and thus to reduce patient anxiety and unnecessary treatment by identifying those individuals who do not have high risk of rupture.

Measurable benefits of @neurIST will include the quantification of risks, including those of intervention and non-intervention. By combining the efforts and expertise of clinicians and industry, patients will benefit from improvements in diagnostics, prevention and treatment including personalised design of endovascular devices.

Aside from improved patient management and anxiety reduction, the potential economic benefit in Europe is enormous: taking into account the prevalence of this disease [1-5%], the annual rupture rate [0.2-1%], and the average treatment and 1st-year follow-up costs of patients [50kEuro], it is estimated that, in Europe alone, the cost of unnecessary interventional or surgical procedures are in the order of thousands of million Euros per annum.



Timetable:
from 01/01/2006
to 31/12/2009

Total cost:
17.356.730 euro

EC funding:
12.605.239 euro

Instrument: IP

Project Identifier:
FP6-2004-IST-
027703

Partners:

Universitat Pompeu Fabra (ES), Université de Genève (CH), The University of Sheffield (UK), Ecole Polytechnique Fédérale de Lausanne (CH), Fraunhofer Institute - Institute for Algorithms and Scientific Computing (D), Institut Municipal d'Investigació Mèdica (ES), Utrecht University Medical Center (NL), Super Computing Solution s.r.l. (I) Philips Medical Systems B.V. (NL), Erasmus Medical Center (NL), Royal Institute of Technology (SE), GridSystems S.A. (ES), ANSYS Europe Ltd (UK), NEC Europe Ltd. (UK), University of Oxford (UK), Cancer Research UK (UK) InferMed Ltd (UK), Advanced Simulation & Design GmbH (D), William Cook Europe ApS (DK), Institut National de la Santé et la Recherche Médicale (F), IDAC Ireland Ltd (IE), Neuroangiografia Terapèutica S.A. (ES), Hospital Clínic i Provincial de Barcelona (ES), University of Luton (UK), Medical University of Pécs (HU), Universitaet Wien (A), Universitätsklinikum Freiburg (D)

Results achieved during the first year

• Retrieving @neurIST relevant information

Classification, standardization and protection of the personal identity of patients are the first steps towards integration of clinical datasets - a process that requires adequate data collection.

The first step of normalisation is the creation of a Clinical Reference Information Model (CRIM). The CRIM is an inventory of data that will be acquired through the @neurIST project. A second release of the document includes an inventory of genetic information. The current version of the CRIM contains primary data attributes (clinical, imaging, genetics). Some derived data attributes are defined but others are expected and will be integrated into the next CRIM version. The CRIM is currently an excel document that will converge progressively into a fully structured form in XML format.

The CRIM served as a support to initiate an @neurIST ontology and was the reference to generate the CRIM automated data acquisition software. It will be continuously synchronised with the @neurIST ontology.

Based on the results above, the Clinical Data Collection Protocols have been designed, describing the collection practices to be followed by the clinical partners. A detailed review on Ethical Issues concerning Biological Samples and Personal Data has been performed. The protocols are now ready to go through the Ethical Committees at every clinical centre during the first months of 2007 in order to start with the data collection.

• Modelling the disease: merging disciplines

The initial conceptual framework (the *Global Schema of the Disease*) for modelling the disease has been delivered. This Schema will go beyond simple integration of databases, and sets the basis for semantic mediation. This document describes the process to establish the global schema for this disease (or any other). The CRIM provided a good coverage for clinical data sources. The collaboration of experts from the wide range of domains within the Consortium is of special relevance for the creation of this schema.

• Prototype Overall System Architecture Released

All the architectural design plans for the different @neurIST subsystems (application suites, clinical infrastructure, Grid technologies, etc.) are combined in the *Prototype System Architecture and Design Document*. This deliverable provides an overview of the initial @neurIST system architecture and design, and the guidelines for the development process, by showing how the architectural drivers for the @neurIST prototype link to the high-level architecture and design.

This document also provides the basis for the implementation, evaluation and deployment of the @neurIST prototypes, and addresses the definition of the reference model.

Of special relevance is the re-use of project results from previous FP5 projects, like GEMSS, as well as the use of robust standards as far as possible.

• Engaging clinical and industrial stakeholders through first prototypes

A first set of independent demonstrators for the application suites and the computational backend service has been released. These prototypes allow obtaining system feedback from end-users, and demonstrate the feasibility of the interactions with the rest of @neurIST components. This feedback is collected every 6 months during End User Workshops, where clinicians, researchers and industrial partners analyse the demonstrators.

As an example of the progress in prototypes, the @neuInfo was used to set up a data service for @neuLink, and the potential use of @neuCompute with the suites has been analysed.

Contractors involved: UPF, UNIGE, USFD, FHG, IMIM, B3C, PHILIPS, MI-EMC, GRIDSYS, INSERM, ANSYS, NEC, UOXF.HJ, CRUK, INF, ASD, COOK, IDAC, NAT/HGC, HCPB, LUT, MUP, UNIWIEN, UKLFR

• Complex information processing workflow specified

The flow of data through the complex information extraction process has been generated, illustrating the interaction between the components. Strong emphasis has been placed on the development of a modular and interoperable tool chain for the structural and computational fluid dynamics solutions.

Significant progress has been made in the research and development of algorithms and computational software components, although they are not yet fully integrated in front-end applications that demo their capabilities. The specifications and requirements of the software components have been expressed in terms of detailed use cases, and first integration results are available.

The specification and design of the libraries to be integrated from WP3 to the corresponding @neurIST suite has been finalised. The integration of one of the libraries (segmentation) has been started.

Contractors involved: UPF, UNIGE, USFD, EPFL, IMIM, PHILIPS, MI-EMC, KTH, ANSYS, NEC, UOXF.HJ, ASD, IDAC

Literature reviews on the occurrence of aneurysms, subarachnoid haemorrhage, their risk factors and prognosis were started.

Health care databases that allow for *in silico* populational studies necessary to underpin the disease model have been identified; protocols have been submitted to review boards, and the conduct of the following *in silico* studies are in progress:

- Assessment of the incidence of subarachnoid haemorrhage, and patterns by age, gender, time
- Description of intervention patterns of subarachnoid haemorrhage over time (clipping vs. coiling) by age, gender
- Complication rates and life expectancy after various interventions for subarachnoid haemorrhage
- Assessment of the prevalence of unruptured aneurysms from diagnosed and 'screened' populations
- Comparison of risk factors between patients with unruptured aneurysms from diagnosed and 'screened' populations
- Quantification of the association between risk factors and subarachnoid haemorrhage



- **First @neurIST ontology draft available gathering all relevant knowledge about the disease (simulation-based knowledge excluded).**

Liaison among ePIdemiology, disease models and @neuRisk strands started.

The release of a @neuRisk prototype served to start the discussions between epidemiological experts and developers, for a better understanding of the model, how it may be extended and what features are missing. @neuRisk prototype also demonstrated a visual way of representing a personalized risk benefit analysis and more complex models may become easier to understand both for the clinician and the patient.

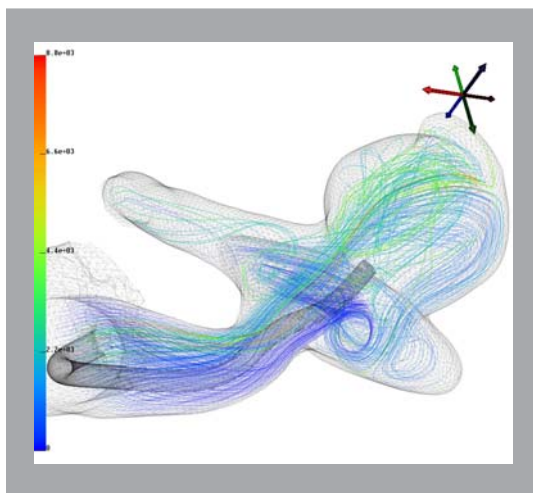
The understanding on how the ontology developed for @neurIST and text mining results serves as input for assessment of associations between these factors and the presence of an aneurysm, or its rupture.

Ontology is essential to support semantic access to information by, for instance, providing the possibility to extract groups of synonyms or related terms. "Related terms" may be broader or narrower terms. In addition, such ontology enables that characteristics of an entity type can be derived by its semantic relations to other types. Therefore, "related terms" may also be possible characteristics of an entity type, for example the possible locations of an intracranial aneurysm, or a list of entity types that have in common to be "risk factors".

In the first project year, terms from the different scientific fields in the project were collected, followed by a structured representation of the identified entity types (concepts) and the design of a synonym

database. The result is a vocabulary with already good coverage in the field of clinical medicine (including entity types describing the disease "intracranial aneurysm", associated diseases, anatomical entities, and patient history and life style factors). There is already an incomplete coverage in the domains epidemiology, molecular biology and simulation, which need to be further enhanced.

Contractors involved: FHG, IMIM, MI-EMC, CRUK, UKLFR



- **Promotion among health professionals**

There is a successful integration of health professionals with the rest of profiles within the project.

This has been facilitated by the fact that four members of the Project Board have clinical or biomedical background (Daniel Ruefenacht, Martin Hoffman, Robert Dunlop and, since more recently, Philippe Bijlenga).

The project procedures guarantee that the clinical parties play a core and active role in the System Development Process, and End User Workshops are in preparation to allow a better understanding of the possibilities offered by the @neurIST approach to clinical practice and to reinforce roles in the @neurIST development process.

- **External @neurIST dissemination plan defined; dissemination activities started**

Project-wide dissemination goals and strategy have been already defined, and a relevant number of dissemination activities have been performed. This strategy also includes description of the collaboration with external projects (e.g. ISUIA) and the establishment of network collaboration between clinical sites.

The strategy for internal knowledge management supports the collaboration amongst different disciplines, with an important focus on health professionals. The @neurIST concept has been presented in several key clinical and scientific international fora like the IEEE Symposium on Biomedical Imaging [ISBI] (Apr 2006, Washington DC, USA), the HealthGrid Conference 2006 (Jun 2006, Valencia, E), the World Congress on Biomechanics (Aug 2006, Munich, D), the European Society of Neuroradiology / Intracranial Stent Meeting [ESNR/ICS] (Sep 2006, Geneva, CH), and will be featured at the International Stroke Conference (Feb 2007, San Francisco, USA).

Contractors involved: UPF, FIMIM, UNIGE, USFD, IMIM, PHILIPS, MI-EMC, NEC, UOXF.HJ, NAT/HGC, HCPB, MUP

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