Third Periodic Activity Report

Project Number:	FP6-2005-IST-026996
Project Acronym:	ACGT
Project Title:	Advancing Clinico-Genomic Clinical Trials on Cancer: Open Grid Services for improving Medical Knowledge Discovery
Instrument:	Integrated Project
Deliverable name:	Third Periodic Activity Report
Period covered:	From 1st February 2008 to 31st January 2009
Start date project:	1st February 2006
Duration:	48 Months
Submission Date:	10/4/2009

COVER AND CONTROL PAGE OF DOCUMENT	
Project Acronym:	ACGT
Project Full Name:	Advancing Clinico-Genomic Clinical Trials on Cancer: Open Grid Services for improving Medical Knowledge Discovery
Document id:	N/A
Document name:	Third Periodic Activity Report
Document type (PU, INT, RE)	RE
Version:	2.0
Submission date:	10/4/2009
Editor: Organisation: Email:	Manolis Tsiknakis FORTH tsiknaki@ics.forth.gr

Document type PU = public, INT = internal, RE = restricted

ABSTRACT:

The current document is the Annual Progress Report of the project for the third year of its implementation, i.e. 1 Feb 2008 to 31 Jan. 2009.

It provides a synthetic view of the work performed by the project and it presents the main achievements of the project during the reporting period.

KEYWORD LIST: Annual Activity Report

MODIFICATION CONTROL			
Version	Date	Status	Author
1.0	07/04/09	Pre-Final	Manolis Tsiknakis, Remi Ronchaud
2.0	10/04/09	Final	Manolis Tsiknakis, Remi Ronchaud

List of Contributors

All WP leaders have made contributions of material regarding the status and work performed by the WP they are responsible for, have reviewed the pre-final version of the report and provided comments, which assisted in the production of the final version.

As a result the list of contributors is:

- Rémi Ronchaud, ERCIM – Project Coordinator, WP 1 Leader
- Manolis Tsiknakis, FORTH – Scientific Project Coordinator
- Norbert Graf, Uds – Quality Manager and WP2 Leader
- Jarek Nabrzyski, WP3 & 4 Leader
- Anca Bucur, WP5 leader
- Stefan Rüping, WP6 Leader
- Luis Martín, WP7 Leader
- Georgios Stamatakos, WP8 Leader
- Stelios Sfakianakis, WP9 Leader
- Nikolaus Forgo, WP10 Leader
- Brecht Claerhout, WP11 Leader
- Christine Desmedt and Dimitris Kafetzopouls, WP12 Leaders
- Thierry Sengstag, WP13 Leader
- Radu Gramatovic, WP14 Leader
- Yannick Legre, WP15 Leader
- Andreas Persidis, WP16 Leader

Content

Publishable Executive Summary

Summary description of project objectives

ACGT is an Integrated Project (IP) funded in the 6th Framework Program of the European Commission under the Action Line "Integrated biomedical information for better health". The high level objective of the Action Line is the development of methods and systems for improved medical knowledge discovery and understanding through integration of biomedical information (e.g. using modelling, visualization, data mining and grid technologies).

ACGT focuses on the domain of Cancer research, and its ultimate objective is the design, development and validation of an integrated Grid enabled technological platform in support of post-genomic, multi-centric Clinical Trials on Cancer. The driving motivation behind the project is our committed belief that the breadth and depth of information already available in the research community at large, present an enormous opportunity for improving our ability to reduce mortality from cancer, improve therapies and meet the demanding individualization of care needs.

In addition to their shear volume, the data collected using a variety of laboratory technologies and techniques are often published without the background information (method of capture, sample preparation, statistical techniques applied) that is needed to reproduce results. In fact, a typical researcher spends as much time trying to understand the origins of a dataset as actually performing new analyses. Rarely is a clinical biostatistician able to make good use of data collected on studies in which they were not directly involved with, largely due to incomplete or non-existent annotation and standardization of the information. Even within a single laboratory, researchers have difficulty integrating data from different technologies because of a lack of common standards and other technological and medico-legal and ethical issues. As a result, very few cross-site studies and clinical trials are performed and in most cases it isn't possible to seamlessly integrate multi-level data.

The ultimate objective, therefore, of the ACGT project is the development of a Semantic Grid infrastructure offering high-level tools and techniques for the distributed mining and extraction of knowledge from data repositories available on the Grid, leveraging semantic descriptions of components and data and offering knowledge discovery services in the domain of cancer research. Special emphasis is been given to the trust that needs to be embedded in the platform and relevant ethical issues, thus creating optimal conditions for its uptake.

In achieving this high level objective, the project focuses on:

- ⇨ the development of a Master Ontology on Cancer. The ACGT Master Ontology is the corner-stone of our semantic integration architecture. The ACGT Master Ontology is meant to constitute a reference ontology for the field targeted by the ACGT project, and its objective is to enable the semantic data integration across its various sections. Our plan is for the ACGT master ontology to be part of the OBO Foundry; The structure, completeness and scalability of the MO is under continuous evaluation as the full range of functions supported by the ontology are implemented and tested.
- ⇨ the development of a "Mediator" to hide the complexity of query translation and data integration. While following the state of the art in the area, it proposes an innovative approach to semantic mediation. In this approach, the user performs queries against a single, "virtual" repository. This virtual repository represents the integration of several heterogeneous sources of information. This integration process relies on a common interoperability infrastructure, based at the conceptual level on the global schema (which in our case is the ACGT MO);
- ⇨ the implementation of a clinical trial management system based on an ontology driven software development process, which should result in semantically consistent clinical trial

systems in the future; The ontology based clinical trial management system for ACGT (ObTiMA) plays a crucial role. ObTiMA supports the design phase of a clinical trial and is a tool allowing an end-user to manage a patient within a clinical trial, to capture data, to report data and to query and analyzed databases used in the trial in a standardized way;

- ⇨ the implementation of open, standards based data access services, thus providing uniform access to heterogeneous clinical trial, genetic as well as public biological databases; The main goal of the data access services is to provide a uniform data access interface to heterogeneous data sources. Web Services have been used as the common interface technology, and SPARQL has been chosen as a common query language. A range of suchdata access services have been implemented for relational databases, medical image databases and databases managing microarray data (BASE compliant).;
- ⇨ the implementation of a range of bioinformatics and other biomedical data analysis and visualisation tools, grid-enabled knowledge discovery tools as well as the seamless discovery, integration and management of these sharable information assets, i.e. data and tools operating on such data. The gridified version of the R package (GridR) is a key such service enabling users to make use of the complete ACGT platform and services by using the (familiar) R language. Additional such analytical services, e.g. literature mining, visualization, etc are also been implemented. At the same time a generic method has been established for the integration and re-use of existing bioinformatics services into the ACGT architectural framework (e.g. BioMOBY services);
- ⇨ central to the workplan of ACGT is the notion of discovery (eScience) workflows. In essence a workflow can be abstracted as a composite service, i.e. a service that is composed by other services that are orchestrated in order to perform some higher level functionality. As a result the project works towards a service composition environment which realizes and validates it. Towards this objective the implementation of a Workflow editing and enacting environment is designed and implemented;
- ⇨ the annotation of services and workflows with semantic descriptions. An adequate and convenient way of annotating workflows with metadata is of paramount importance for their posterior discovery among repositories of useful workflows based on their purpose, internals and field of application characteristics; The main outcome of our work to date is the definition of a generic semantic service integration architectural framework using Semantic Web technologies, standards, and tools. Such a framework provides the semantic integration of not only ACGT services but also other third party services like BioMOBY.
- ⇨ the definition of an integration architecture, which has a complex layered organization, involving security, data anonymization, GRID-distributed computing, uniform database access, etc which enables the seamless semantic publication and discovery of data, tools and services as well as their dynamic composing in e-science discovery workflows and their execution on the Grid. An important dimension of this architecture is its “security view”. Analysis of the ethical and legal requirements that the project must adhere too has led to the specification of the demanding “security architecture”, and a range of required tools and procedures, thus making sure that a totally secure computational environment is delivered to end users.

Contractors Involved

The project’s scientific coordinator is Manolis Tsiknakis from FORTH, Greece (tsiknaki@ics.forth.gr) and the network administrative coordinator is Remi Ronchaud (remi.ronchaud@ercim.org) from EEIG ERCIM, France.

The participants to the ACGT project are the following:

GEIE ERCIM, FORTH, INRIA, University of Amsterdam, Philips S.A., Institute Jules Bordet, SIB, Lunds University, University of Malaga, UPM, FhG, BIOVISTA O.E., University of Crete,

University of Hannover, PSNC, Custodix, Healthgrid, Institute of Communications and Computer Systems, University of Saarland, SIVECO S.A., FUNDP, University of Hamburg, University of Oxford, Hokkaido University, and European Institute of Oncology.

Work performed

User Needs

The main focus was laid on clinical aspects of the project. The search for new clinical trials that can run within ACGT was a major workload. In this respect the work was concentrated on the following major areas during the third period of ACGT:

1. Continuation of work regarding user requirements and functionality of the Ontology based clinical data management system (ObTiMA)
    a. User needs for clinicians and basic researchers for ObTiMA including the user friendly integration of the Master Ontology
    b. Clinico-genomic integration, including technological, legal and ethical issues, security and quality control within ObTiMA
2. A range of clinico-genomic scenarios that were implemented in the clinical studies as defined in WP12 are further developed and discussed how to integrate them into the trial builder
3. New clinical trials and scenarios were defined to use the ACGT platform. They are listed and described in D2.4.

Clinical Trials

The status of implementation of the two originally defined trials is being continuously monitored. These two trials are contributing data for the third “trial”, i.e. the oncosimulator.

Additionally, IEO carried out the clinical part of the Trenett study, and started collecting and pre-validating the data as well as planning the statistical analyses to be carried on through the ACGT tools and services (GridR, Workflow, etc). The clinical partners are also continuously interacting with the other WPs to answer all the questions they may have regarding these trials.

Also, in order investigate the various harmonization issues related to cross-platform and multi-centric post-genomic data collection and analysis, we developed a study which aims to assess the variability in gene expression microarrays, and of the prognostic and predictive profiles obtained from this technology, performed at different sites and using different array methodologies in human breast cancer samples. To this end we are comparing reproducibility of results obtained in two different ACGT partners institutions (IJB and UOXF) using two different but well established technologies for gene expression microarrays; namely, Affymetrix gene expression arrays (processed at IJB) and Illumina arrays (processed at UOXF). A lot of time has been spent to define and agree on the ethical and legal requirements to share clinical and genomic data, to update the clinical database and to formulate research-clinical meaningful data mining scenarios for the review demonstrators.

Finally, different initiatives have been taken to promote post-genomic studies conducted in the context of ACGT as well as to get feed-back from the clinical community.

Ethical and Legal framework

According to the legal requirements previously analysed, technical solutions to safeguard data protection were developed and tested. The focus was on the implementation of the proposed ACGT Data Protection Framework, on the negotiation and signing of the produced contracts between ACGT partners, the established Center for Data Protection and on a Risk analysis together with WP11 with regard to data protection.

Furthermore, the work on the projected comparative survey on patients' perspectives and needs regarding informed consent and data protection was continued and implemented.

Validation of the initially defined ACGT Architecture.

An architecture based on services and their interactions has been defined, during the reporting period one, for the development of the ACGT infrastructure, which is intended to describe the structure of a system in terms of computational components and their interactions, patterns that guide their composition and constraints on these patterns. In the general ACGT environment the workflow authoring and management tasks play a central role as a means to support the knowledge discovery process.

The security layer of the architecture has been defined in detail: Access rights, security (encryption), trust buildings are been issues to be addressed and solved on this layer, based on system architectural and security analysis. Implementation of domain specific security services, such as pseudo-anonymization and anonymization services, which are modelled and invoked through this layer, has been completed. In specific:

- ⇨ The Custodix Anonymisation Tool (CAT) has reached version 1.0. Further development has been done to make a Command Line Interface (CLI) available.
- ⇨ Modules for the monitoring system were created and deployed to monitor the stability and function of the security services.
- ⇨ The Gridge Authorization Service (GAS) was further developed and improved.
- ⇨ The meta-data repository was extended to support data set identifiers.
- ⇨ More services were integrated in the ACGT security framework. Amongst those was the metadata repository where changes in services and workflow metadata should be restricted and subject to appropriate permission as specified in GAS.
- ⇨ Specification for the role based secure access to ObTiMA and user roles and rights management has been specified.

In addition to the above, significant progress with regards to the development of the ACGT platform occurred during the reporting period. Two large scenarios (PseudoTOP and MCMP) were developed and used to test the logical and execution architecture in general as well as separate tools and services. Based on the experiences gathered in building and demonstrating these end-to-end demonstrations and also on the feedback received from a first evaluation-and-training session with end users which took place in Vienna, a range of activities have been defined and executed with the objective of a) increasing robustness, b) reducing technical complexities in using the systems/services and c) increasing the usability of the whole platform. Specifacally the more critical activities that were performed include:

a) Grid Layer

- grid testbed were maintained and extended with new resources to provide more computational power and storage space for the project.
- the framework for monitoring grid resources and services was introduced .
- implementation of automatic testing procedures with a portlet for presentation the results.
- continuous work on the improvement of the grid services responsible for resource management, data management and authorization decisions.
    a. ongoing work on integration of DMS service with global authorization framework and VO management,
    b. implementation of the parametric job support in resource management system in the grid,
- design and implementation of new security policies in the context of Virtual Organization management.

b) The ACGT Master Ontology

- Review/Extension of ACGT MO.
- Addition of anatomical classes.
- Re-evaluation of NCI Thesaurus (caBIG, caCORE).
- Ontology-focussed validation of CRF creation.

c) ObTiMA

- Advanced CRF Creator and Ontology viewer.
- Extension of the ObTiMA database for the Trial Outline Builder.
- Further integration of ObTiMA with the ACGT Mediator.
- Export clinical trials into CDISC ODM format.
- Multi-language support during CRF creation.
- Web Service for accessing the ObTiMA database from TOB.
- Web Service interface specification for accesing the Ontology Submission System from ObTIMA.
- Roles and Rights MAnagemnet System specified and implemented (version 1).

d) Data Access Services

- Developed data access service for retrieving microarray data. Real life evaluation of the services with the BASE database.
- Extended data access services to meet requirements of pseudoTOP, MCMP, and SIOP data analysis scenarios. Added functionality to deliver files to DMS.
- Increased query functionality by supporting custom SPARQL functions.
- Integrated data access services into the ACGT security infrastructure.

e) The ACGT Mediation technologies

- Design, Implementation and Testing of the mapping and query tools.
- Definition of new version of the Mapping API, covering Obtima requirements .
- Updating of mapping format to cover new cases of heterogeneity.
- Improving the mediation algorithm, avoiding data overriding issues and covering cross database references.
- Integartion of the mediation tools in the portal.

f) ACGT Analytical Services

- Reference implementations of ACGt compliant analytical services (literature mining) and documentation of experiences.
- Implementation of new features in the GridR tool, and bugfixes .
- Publication of the GridR tool under the R open source repository CRAN.
- Implementation of of visualization services in the backend for use by Hokkaido University in the Subjunctive Interface.

g) The ACGT Workflow Environment

- design and implementation of the ACGT web based workflow authoring and execution tool and its integration in the ACGT portal.
- design and implementation of appropriate security infrastructure so that the workflow execution is seamlessly integrated with the underlying Grid security mechanisms of ACGT.
- Implementation of required functionality in support for Grid Security and credential delegation.
- Implementation of a generic architecture of proxy services allowing the integration of Grid and non-Grid based technologies at the workflow layer and will also permit the incorporation of “third party services”.

h) Semantic framework for ACGT Services and Tools

- Definition of the semantic framework for the services, data, and workflows of ACGT. Reported in D9.4, and its initial implementation.

i) Technologies for in-silico modelling and simulation

- Development of the initial version of the (semi)integrated Oncosimulator including the simulation and the technological components.
- Implementation of an extensive numerical study of the algorithms and codes including convergence and stability.
- Code optimization so that convergence can be ensured automatically and stability is improved through several arithmetic adaptations.

j) The ACGT Portal

- Redesign of the front-end and content contribution in the ACGT Portal.
- Redesign of the ACGT Portal back-end from the needs for “evaluation and validation” point of view.
- Deployment of Gridsphere portal technology.
- Integration of the workflow environment in the ACGT Portal and the implementation of a "single-sign-on" (SSO) seamless access to it.
- Development of the DMS Portlet v2.
- Updating of the Metadata Registration Portlet.
- Development of the GridR Console Portlet.
- Development of the VO Management Portlet.

Apart from these specific implementation activities, we have focused on verification (end-to-end) of the architecture. Towards this objective we monitor very carefully all technical decisions taken regarding the implementation of the services at the various layers of the architecture. We have continued defining new se cases: based on the requirements, but also on the project scope, while talking to users. We have continued working on scenarios, which were investigated and explored their implications for the architectural decisions already taken.

Results achieved

Significant progress with regards to the development of the ACGT platform occurred during the reporting period. Two large scenarios (PseudoTOP and MCMP) were developed and used to test the logical and execution architecture in general as well as separate tools and services. Based on the experiences gathered in building and demonstrating these end-to-end demonstrations and also on the feedback received from a first evaluation-and-training session with end users which took place in Vienna, a range of activities have been scheduled with the objective of a) increasing robustness, b) reducing technical complexities in using the systems/services and c) increasing the usability of the whole platform.

Key services at the various layers of the architecture have gone refinement and advanced versions of them are tested in the various end-to-end validation scenarios established.

Such mature versions of key architectural components include:

- the ACGT Master Ontology
- the ACGT Mediator tools and technologies (mapping tool, etc)
- the Ontology based Trial Management System
- Data access services
- the ACGT Portal
- VO management services
- analytical tools (GridR, literature mining)

- workflow editing environment and workflow enactment services
- the ACGT Semantic Services Framework (i.e. metadata repository)
- the Oncosimulator
- interactive visualisation services on the Grid,
- as well as the services of the advanced Grid layer are available.

In parallel to these activities, we have been working towards promoting the ACGT CDP on the European level, and begun addressing the intellectual property issues from the legal point of view. Also the international and national survey on patients' and parents' perspectives and needs regarding informed consent and data protection was designed and set up.

Expected results

The project aims at improving quality of European clinical trials leveraging on latest advances in information technology and computer science. The improvement in clinical trials are going to be achieved through a fully integrated handling of patient's biomedical profile, which requires a deep semantic integration of all data sources related to the subject involved in the trial, and by making this highly integrated set of data and computational assets available to end users with compelling user interface.

Although the targeted areas chosen are focused on Paediatric oncology and Breast cancer, the infrastructure which the project is aiming to develop and deploy could be easily exploited by and extended to any other disease area, after appropriate tailoring. Ultimately, the most important beneficiaries of ACGT will be the cancer patients themselves and the public at large.

The ultimate objective, therefore, of the ACGT project is the development of a Semantic Grid infrastructure offering high-level tools and techniques for the distributed mining and extraction of knowledge from data repositories available on the Grid, leveraging semantic descriptions of components and data and offering knowledge discovery services in the domain of cancer research.

The expected results of the ACGT project comprise:

- The Engineering of a Master Ontology (MO) on Cancer: In order to ensure the means of the ACGT MO quality management, we have decided to aim at incorporating our ontology into the OBO Foundry, which is a collaborative effort, involving a group of ontology developers who have agreed in advance to the adoption of a growing set of principles specifying best practices in ontology development.
- Developing software tools and research strategies that enable users to move away from labor-intensive case-by-case modelling of individual applications, and allow them to take full advantage of generic adaptive and self-learning solutions that need minimal supervision
- Workflow Management: In a clinical trial environment there are combined processes based on previous results and materialized through a multi step stateful operation. To support automation of these kinds of processes, workflow management become an essential part of our architecture.
- Improving ease of use by enabling data, service and workflow descriptions at high semantic levels. The semantic services framework defined will enable us in delivering recommendation services assisting users in the design and/or discovery of their analytical workflows.

- Developing disease models: Accurate models can be utilized as the components of complicated simulations with the purpose to study and analyze the interrelations between patient organism types, disease factors, possible treatments, etc. Such procedures can provide critical intelligence and look-ahead on treatment possibilities or indeed any process that can be described by means of the models.
- Spreading of expertise and excellence through dissemination, training and industrial liaison, contribute to the distribution and uptake of the technology by relevant end-users.

Intentions for use and impact

Europe needs more integrated clinical trials, and therefore the end results of this project are still extremely relevant since these can have a profound impact on Europe's needs in this field. It is needed to get the research information rapidly flowing into the clinical trial design and assessment, in a coordinated way.

ACGT's vision is to become a pan-European voluntary network or grid connecting individuals and institutions to enable the sharing of data and tools, creating a European Wide Web of cancer clinical research; the ultimate goal being to speed the delivery of innovative approaches for the prevention and treatment of cancer. ACGT will offer the benefits of open access to a rich pool of interoperable tools, shared data and standards to the Cancer Research Community, and also the ability to participate and contribute without compromising individual innovation and creativity.

We have already mature demonstrations of all technological components, functioning as a whole, required to realize this vision. We believe that by the end of the project we will deliver a solid platform for use by end user communities.

At the same time we fully agree with the statement of our Reviewers (see Consensus Review Report/Dec 2008) that:

"The full development, dissemination and exploitation of the ACGT infrastructure is clearly a 5-10y endeavour and will require a detailed business and scientific strategy – embracing formal organisational partnerships, commercial activity and participation in open scientific communications. It remains important to make sure that goals are realistically prioritised so that the really important practical outcomes that are looked to from this project are not compromised by spending too much resource on goals that will take longer to achieve. The project needs to leave a solid platform for what comes next and capturing fully the knowledge gained within the consortium is essential for this."

Project Objectives and Major achievements during the reporting period

General Project Objectives

In order to achieve its goals and objectives, ACGT will create and test an infrastructure for cancer research by using a virtual web of trusted and interconnected organizations and individuals to leverage the combined strengths of cancer centers and investigators and enable the sharing of biomedical cancer-related data and research tools in a way that the common needs of interdisciplinary research are met and tackled.

Strategically, the ACGT project addresses the following needs and challenges related to biomedical, technological and scientific aspects:

- ⇨ Integration of Clinical Research Centers on Cancer with varying needs and capabilities in a common network for sharing data, applications, and technologies.
- ⇨ Development of a useable and scalable biomedical grid that Clinical Research Centers on Cancer will actively use for added value clinical trials.
- ⇨ Demonstration of new enabling tools for supporting multi-centric Cancer Center research.
- ⇨ Development of new component-based data analysis and knowledge discovery tools and modification of existing ones so as to utilise the advantages of grid computing, and enable high-performing data-mining and biomedical knowledge extraction operations.
- ⇨ Utilisation of clinical trial management systems based on standards-based and components-based clinical trial management systems, integrative cancer research applications and innovative tools to support (a) ontology-based integration and sharing of data and biomedical information and (b) advanced data mining and biomedical knowledge extraction.
- ⇨ Sharing of biomedical information and data upon common standards and utilisation of and in a manner that protects data privacy and security.
- ⇨ Fostering common usage of vocabularies, common data elements and the formation of a unifying architecture for the support of the advanced clinico-genomics clinical trials of the future.

Integration targets all levels – from molecular to the human and the population. GRID-enabled mediation functionality (realised by respective software components, tools and services) compose the mean toward a knowledge-enriched, effective and reliable integration.

Current relation to the state of the art

The following is an extract from the paper “Morris A. Swertz and Ritsert C. Jansen. Beyond standardization: dynamic software infrastructures for systems biology”, published in Nature Reviews, Vol. 8, March 2007, pp. 235-243.

“…Systems biology can (and should) move from slow and expensive, almost one-at-a-time, practice to a much more cost efficient many-of-a-kind practice in which biologists can quickly obtain customized software infrastructures that meet their specific needs. What must be done to make the most of it?

A repository to share DSL models, or modules thereof, will help to keep different research groups on the same track, because they can oversee the few changes in a single DSL file much better than they can oversee many related changes that are spread throughout software code. The Online Showcase (BOX 2) demonstrates how that could work: everyone involved can find, learn, reuse and customize infrastructure variants for sequences,

microarrays and systems genetics using just one simple DSL. An accompanying repository of code generators and reusable assets helps to share and evolve resources at the software level. These efforts could result in an infrastructure platform for systems biology, analogous to the R-project.

Variants from separate software families need to be 'pluggable' to allow comprehensive infrastructures that, for example, integrate data management and analysis. …….This also requires some common software standards, such as web services. The other families must bridge their incompatible reusable assets in a similar way, which could result in a 'software population'68 for systems biology in which software infrastructures from all families can work seamlessly together."

It proves, we believe, the fact that the ACGT project is focused in delivering a much-needed infrastructure. If successful, the implications of the project will be significant.

We also believe that the project is providing state-of-the-art solutions in its main sub-domains of activity. The project has evaluated the results of many relevant projects and initiatives, has selected appropriate results for adoption, whilst it proceeds with the design and development of new tools and technologies that are required and specifically tailored for the domain of post-genomic clinical trials.

Recommendations from the last review

The recommendations from the last Annual project review (May 2008) were:

- Consider a project diary, to capture the project narrative and encourage wide involvement of project participants in describing and explaining the project to wider audiences.
- Establish reference group. Members in this group should be: ACGT members, clinicians within the cancer field, Bio-medical researchers.
- Reinforce efforts to establish planned advisory/governance structures.
- Prepare an end-to-end demonstrator for the next review, with as much real clinical trials and genomic data as possible in evidence.
- Maintain focus on Obtima as means to drive standardisation of clinical trials data capture.
- Put more resources into ObTiMA.
- Maintain fuller formative documentation and evaluation of the evolving MO and its roles, relationships and performance with respect to Obtima functionalities, the interface with domain ontologies such as GO and FMA, and with metadata used in querying finally assembled ACGT data repositories.
- Critically review the planned evaluation methodology of the onco-simulator; is it to be focused principally on demonstrating clinical utility or on the validity of its physiological modelling? Both are worthwhile goals, but they are not the same.
- Critically review how research metadata services and the master ontology will interact in delivering end-to-end functionalities of the platform and their evolution through new versions, over time, as the genomic science and clinical trials requirements change.
- Consider future external usability analysis in evaluation of the platform.
- Consider future external risk analysis and testing of security framework.
- Continue to present the project at different scientific meetings within the cancer field.

The project's management board believes that these recommendations are correct, and indeed correspond to issues that the project needs to successfully address.

In addition the main recommendation from the December 2008 Review of the project was:

- The project should focus on testing and evaluation with real clinical data.

Obviously some of these recommendations are more difficult or complex to respond to, but in all cases specific measures have been taken in our attempt to respond. These are reported at various sections of this document and will also be synthetically addressed at the forthcoming annual project review.

Summary of objectives for the reporting period, work performed, contractors involved and the main achievements in the period

The main objective for the reporting period had been to validate the relevance and adequacy of the initial ACGT architecture through the implementation of a range of demonstrators. For this reason we initially worked hard for setting up an end-to-end demonstration scenario with various scenes. Our main objective was integration. Having gone through the experiences of setting up and developing such "integrated demonstartors" several other issues became important, such as usability, ease of use, scalability, robustness, etc.

We have collectively identified the main issues to be addressed, prioritized them and focused our implementation activities around a limited set of such issues at a time. This becomes obvioys by reading the description of work done by eaavh workpackage.

During the third implementation period all partners have been very actively engaged in the various activities, relevant to them. The collaborative activities of contractors and their interaction has been regular, and of high quality. The technical work performed has been of a high level, and it was produced with the active involvement of all contractors.

One very significant achievement of the project during this implementation period has been its success in getting closer to its target end-users. Our decision to replace our initial plan of organizing a project conference with a series of scientific events in places where our future users will naturally be (i.e. their own scientific conferences) has so far paid dividends. This is, in our view, expressed by the decision of EORTC to link and get involved closely in the project, but also by the fact that the Brest International Group (BIG) has lloked at ACGT for long term solutions to their data integration challenges in the context of their neoBIG studies.

Most important problems during the period including corrective actions undertaken

The main problem we had to address during the reporting period related to the fact that a limited set of planned activities and few Deliverables proved that they were not really mature for implementation and production. We specifically refer to:

- D14.3 - Demonstration and Report of training modules, due on month 21. Most of the activities of WP14 during the period were related to collaborating with the various other technical workpackages for delivering the end user interfaces at the portal level. In parallel most tools and technologies have been evolving, with newer version and functionalities implemented. Producing training material for "evolving tools" proved to be a problem. We have produced a "reference implementation of such a traingin module (the ontology viewer) for gathering experience. We propose to move this Deliverable forward into the 4th Implementation Period (i.e. month 48) – in view of the fact that the project has extended its implementation period by 6 months.

- Workshop Training for end-users on ACGT Technologies & Methodologies. We have organised 2 such training/evaluation workshops with end-users. Yet, it is not what we have really planned for. The reason for this has, again, been the evolution in functionality and technologies and the lack of a really stable version of the platform – upon which we train and evaluate. These activities will accelerate in the last 18 months of the project.
- For the same reason as above (volatility of technologies, evolution, etc) we have not been in a position to produce the following Deliverables: a) D3.2 The ACGT technical Architecture – Final Specifications, and b) D11.5 Finalized ACGT security Architecture. We plan to complete these activities and Deliverables by month 42 (i.e. six months delay).

Workpackage progress of the period

All project WPs were active during the reporting period. An overview of the activities carried out by each WP is given in the subsequent sections.

WP 1 – Project Management

Partner Responsible: ERCIM and FORTH

Contributing partner(s): FORTH, Philips, UPM, FHG, PSNC.

Reporting Period: 01/02/2008 – 31/01/2009

Workpackage objectives and starting point of work at beginning of reporting period

The objective of this Workpackage is to ensure a strong and coherent administrative and financial management of the project. This activity can be subdivided in two main parts:

1) Administrative and Financial Coordination;
2) Scientific Coordination.

This activity is lead by ERCIM, represented by Remi Ronchaud, with the support of the ERCIM Office team.

The administrative coordination was concerned first and foremost with efficiency and sustainability of the project's management architecture, including decision-making processes, and the maintenance of the efficient communication mechanisms for knowledge and information exchange. The co-ordination of the large number of activities composing the ACGT project and the validation of the quality of the produced results required a strong managerial effort.

In particular, from the scientific point of view the project activities were monitored and coordinated through several exchanges with the partners both by participating in official meetings of the project's governing boards (i.e., Management Board, Steering Committees) and by a large number of personal phone and e-mail exchanges. Much effort has also been dedicated to guaranteeing that all of the activities are performed in the scheduled time and to manage unplanned situations, such as the need for more extensive experimentation.

The Management Board is composed of one representative from each work package. The objective of this committee, created to favour and speed-up the test-bed development, is to discuss technological choices and agree on solutions that affect the design of multiple services. This committee is headed by Manolis Tsinakis, FORTH, and benefits from the commitment of the Quality Manager, Norbert Graf, UoS.

Emphasis was placed on the establishment of certain cornerstones of proper project management: quality assurance and risk management being the leading priorities. First, quality control procedures have been discussed at length to ensure that deliverables and reports achieve the standards of quality expected by the project's governing boards and to monitor the image ACGT exposes to the external environment via dissemination activities.

During this third year of activity, the administrative coordination was concerned also with the timely delivery of all deliverables and with the efficient preparation of the Official European Commission project review. In Particular, focus was on the preparation of an integratred demonstration of the ACGT system. WP1 has also maintained the project's management architecture, including decision-making processes, and the establishment of efficient communication mechanisms for knowledge and information exchange (e.g., BSCW shared workspace, mailing lists, on-line reporting tools).

During this third year of activity, the main activities and achievements of the Managements have been focusing on:

- Maintenance of the project's general organization and sustainability of the management architecture.
- Coordination of all periodic management and scientific ACGT meetings.
- Monitoring of WP activity, with a particular focus on the timely production of deliverables.
- Coordination of the periodic reporting for the entire project. Preparation of the Six monthly activity Report. Regular efforts were devoted to the collection of every partner's contribution to the periodic report (work description and effort figures in person-months).
- Reminder of procedures and guidelines across all partners' institutions (reimbursement, costs claims, votes and communication protocol).
- Preparation and Validation of partners' Periodic Management Reports
- Reception and transfer to all partners of the third advance payment.
- Permanent assistance and support to Scientific Management.
- Organisation of periodic meetings and audio-conferences to ensure a coherent information flow within ACGT. Supervision of the information flow within the project and support of collaborative tool (BSCW).
- Review and analysis of effort consumption across all ACGT Partners. Definition of a minimal budget redistribution plan to optimise resources allocation across institutions and Workpackages.
- Validation and monitoring of partners efforts and contributions to the project.
- Cooperation with University of Hokkaido (UoH) to enhance national Japanese funding opportunities to support UoH activities within ACGT.
- Preparation of periodic project reviews and of corresponding demonstrators.
- Preparation of the Final Detailed Implementation Plan for months 37 to 54.
- Contribution to the dissemination strategy and to the production of promotional material: ACGT poster, leaflets, Newsletter and give away material.
- Preparation for the production of a promotional video (budget planning and definition of target audience and key messages)
- Interaction with related initiatives to lay the ground for cooperation
- Preparation for participation to European international cooperation events (EU-Japan).
- Integration of EORTC as subcontractors to Jules Bordet
- Interaction with Breast Cancer International group (under non-disclosure agreement)

The Management has also been preparing and organising the plenary project meetings during the reporting period. Additional Management board and technical meetings have also been organised to support the scientific coordination effort across disseminated teams and Workpackages.

- ACGT consortium Meeting, Italy (Milano), February 5th – 7th
- WP8 Meeting, Italy (Milano), February 8th
- ACGT technical meetingj Germany (Berlin), 14th April
- Technical Pre-Review Meetingj Eindhoven, 08.05.-09.05.2008
- ACGT integration meeting, Holland (Eindhoven), 8-9th May
- ACGT Reviewj Eindhoven, May 26th – 28th
- ACGT Consortium Meetingj September 22nd – 24th 2008, , Heraklion, Crete, Greece
- ACGT Review, December 8th -11th 2008, Brussels, Belgium
- ACGT Consortium Meeting, January 27th -30th 2009, Vienna, Austria

The complete list of technical meetings (including presentations and minutes) is available on the BSVCW server at: https://bscw.ercim.org/bscw/bscw.cgi/98381

WP2 - User Needs Analysis and Specifications

Partner Responsible: USAAR

Contributing partner(s): Forth, UvA, Philips, IJB, SIB, LundU, UMA, UPM,, FHG, Biovista, UOC, PSNC, Custodix, ICCS, USAAR, SIVECO, UOXF.BP, UHoK, IEO

Reporting Period: 01/02/2008 – 31/01/2009

Workpackage objectives and starting point of work at beginning of reporting period

The Workpackage has the following major objectives:

This WP will continue to elaborate on the various requirements from a clinical point of view that are necessary for the proposed ACGT platform.

- To update guidelines for clinical trials (e.g. ICH and GCP), tools and software for the management of clinical studies and needs for clinico-genomic integration (including technological, legal issues, ethics, security, quality control, etc.).
- To refine requirements and assessment of the relevance (from the point of view of the clinical research) of the architectures and applications that are developed.
- To ensure the feasibility of implementing and to increase the number of clinical studies for cancer into ACGT based on specific clinicogenomic scenarios
- To define and implement usability criteria as part of the quality process for the evaluation of developed tools and software driven by clinicians and other endusers.
- To define criteria for a submission system for tools, software and data from an enduser perspective
- To define criteria for the selection of tools, software and data from a clinical perspective.
- To elaborate maintenance criteria for ACGT (together with WP16)

Objectives during reporting period

The main focus was laid on clinical aspects of the project as done in the last periods. The search for new clinical trials that can run within ACGT was a major workload. In this respect the work was concentrated on the following major areas during the third period of ACGT:

1. Continuation of work regarding user requirements and functionality of the Ontology based clinical data management system (ObTiMA)
   a) User needs for clinicians and basic researchers for ObTiMA including the user friendly integration of the Master Ontology
   b) Clinico-genomic integration, including technological, legal and ethical issues, security and quality control within ObTiMA
2. Those specific clinico-genomic scenarios that were implemented in the clinical studies as defined in WP12 are further developed and discussed how to integrate them into the trial builder

3. New clinical trials and scenarios were defined to use the ACGT platform. They are listed and described in D2.4
4. Two deliverables were finished during this period:
   a) D2.3: User requirements for the evaluation of developed software and tools regarding usability criteria
   b) D2.4: Report on additional user-driven scenarios in post-genomic clinical trials on Cancer

- **Progress towards objectives**

Further progress was done in developing requirements and functionality of ObTiMA to get a tool for clinicians that will help to increase the number of clinical trials in ACGT.

Tasks worked on and achievement made with reference to planned objectives, identify contractors involved.

The main tasks carried out by USAAR can be summarized in:

The main focus was laid on the user requirements and the functionality of ObTiMA and the search for new trials and scenarios for ACGT. This task is leaded by USAAR (Norbert Graf). Deliverables D2.3 and D2.4 were finished and submitted. Both are available at the BSCW Server. Input for these deliverables was given by all participants of WP2. Over the entire period IFOMIS stayed in contact with Saarland University Hospital and FHG [IMBT] in order to discuss ontology related questions regarding the development of the Trial Builder. Major progress is done regarding the Clinical view and the maintenance of the Master Ontology. Multiple meetings and discussions about technical issues with project partners (FHG [IBMT], Hokkaido University, Custodix, IFOMIS, FORTH) took place to enhance feedback between developers of ObTiMA and the users. Since February 2008 one person (Jochen Boehm) is only dealing with optimizing the usability of ObTiMA keeping a close contact with the developers of the software and the endusers.

This WP continued to elaborate on the various requirements from a clinical point of view that are necessary for the proposed ACGT platform. The main points of investigation as defined in the first two years were supplemented by defining criteria for the evaluation of developed software and tools. The corresponding deliverable 2.3 (User requirements for the evaluation of developed software and tools regarding usability criteria) was finished and submitted on the 15th of March 2008.

A main focus was laid on answering the question, what are the requirements and needs for clinicians to use ObTiMA as a clinical data management system. The issue of maintaining ACGT and ObTiMA was founded to be the most crucial point, before clinicians will use ObTiMA for their clinical trials. The integration of ObTiMA in the ACGT Portal, the ACGT roles and rights management and the Custodix anonymisation tool (CAT) for the use with ObTiMA was decided and will be evaluated by end-users.

As can be seen in the list of meetings and dissemination activities, ACGT and ObTiMA was presented to different clinical groups in different workshops and meetings to increase the number of clinical trials for cancer. Special focus was given to EORTC, SIOP and GPOH. These groups all are interested and are willing to use the ACGT infrastructure, if a guarantee is given that ACGT and ObTiMA will be maintained.

To increase the number of clinical trials for cancer into ACGT a lot of effort was done in organizing local meetings and attending other meetings. Deliverable 2.4 was submitted

in time regarding this topic. The Rhabdoidtumour Registry will use the TrialBuilder as soon as there is a functioning prototype. The same will be done with the next SIOP nephroblastoma trial. The clinical partners of the University of Oxford and the Instituto Europeo di Oncologia in Milano are on board increasing the number of clinicogenomic scenarios. At different meetings active participation of the WP2 leader (Norbert Graf) promoted ACGT to a greater and especially clinical auditorium. Regarding the InSilico Oncology further progress is done regarding the workout of the scenarios and the need for clinical validation of the InSilico experiments. More anonymised DICOM data together with clinical data are available at ICCS for use in the simulator.

Together with WP16 the elaboration of criteria for maintenance of ACGT has been started.

During this period the state of the art review was updated on a regular basis, regarding current guidelines for clinical trials, the assessment of tools and software for the management of clinico-genomic studies and trials. The user needs for clinico-genomic integration (including technological, legal issues, ethics, security, quality control, etc.) was consolidated within the corresponding WPs.

Regarding the InSilico Oncology further progress is done regarding the workout of the scenarios and the need for clinical validation of the InSilico experiments. Anonymised DICOM data are now available at ICCS for use in the simulator. A tool for the segmentation of tumour in DICOM files is developed by Fraunhofer and used by clinical partners for submission to the InSilico scenario.

The main tasks carried out by IFOMIS can be summarized in:

Review/Extension of ACGT MO

The ACGT Master Ontology is constantly reviewed with respect to usability (by the ACGT services, namely the mediator and ObTiMA) and completeness. The clinical partners were constantly asked to hand in reviews on the coherence and correctness of the representation of clinical reality. However, we experienced that these activities led to only minor adjustments over the last months. By using the MO in ObTiMA we needed to extend the ontology considerably with respect to constraints and axioms. We have done so and reported ongoing work (**Documentation on Ontology Development February to July 2008)** and will provide another document in March. The results of this process are evaluated in the **Ontology focussed validation of CRF creation** (s.b.) until end of February 2009. The consistency of the MO is constantly checked while working with the owl-file, using the Pellet Reasoner (Pellet 1.5 until Dec 2008; Pellet 2.0 from Jan 2009).

Addition of anatomical classes

An unforeseen problem did arise quite before the reporting period: With respect to anatomy we were always very confident that we will be able to re-use the Foundational Model of Anatomy (FMA) one way or the other. Basically, we hoped for a re-usable, open source owl-implementation. Even though two such implementations exist, they confronted us with a severe problem. Copying an owl-Implementation of the FMA in its entirety would probably result in an ontology to large to check with a reasoner and rather slow in use for both ObTiMA and the mediator. Realizing this problem we decided to look around for alternatives. Alan Rector proposed to talk to Jay Kola who developed an anatomy ontology which is not part of the OBO Foundry and is based on ontology terms from the NCI Thesaurus (s.b.). After reviewing this ontology, which was rather small, but not build to the quality criteria formulated for ACGT we had to find an alternative. We decided to create the anatomical classes as needed in the domain (used in the CRFs) in accordance with the FMA. This means that we added most parts of the middle layer of the FMA ontology, but restricted the leaf nodes to those needed in ObTiMA at the moment. Adding new classes will, however, be not problematic since

all that the curators need to do is search the FMA and add the content. This method provides the best solution for the problem at hand. The conceptual modelling we make use of is the best available representation of anatomy that is on the market. Furthermore, the FMA is open source and there are no restrictions for re-use.

Provided mappings for the SPARQL query

In order to support the query tools IFOMIS provided mappings for the SPARQL queries. This task was done in close collaboration with UPM and Philips.

Re-evaluation of NCI Thesaurus (caBIG, caCORE)

Since the start of ACGT the project, and especially WP7 is confronted with questions whether the NCI Thesaurus would not be a better terminology resource than the newly developed ACGT MO. This situation became urgent again by the fact that the NCIT is distributed and advertised under a number of new names, respectively in a number of different systems, for instance caCore. Given requests of colleagues we understood that it is our responsibility to re-evaluate the NCIT. Doing so we, sadly, came to the result that the grave problems already described in Deliverable 7.1 have not been corrected and thus, the assessment of the NCIT reaches the same result as before.

Providing D7.7

The review in May 2008 showed a still existing lack of clarity with respect to the design principles and the design decision behind the ACGT MO. Therefore, IFOMIS volunteered to provide another deliverable addressing these issues. The deliverable was written in autumn 2008 to be presented in the December review. It was uploaded on the BSCW server November 23. D7.7 does not only provide descriptions of basic principles of the MO development, but also documents design decisions to facilitate cooperation in further developments of the MO. The deliverable does not only consist of text, but also provides a multitude of instructive examples from the MO and illustrations.

Furthermore, IFOMIS intensified the documentation effort in every respect and provided further documents to demonstrate the work on the ACGT MO.

Ontology-focussed validation of CRF creation

Since December 2008 IFOMIS is active in the evaluation of the CRF creation process in ObTiMA. IFOMIS' task here is to check and prove the possibility to create all items on the CRF utilizing the ontology. This process is a major evaluation effort with respect to the ontology since missing or wrong restrictions can be spotted. The deadline expected for the evaluation of the SIOP CRFs is February 28.

Efforts towards validation of conceptual design by means of automated term extraction

A critical aspect for the success of the ACGT MO is whether we manage to provide a correct and complete representation of the given domain. In order to validate our conceptual design we decided to collaborate with terminology experts outside ACGT to get an impression on the completeness of our representation.In this task we co-operated with the Institut für Angewandte Informationsforschung (IAI, Institute for Applied Information Science) located at Saarland University. We were in contact with the director of the institute, Prof. J. Haller, and a PhD student (G. Grigonyte). The AIA offered to extract a terminology from domain specific abstracts. We decided to use 200 abstracts on clinical trials, mostly in nephroblastoma and breast cancer. The abstracts where provided by our clinical partner in Homburg, namely Alexander Hoppe and Norbert Graf. The IAI provided us with a 19-page list of terms extracted automatically from the abstracts early in July. The final analysis of the ACGT MO and its accordance to the extracted terminology had to be postponed until middle of August due to our efforts in adding the anatomy branch to the ontology. However, our first survey of the

terminology led to the result that more abstracts are needed to gain more statistical opportunities for term extraction.

Intra-project communication on ontology development

It was decided that the submission tool for the ontology which will play a major role in maintenance will be developed by FORTH. IFOMIS is actively reviewing and commenting the process of developing the submission system. Deliverable D2.5 will address this issue.

Networking with the OBO Foundry/NCBO BioPortal

IFOMIS is keeping contact with the OBO Foundry to make the ACGT MO part of the Foundry. We planned the submission for February 2008, but due to the project critical efforts on CRF creation in ObTiMA this is postponed to the second half of 2009. Nevertheless, since November 2008 the ACGT MO can be explored using the NCBO BioPortal (http://bioportal.bioontology.org).

New collaborations/New users of the ACGT MO

In November 2008 both curators of the MO visited the FOIS (Formal Ontology in Information Systems) 2008 conference. Even though no paper was presented the goal was to find possible new users for the ACGT MO. This turned out to be a successful enterprise. In December 2008 Siemens informed us that they and the German Research Center for Artificial Intelligence (DFKI) will use the ACGT MO in a German project called “Theseus” funded by the German Federal Ministry of Economics and technology (http://theseus-programm.de). The ACGT MO will be used in the Theseus medico branch. It replaces the NCI Thesaurus which did not provide the information relevant to the task carried out by Siemens and DFKI. Furthermore, a German representative of the IHE (Integrating the Healthcare Enterprise) got in touch with IFOMIS asking for possibilities to use the ACGT MO to bridge HL7 Version 2 and HL7 Version 3. This just occurred in December and no further consultations took place until now, but IFOMIS agreed to support the effort.

The main tasks carried out by Philips can be summarized in:

Philips continued to collect requirements for an ACGT-specific clinico-genomic electronic health record (EHR).

The main tasks carried out by UPM can be summarized in:

UPM continued to gather and interpret user requirements for querying clinical databases (SIOP and TOP) using SQL predefined queries. Natural language is used for the interpretation of concepts contained in the SIOP and TOP databases

The main tasks carried out by UMA can be summarized in:

UPM group has developed a requirement gathering process involving the mapping tool and query tool user interfaces. It has been a main goal to make these interfaces user-friendly. The requirements were gathered from different points of view, with the aim of generating personalized interface for different profiles. UPM has worked closely with end-users as well in defining use-case scenarios for demonstration purposes

The main tasks carried out by UvA can be summarized in:

- Data exchange (DICOM) from USAAR to UvA for provisioning the OncoSimulator visualization
- Design discussions concerning OncoSimulator experiments

The main tasks carried out by IEO can be summarized in:

In the framework of WP2, they mainly developed theoretical research activities, by continuing focusing on antiangiogenic therapy.

To support the biological inferences of the ACGT clinico-genomic study "Trenett", IEO deployed a series of theoretical studies focused on biophysics of anti-angiogenesis therapies in combination with chemtotherapies. In particular, they focused on:

I) elaborating a mathematical model of an optimal combined therapy in absence of effects of normalization of tumour blood vessels ("the pruning effect"), in collaboration with U. Ledzewicz ,Southern Illinois University USA, and H. Schaettler, G. Washington University, USA [1];

II) Definition, analysis, simulation and inferences of the efficacy of combine therapies in presence of pruning effect [2].

Finally, extensive work has been done for the final revision of the works [3] and, mainly, [4] and [5], described in previous report.

[1] Alberto d'Onofrio, Urszula Ledzewicz, Helmut Maurer and Heinz Schaettler, Optimal Control of chemotherapic drugs also having antioangiogenic effects, Submitted to Mathematical Biosciences

[2] A. d'Onofrio (c.a.) and A. Gandolfi. "Modelling the pruning effect in the chemotherapy in conjunctio to antiangiogenesis anticancer therapy".mansucriopt in preparation

[3] A. d'Onofrio (c.a.) and P. Cerrai A bi-parametric phenomenologic model for the tumor angiogenesis and anti-angiogenesis therapy. In press on Mathematical and Computer Modelling 49 1156-1163 (2009)

[4] A. d'Onofrio (c.a.) and A. Gandolfi "A family of models of angiogenesis and anti angiogenesis therapy". In press on Mathematical Medicine and Biology

[5] "The cooperative and nonlinear dynamics of tumor-vasculature interaction suggests low-dose, time-dense antiangiogenic schedulings". In press on Cell Proliferation

The main tasks carried out by ICCS can be summarized in:

ICCS contributed to the definition of the Oncosimulator particular module specifications and their interdependencies from both the end user (clinician, basic researcher, general public) point of view - in tight collaboration with the clinical partners (USAAR, IJB) - and from the technical point of view in tight collaboration with the technical partners (UvA, INRIA, FORTH, FHG, PSNC, UHok et al.)

The main tasks carried out by UoC can be summarized in:

UoC, in close collaboration with FORTH, has participated into the formation of a scenario that is based on the Prognochip clinico-genomic study and aiming at extending pathological characterization of samples, completing clinical information about the patients and capturing the requirements for deployment of the ACGT infrastructure.

The main tasks carried out by Biovista can be summarized in:

Experiments performed with Biovista lit mining tools in collaboration with University of Oxford to determine utility in their workflow. This is an ongoing effort. The question of how to maintain ObTiMA is part of the dissemination task.

The main tasks carried out by SIB can be summarized in:

SIB conducted an analysis of bioinformaticians/data miners' requirements in the context of the scenarios adopted for demonstration and testing:

- TOP/PseudoTOP: Data mining on breast cancer data (in-depth analysis of data

collected at a single site)
- MCMP multi-centric multi-platform scenario (integration of datasets collected at two different sites and using different microarray platforms in clinical research)
- SIOP (integration of ObTiMA with the ACGT data mining environment)

The user requirements for the TOP/PseudoTOP and MCMP have lead to scenarios that have been shows in the reviews that took place during the reporting period.

The user requirements for the SIOP clinical trial (Wilms tumor) have started to be analyzed at the very end of the period. This process is currently ongoing.

SIB organized a workshop between CHUV (University Hospital in Lausanne, CH) and ACGT. The workshop allowed physicians, researchers and medical IT representatives of the hospital to understand the goals of the ACGT environment and to express their needs for such an infrastructure in a daily practice environment. The main conclusion of this meeting was a confirmation that the broad lines of the project were in-line with the needs of researchers in clinical environment.

The main tasks carried out by Custodix can be summarized in:

A short review of user requirements regarding VO and resource management was performed. The different use case scenarios were evaluated and possible needs were discussed with end-users.

Custodix also participated in the workshop organised by SIB between CHUV (University Hospital in Lausanne, CH) and ACGT to determine the specific security needs for a hospital before it can use the ACGT infrastructure.

The main tasks carried out by UOXF can be summarized in:

In the framework of WP2, they continued to develop research activities in the context of the MCMP scenario described in WP12 and more generally methods for the development and validation of prognostic/predictive signatures, and meta-analysis of publicly available datasets. Furthermore, they have been assessing feasibility and usability of the ACGT platform in the context of genomic clinical studies and trials carried out at OXF.

- **Deviations from the project work programme, and corrective actions taken/suggested**

.

Identify the nature and the reason for the problem, identify contractors involved

Deviation according to the plan is in WP 5, WP 7 and WP 14. In WP 5 and WP 7 more PM were necessary. In WP 14 less PM is spend. In all other WPs the spent PMs is as proposed.

WP5: Because ObTiMA is a central tool, it was necessary to spend more PM in this WP. There was the need for an intensive feedback with the IT People to optimize ObTiMA. The design and GUI of ObTiMA was to be done user friendly, CRFs and Trial outline was to be evaluated and validated in cooperation with IT people and with WP 13.

WP7: The Master Ontology is of central importance. More PM was needed to use it in ObTiMA and other tools. There was a lack of PM in the year before. Therefore mor PM were available during this period.

WP14: There was not much training possible, due to the lack of further PM.

This deviation was without influence an the Implementation plan, because more work was done as forseen.

- **List of deliverables, including due date and actual/foreseen submission date**

  D2.3: User requirements for the evaluation of developed software and tools regarding usability criteria. Submitted 15th March 2008

  D2.4: Report on additional user-driven scenarios in post-genomic clinical trials on Cancer. Submitted 27th November 2008

  D2.5: Report on requirements for an ontology submission system and for the selection of tools, software and data within ACGT. Due to T0+36. This deliverable will be postponed due to ongoing work.

- **List of milestones, including due date and actual/foreseen achievement date**

  Milestone 2.1 was achieved at month 6. No further milestones

WP3 – Architecture and Standards

Partner Responsible : PSNC

Contributing partner(s): FORTH, UvA, Philips, LundU, UMA, UPM, FhG, BIOVISTA, Custodix, ICCS, USAAR, FUNDP, UH, UHok

Reporting Period: 01/02/2008 – 31/01/2009

Workpackage objectives and starting point of work at beginning of reporting period

This WP will design the architecture of the ACGT environment with special emphasis on the design of the distributed data access, ontology mediation services and 'secure' grid technology. The development of an appropriate architecture will provide the guidelines for integrating the technological components of ACGT into a powerful environment for cancer trials.

The WP will consider the existing grid architectures and toolkits, such as UNICORE and Globus. Gaps in these architectures that do not allow for the support of topic ontologies to be treated in a uniform way inside the grid will be identified. For example, it would seem appropriate to add some semantic data services next to the basic grid functions, such as GRAM, GridFTP and MDS, as well as a plug in for an arbitrary ontology to complement with the generic grid services layer.

This WP will take into account and will strongly collaborate with WP2 aiming to use grids to solve interoperability problems, which is a new idea. The ACGT project will work with respect to this goal within the GIN initiative. Current state of the art in interoperability, in general, and in the biomedical sector, in particular, will be studied. This will be based, in part, on work done in some of the FP5 projects, such as ROADCON, ICCI, caBIG, and others. State of the art in grids in other domains will also be continuously reviewed.

This WP also aims to include methodological state of the art, such as a study of the design methodologies for web-services and grids.

The objectives of this WP are therefore:

- to invent and define the reference grid architecture to support complex project collaboration and to provide a blueprint for grid implementations in this project and beyond.
- to design the overall architecture of a grid based interoperability system for the biomedical sector and make a substantial contribution to standards.

Progress towards objectives

Having defined the initial layered, ontology driven and grid enabled service architecture during the previous period, the activities performed in this Workpackage during this reporting period include:

- Focus on verification of the architecture. Towards this objective we monitor very carefully all technical decisions taken regarding the implementation of the services at the various layers of the architecture.
- Continue defining use cases: based on the requirements, but also on the project

scope, while talking to users, we proceeded to define indicative usecases.
- Continue working on scenarios: We focused on the developed scenarios for all user/actors groups, usually involving more than one actor. We investigated the various scenarios and explored their implications for the architectural decisions already taken.
- Taking into consideration the initial implementation experiences as well as new requirements coming out from the newest scenarios to be supported as well as the final legal and security requirements, as defined in WP10, we have extended and modified the original architecture.
- PSNC is also getting involved within the GIN initiative (Grid Interoperability Now), an activity held in the framework of the OGF work, under the umbrella of the GIN working group.
- Since we foresee that the final architecture of the ACGT system will not change dramatically from the current version of the architecture, we decided not to spend much effort on this part of the WP, but to devote additional efforts in following the Grid standardization efforts, but also on the biomedical standards works.

Deviations from the project work programme, and corrective actions taken/suggested

.

There were no deviations from the workplan.

List of deliverables, including due date and actual/foreseen submission date

In the reporting period the most of work on final architecture specification deliverable was done. The deliverable will be submitted at the beginning of the next reporting period.

List of milestones, including due date and actual/foreseen achievement date

Milestone MWP3.2 - The ACGT updated architecture (month 28) was accomplished

WP4 – Biomedical Grid Technology Layer

Partner Responsible: PSNC

Contributing partner(s): FORTH, UMA,FhG, Custodix, Siveco, UHok

Reporting Period: 01/02/2008 – 31/01/2009

Workpackage objectives and starting point of work at beginning of reporting period

The objectives of this WP are:

- to provide grid services that take advantage of the grid functionality, such as security, resource management, data management
- to provide interfaces to state-of-the art grid databases
- to define and provide the information grid that is capable of secure, safe, semantically rich, and ontology committed information
- to enable an ontology aware biomedical grid infrastructure into which all biomedical information, handled by sector applications is stored
- to provide access capability to distributed computational resources, mainly relying on existing functionality of the grid toolkits, but taking into account the possible exploitation of the higher level semantics that will be built into the grid in WP7
- to extend existing toolkits with decentralised VO management tools and workflow systems based on widely adopted standards, such as BPEL.

The infrastructure will mostly be based on the PSNC's Gridge bag of grid services, enriched with some other selected tools and features, such as workflows, VO management tools, services coordination tools.

Progress towards objectives

The objectives planned for the reporting period were achieved.

- grid testbed were maintained and extended with new resources to provide more computational power and storage space for the project
- the framework for monitoring grid resources and services was introduced
- implementation of automatic testing procedures with a portlet for presentation the results
- all ACGT service developers were supported in implementation of ACGT compliant services with regard to web services technology and security mechanisms
- support in implementation of clients for the grid services
- continuous work on the improvement of the grid services responsible for resource management, data management and authorization decisions.
    1. ongoing work on integration of DMS service with global authorization framework and VO management,
    2. implementation of the parametric job support in resource management system in the grid,
- design and implementation of new security policies in the context of Virtual Organization management,

- design and implementation of the new scenarios for the Oncosimulator application submission in the grid environment including integration with visualization environment and results presentation layer

Deviations from the project work programme, and corrective actions taken/suggested

.

There were no deviations from the workplan.

List of deliverables, including due date and actual/foreseen submission date

Required deliverables were submitted in time

List of milestones, including due date and actual/foreseen achievement date

All planned milestones were achieved in time.

WP5 - WP Distributed Data Access and Applications

Partner Responsible: Philips

Contributing partner(s): FORTH, IJB, LUNDU, UMA, UPM, FhG, BIOVISTA, UOC, ICCS, UdS, UOXF.BP, UHOK

Reporting Period: 01/02/2008 – 31/01/2009

Workpackage objectives and starting point of work at beginning of reporting period

The Workpackage has the following major objectives:

1. To provide seamless and interoperable data access services to heterogeneous distributed data sources by developing a set of compatible software key modules / services based on Web Services.

2. To provide services for ontology-based ubiquitous interoperability within the integrated ACGT environment.

3. To define a generic architecture that enables distributed access to all relevant patient data (clinical, imaging, genomic/proteomic, etc.) available across the clinical trial sites.

Progress towards objectives

The main activities corresponding to the reported period were:

1. **Data Access Services:**
- Developed data access service for retrieving microarray data. Cooperated with Lund to implement and test interface with BASE database. (Philips, LundU)
- Extended data access services to meet requirements of pseudoTOP, MCMP, and SIOP data analysis scenarios. Added functionality to deliver files to DMS, after optional compression into zip archive, including support for asynchronous retrieval (of large data sets). Increased query functionality by supporting custom SPARQL functions. (Philips, UPM)
- Integrated data access services into the ACGT security infrastructure. While waiting for completion of the required OGSA-DAI GAS-plugin, developed Axis2-based version of the relational data access services, to progress integration. Cooperated with PSNC to accomplish development of required GAS authorization module. Subsequently installed and configured module for handling access to data resources. Close cooperation with Custodix to configure access to over a dozen data resources. Extended data access service file transfer functionality to use delegated user credentials for authentication. Cooperated with Lund to secure web-service log-in to BASE server, and to secure microarray data transfer from BASE server to data access services. Extended OGSA-DAI data access client to support invocation of secure services using credentials manged by myProxy service. (Philips)
- Provided guidance to Fraunhofer (IBMT) to add ACGT data access interface to Obtima database, using OGSA-DAI and service implementation developed by Philips.
- Improved deployment set-up of static data resources to reduce time needed to deploy new data sources, and to increase overall robustness of ACGT platform. Data resources are now deployed using data source type specific template configuration files. Set-up four web service containers for hosting data access services: unsecure development, secure development, unsecure stable and secure stable.
- Extended documentation of data access services. Added documentation on project wiki describing installation and usage of secure data access services. Also added description and usage examples for all new deployed data resources.

- Cooperated with PSNC to achieve automatic monitoring of data access services with status reports accessible from the web. Extended data access services to support efficient testing of query functionality and data transfer functionality.
- Developed functionality to support dynamic deployment and subsequent un-deployment of data access services to speed up integration of new data sources into the ACGT platform. Cooperated with Siveco to make functionality available inside the ACGT portal by way of dedicated portlet. Cooperated with Custodix and PSNC to enable access to dynamically deployed secure data resources. (Philips)
- Contribution to the review scenarios and demonstrators (May and December 2008).

2. **Clinico-Genomic EHR**
- Based on interviews with end users we have extracted requirements for a future post-genomic EHR. We have used these requirements to build several scenarios supporting the need for preserving genomic data in a future clinico-genomic EHR. (Philips, FORTH)
- The HL7 Clinical Genomics special interest group is one of the few initiatives on the standardization of clinic-genomic information. The core model in this initiative is the Genetic Locus model. This model describes data related to a genetic locus, i.e., a fixed position on a chromosome such as the position of a biomarker that may be occupied by one or more genes. To get a better understanding of the Genetic Locus model, we have implemented it using the VAMPIRE framework. The main idea of this framework is to capture domain knowledge by means of models and to develop (parts of) applications by instantiating these models and generating the code, documentation, and other artefacts automatically. (Phlips)
- Based on the review of existing standards we proposed high-level a data model for incorporating microarray data into an EMR/EHR system and we have carried our a walkthrough the model for all the defined scenarios. (Philips)
- Wrote paper about ACGT data access services, and submitted it to BMIINT workshop. (Philips)
- Paper “The need for integration of genomic information in a future EHR: An ACGT case study” submitted and presented at IHIC2008 (Philips, FORTH, Biovista)
- ACGT report D5.5 “Initial high-level model definition of an ACGT-specific Clinico-Genomic EHR” (Philips)

3. **Further development of the ontology based Trial Management System** (ObTiMA):
- Advanced layout design (based on IceFaces implementation of JavaServerFaces web technology)
- Advanced CRF Creator and Ontology viewer
- Extension of the ObTiMA database for the Trial Outline Builder
- Further integration of ObTiMA with the ACGT Mediator
- Export clinical trials into CDISC ODM format
- Multi-language support during CRF creation
- Web Service for accessing the ObTiMA database from TOB

4. **Demonstration of ObTiMA**:
- February 5th – 7th 2008, ACGT Consortium Meeting, Milano, Italy,
- Mai 2008 - Review (Eindhoven,)
- July 20th – 22nd 2008, Demonstration of ObTiMA on the meeting in Lausanne regarding Clinical trials and data exchange between ACGT and Hospital Information Systems, Lausanne, Switzerland (participants, SIB, Custodix, USAAR, Oxford, members of the local hospital)
- September 22nd – 24th 2008, ACGT Consortium Meeting, Heraklion, Crete, Greece,
- December 9th -10th 2008, ACGT Review, Brussels, Belgium
- January 27th -30th 2009, ACGT Consortium Meeting, Vienna, Austria,

5. **Development of:**

- D5.4 “Conceptual specification and a first prototype for an ontology based Clinical Data Management System and for the Trial Builder”
- Specification for the role based secure access to ObTiMA and user roles and rights management (together with FORTH).
- Specification for the integration of Trial Outline Builder into ObTiMA
- Contribution to the specification of scenarios for the first integrated demonstrator of the ACGT platform

6. **Collaboration and demonstration of ObTiMA**:
- Jun 2008 – presentation of ObTiMA at TMF meeting (Berlin, Germany)
- August 18th 2008, Meeting (via Adobe Connect) regarding on the specification of the Trial Builder of ObTiMA. Participants: Prof. N. Graf, Jochen Boehm (USAAR) , Prof. Y. Tanaka, J. Fujima, A. Lunzer, M. Kuwahara (University of Hokkaido) and F. Schera (IBMT FHG)
- July 3rd 2008, local meeting to prepare demonstration of ObTiMA on the meeting in Lausanne regarding Clinical trials and data exchange between ACGT and Hospital Information Systems, on July 20th – 22nd 2008 in Lausanne, Switzerland. Place: Homburg, Germany. Participants: USAAR, IFOMIS, Fraunhofer IBMT
- participation in the Technical Parallel Session of the Consortium Meeting (Crete, November 2007)
- October 31st – November 5th 2008, ObTiMA Meeting regarding Trial Outline Builder, Ontology Viewer, Secure access and User Roles and Rights, St. Ingbert, Germany, (participants: USAAR, Fraunhofer IBMT, UHok, FORTH)
- 22.-24. November 2008 - presentation and demonstration of ObTiMA on MEDICA - 40th World forum for medicine (Duesseldorf, Germany)
- January 21st 2009, ObTiMA Meeting regarding the integration of ObTiMA with the ACGT Mediator, Homburg/St. Ingbert, Germany, (participants: USAAR, Fraunhofer IBMT, University of Madrid)

Deviations from the project work programme, and corrective actions taken/suggested

List of deliverables, including due date and actual/foreseen submission date
D5.4 “Conceptual specification and a first prototype for an ontology based Clinical Data Management System and for the Trial Builder” submitted
D5.5 “Initial high-level model definition of an ACGT-specific Clinico-Genomic EHR” submitted

List of milestones, including due date and actual/foreseen achievement date
No milestones due within this reporting period.

WP6 - Data Mining and Knowledge Discovery Tools

Partner Responsible : FHG

Contributing partner(s): FORTH, INRIA, UvA, SIB, LundU, UMA, UPM, Biovista, IEO, UOXF

Reporting Period: 01/02/2008 – 31/01/2009

Workpackage objectives and starting point of work at beginning of reporting period

The main objectives of WP6 according to the DOW are:

-To adapt standard analysis modules for descriptive statistics and visualization, hypothesis tests, discriminant analysis, and survival analysis to the ACGT environment.

- To adapt advanced data mining and text-mining modules to the ACGT use cases.

- To provide an innovative and user-friendly interface to the analysis tasks.

-At the beginning of the reporting period

At the beginning of the reporting period, an initial version of the GridR tool as the core knowledge discovery (KD) tool in ACGT had been demonstrated. In addition, literature mining and the clustering tool “chavl” had been demonstrated as examples new, gridified KD tools. A repository for knowledge-discovery-relevant metadata had been implemented, and a corresponding meta data schema has been developed.

Progress towards objectives

*I*n this reporting period, work in WP6 has focused on 3 major objectives towards an integrated analysis platform, as described in Deliverable D6.5: the improvement and portal-integration of the GridR tool, the development of metadata schemas and metadata-aware tools, and the devlopment of visualization tools. In addition, the current status of the analysis environment has been presented in the MCMP scenario, a real-world data analysis scenario.

- Implementation of new features in the GridR tool, bugfixes (FHG)

- Publication of the GridR tool under the R open source repository CRAN (FHG)

- Demonstration of the GridR tool in a tutorial at the R user conference useR2008, Dortmund, Germany. (FHG)

- Implementation of an initial GUI for GridR in the context of the ACGT Portal (FHG)

- Design of the Web Service interface of the GridR system and guidelines for its implementation (FORTH, FHG)

- Integration of the GridR service in the workflow environment and implementation of the needed “proxy service” for the realization of the “scripts as services” concept. (FORTH, FHG)

- End-user testing of GridR aspects of data mining environment (SIB, FHG)

For the metadata development, the following tasks have been addressed

- Discussions about file-related metadata and the different approaches for supporting them. (FORTH, FHG, UMA, UPM)

- Creation of metadata format associated to query results, and updating of the mediator to retrieve metadata files. (UPM, FHG)

- Updating of results datasets format to fit the requirements of the KDD tools. (UPM)

- Configuration of the communication of the mediator with KDD tools for different scenarios. (UPM)

For the user interface and visualization tools, the following tasks have been addressed

- Bringing data miner end-user view into the TMC meetings. (SIB)

- UvA continued the availability of visualization services in the backend for use by Hokkaido University in the Subjunctive Interface. (UVA)

- Collaboration has continued with Hokkaido University, Japan, for the integration of the visualization services into an interactive environment known as the "Subjunctive Interface". This collaboration will result in an environment that enables parametric studies of the in silico simulation software through an interactive graphical interaction and representation interface. A number of meetings between partners in WP8 have resulted in significant steps forward into achieving this goal. (UVA, UHok)

- UvA has taken first steps for the implementation of new algorithms for the interactive visualization of networks and graphs. An initial prototype has been demonstrated on a multi-touch table at SuperComputing 2008 (SC08), Austin, TX. (UVA)

For the MCMP scenario, the following tasks have been addressed

- Implementation and integration of data, scripts and workflows the MCMP scenario presented in December 2008 review. (SIB, UOXF, FHG, FORTH)

- Contribution to the deliverable D6.4 concerning the "Matching Gene Expression Profiles and Regulatory Networks" scenario. (FORTH)

- Development of R routines and analyses workflows in relation to MCMP (UOXF)

- Development and validation of tools for analysis and meta-analysis of clinico-genomic datasets. (UOXF, SIB)

Finally, the following additional tasks have been addressed

- Writing of several conference papers. (FHG, FORTH, SIB)

- Research and integration of new data preprocessing algorithms in the mediator. (UPM)

- Study to assess predictive accuracy of literature mining (Biovista)

Deviations from the project work programme, and corrective actions taken/suggested

nil

List of deliverables, including due date and actual/foreseen submission date

D6.4 and D6.5 have been integrated into one documents as discussed in the December review. Both are in their final stages and will be submitted March 2009.

WP7 - WP7 - Ontologies and Semantic Mediation Tools

Partner Responsible: UPM

Contributing partner(s): FHG, USAAR, INRIA, PHILIPS, LUNDU, FORTH, BIOVISTA, SIB, IJB, UOXF, IEO, UMA

Reporting Period: 01/02/2008 – 31/01/2009

Workpackage objectives and starting point of work at beginning of reporting period

The Workpackage has had the following major objectives during this period:

- To provide friendly access to the mediation service to both end users and client layers within the
  ACGT platform. This goal encloses the following sub-goals:
  - To develop a web-based friendly user interface that aids clinicians in formulating queries for the mediator.
  - To include a series of services in the Mediator dealing with providing additional information on the integrated repositories—i.e. global constrained schema and other types of required metadata.
- To provide a means to cooperate in the building of mappings overcoming the semantic issues present in the data sources. This goal implies the development of a web based mapping user interface and its subsequent inclusion in the ACGT portal.
- To research in the way to speed up the mapping process by the construction of a framework for the automatic generation of mapping suggestions.
- To research in techniques for the optimization of query execution in the mediator, such as the
  utilization of a cache system storing subquery translations.
- To design the formal procedures for the ontology submission system.

Progress towards objectives

The main activities, output and achievements of the WP during the reporting period were:

- Design, Implementation and Testing of Mapping and query tools (UPM)
- Implementation of new version of the Mapping API, covering Obtima requirements (UPM)
- Updating of mapping format to cover new cases of heterogeneity (UPM)
- Improving of the mediation algorithm, avoiding data overriding issues and covering cross database references (UPM)
- Analysis of the issue of maintenance and extension of the ontology (FORTH)
- Requirement analysis of a submission system for ontology evolution (FORTH)
- Analysis of Specifications for the Ontology Submission tool (FORTH)
- Development of the first prototype of Ontology Submission tool (FORTH)
- Review/Extension of ACGT MO (FORTH)
- Review and refinement of the ACGT Master Ontology (FORTH)
- Study of existing ontologies (Feta, INB, emb.net) for semantic annotation of web-service functionality. Purpose is to use these ontologies as a base when developing ontologies for services and data types and integrate with semantic mediator (UMA)
- Support for storing and sharing mediator queries in the ACGT metadata repository. The queries are thereby possible to integrate in workflows using the workflow editor (UMA)
- Review/Extension of ACGT MO (IFOMIS)
- Addition of anatomical classes (IFOMIS)

- Re-evaluation of NCI Thesaurus (caBIG, caCORE) (IFOMIS)
- Ontology-focussed validation of CRF creation (IFOMIS)
- Efforts towards validation of conceptual design by means of automated term extraction (IFOMIS)
- Intra-project communication on ontology development (IFOMIS)
- Networking with the OBO Foundry/NCBO BioPortal (IFOMIS)
- Development of the advanced CRF Creator and Ontology viewer for ObTiMA (FhG)
- Contribution to ACGT Master Ontology: further specification of requirements and review (FhG)
- Contribution to the development of the mapping format for the mapping of data sources to the ACGT Master Ontology (FhG)
- Preparation of demonstrations for the reviews: creation of mappings, interfaces and queries for the different scenarios (UPM, PHILIPS, FhG, IFOMIS, UMA, USAAR)

Deviations from the project work programme, and corrective actions taken/suggested

The only deviation from the original planning was the production and delivery of D7.7, a new deliverable on Design principles of the ACGT Master Ontology: Examples and Discussion, not included in the original DOW description. This deliverable was decided to be produced after receiving feedback from the reviewers in December 2007, and has the main aim of clarifying the process of building and curating the Master Ontology.

List of deliverables, including due date and actual/foreseen submission date

D7.4 Consolidated approach for semantic mediation and integration of heterogeneous data sources for clinical trials (T0 + 24)

D7.5 Demonstration of final mediation access tools and services (T0+32)

D7.7 Design principles of the ACGT Master Ontology: Examples and Discussion (T0+32)

WP8 - Technologies and Tools for In Silico Oncology

Partner Responsible : ICCS

Contributing partner(s): FORTH, INRIA, UvA, IJB, FHG-IGD, ICCS, USAAR, UoH, IEO

Reporting Period: 01/02/2008 – 31/01/2009

Workpackage objectives and starting point of work at beginning of reporting period

The objective of this WP is to develop the "Oncosimulator", a technologically advanced and user friendly system able to spatiotemporally simulate within well defined reliability limits tumour growth and tumour and to a lesser extent normal tissue response to chemotherapy, for the cases of breast cancer and nephroblastoma (Wilm's tumour), in the patient's individualized context. The constituent simulation models are based on the essentially "top-down" modelling approach developed by the In Silico Oncology Group, ICCS-NTUA

Pertinent clinical, imaging, histopathologic and molecular data in conjunction with the ACGT clinical trials are being exploited in order to validate the model both prospectively and retrospectively. More specifically, the in silico oncology trial is based on the two clinical trials (nephroblastoma SIOP 2001/GPOH, University of Saarland, and breast cancer TOP trial, Institute Jules Bordet) following their considerable enhancement in terms of data collection.

During the 3rd reporting period (3rd year of ACGT's lifetime) the following fundamental clusters of activities took place:

CLUSTER 1: Initial version of the (semi)integrated Oncosimulator.

CLUSTER 2: Numerical studies and code optimization.

Progress towards objectives

CLUSTER 1: Initial version of the (semi)integrated Oncosimulator.

Development of the initial version of the (semi)integrated Oncosimulator including the simulation and the technological components. The technological components concern the following tasks:
1. Image processing (tumour segmentation, interpolation, 3D reconstruction, homogenization of the discretization mesh).
2. Simulation code execution optimization.
3. Execution driving through the parametric study portal "RecipeSheet".
4. Cluster/grid execution of the code in order to simulate several candidate treatment schemes and/or several virtual instances of the patient.
5. Standard and virtual reality visualization of the predictions

CLUSTER 2: Numerical studies and code optimization.

Implementation of an extensive numerical study of the algorithms and codes including convergence and stability.

Optimization of the previously mentioned codes so that convergence can be ensured automatically and stability is improved through several arithmetic adaptations.

Furthermore, use of the SVN and Eclipse platforms in order to facilitate collaborative optimization of the codes by the various distantly located involved partners.

From the participating institutions perspective the following contributions have been made:

ICCS

ICCS has coordinated the entire workpackage. It has produced and provided the simulation codes in order to serve as the basis for the development of the technological modules. ICCS has checked the performance of the technological modules from the simulation perspective. It has also performed several code optimization tasks and numerical analysis studies.

Refinements, extensions and numerical checks and explorations of the simulation model have been performed. Particular focus has been assigned to the novel tumour initialization technique, the study of its convergence and the numerical study of the sensitivity of the model to several critical parameters or parameter combinations.

The outcome of an initial step towards the clinical adaptation and validation of the system has been presented and discussed in D8.3. Use of anonymized real data before and after chemotherapeutic treatment for the case of the SIOP 2001/GPOH nephroblastoma and TOP breast cancer clinical trials constitute the basis of the clinical adaptation and validation process.

Functioning of the initial Oncosimulator platform, including both basic science and technology modules, was demonstrated during the Eindhoven ACGT annual review (May 27-28, 2008). By using real medical data concerning nephroblastoma and breast cancer in conjunction with plausible values for the model parameters (based on available literature and/or logic) a reasonable prediction of the actual tumour volume shrinkage has been made possible.

The successful performance of the initial combined Oncosimulator platform has been a particularly encouraging step towards the clinical translation of the system, being the first of its kind worldwide.

USAAR

USAAR has provided the nephroblastoma medical data for the development and clinical validation of the Oncosimulator. See also WP2 PAR.

IJB

IJB has provided the breast cancer medical data for the development and clinical validation of the Oncosimulator. See also WP12 PAR.

UvA

The University of Amsterdam has continued their work on the visualization services. A prototype version of the interactive web based visualization services have been successfully integrated into a number of scenarios, some of which have been demonstrated at the ACGT review in Eindhoven, May 2008. Several performance issues have come up during this integration that have given us pointers to improve performance.

Collaboration has continued with Hokkaido University, Japan, for the integration of the visualization services into an interactive environment known as the "Subjunctive Interface". This collaboration will result in an environment that enables parametric studies of the in silico simulation software through an interactive graphical interaction and representation interface. A number of meetings between partners in WP8 have resulted in significant steps forward into achieving this goal.

UvA has obtained additional anonymized DICOM patient data from Saarland University, both before and after chemotherapy. This data will be used as respectively initial conditions and "ground truth" validation data for the visual comparison of in silico simulation results and imaging data in the parametric study scenario. This is a complex scenario, involving six partners in WP8, and UvA has taken the initiative to play an active role into managing this complexity and identifying possible problem areas.

UvA has taken first steps into integrating support for PSNC's Data Management System (DMS) into the visualization architecture. Shortcomings of this system for the purpose of the parametric study scenario have been identified.

PSNC
PSNC has contributed to the development of the Oncosimulator regarding the automatic execution of the entire workflow on a grid infrastructure. It has also extensively contributed to the Document Management System (DMS) to be used in conjunction with the Oncosimulator.

INRIA
During the first part of this period, INRIA prepared the code of the Oncosimulator for the "Annual Review" which took place in April 2008 in Eindhoven (The Netherlands). During this review, a demonstration of a first exploitation of the ACGT Grid with WP8's technologies has been made. INRIA worked closely with ICCS developers and PSNC people to optimize the Oncosimulator code for Grid execution.

In addition, INRIA in collaboration with ICCS has decided to exploit the cooperative tools and services offered within the ACGT project such as the SVN Repository server provided by FORTH (see https://iapetus.ics.forth.gr/ACGT_Repository/) and has standardized the development tools for future activities on the Oncosimulator code. "GCC (http://gcc.gnu.org) / Eclipse IDE (for Integrated Development Environment, http://www.eclipse.org/cdt) / SVN (http://subversion.tigris.org/)" has been chosen as a unique environment to develop and collaborate on the code of the Oncosimulator.

At the same time, INRIA has carried on the various parallelization activities. After many researches on conceiving a distributed execution of one single Oncosimulator instance on a Cluster, INRIA has concluded that this method was not reliable with the amount of memory access needed by the application. Nevertheless, INRIA is now working on a parallelization on multi-core processors
where the memory can be shared between different threads (ie. soft processes). The results of the first implementation of the multi-threaded version are encouraging but their validity has to be discussed thoroughly with ICCS.

FORTH
FORTH extended and adapted semi-automatic image segmentation algorithms to be applied on the actual ACGT DICOM data.

FHG-IGD
The following image processing procedures were undertaken by FHG IGD in Darmstadt:

- Provision and development of tools for manual slice wise tumour contouring

- Storing of contours as binary data sets
- Resampling and interpolation of binary segmentations using level set methods
- Cropping of resulting data sets in order to reduce the amount of voxels that enter the tumour growth simulation
- Examination of methods for 3D tumour segmentation

UoH
UHok continued to work with UvA, ICCS and others on deploying the RecipeSheet software as the interface for running Oncosimulator jobs, and for requesting and controlling 2D and 3D visualisations of their results. As a first stage, a setup for browsing pre-computed results was demonstrated at the annual review. Work since then has focussed on the validation and calibration of the Oncosimulator code, requiring ways for users to handle larger numbers of parameters, and full integration with Grid security mechanisms. UoH has also worked with UvA to prototypeWeb-service-based approaches to synchronising multiple related visualisations.

IEO
IEO in collaboration with ICCS and USAAR has started exploring the feasibility of the eventual inclusion of an additional module into the Oncosimulator dealing with the immune system (IS) responses to the tumour and possibly with the effect of immunotherapies in the final stage of the ACGT lifetime.

Although no clinical validation for this more qualitative module has been planned, its aim would be to deepen the understanding of such phenomena and of the follow-up period after the end of chemotherapy when as in the initial stages of tumorigenesis an important role might be played by the immune surveillance, alone or enforced by a suitable immunotherapy (either active or passive).

The Oncosimulator might be particularly fit to this task since it provides a satisfactory way to model spatial dynamic phenomena such as the ones taking place during the interaction of IS with a solid tumour. This might be particularly valuable in the field of tumour immunology, where the literature concerning spatio-temporal aspects is in its first phase of development.

A more detailed description can be found in D8.3.

Deviations from the project work programme, and corrective actions taken/suggested

Due to a delay in the provision of the expected medical data from the clinical partners (due to administrative and other reasons) there has been a slight delay in the clinical adaptation and validation procedure. However the mainstream of the workpackage is flowing without any serious problems.

List of deliverables, including due date and actual/foreseen submission date

Production and submission of deliverable D8.3.

WP9 - The Integrated ACGT Environment

Partner Responsible: FORTH

Contributing partner(s): UvA, Philips, IJB, SIB, LundU, UMA, UPM, FHG, BIOVISTA, UoC, PSNC, Custodix, ICCS, UHok

Reporting Period: 01/02/2008 – 31/01/2009

Workpackage objectives and starting point of work at beginning of reporting period

The main objectives of WP9 according to the DoW are:

- To demonstrate large scale system integration within the ACGT environment
- To implement the workflow layer for achieving composability of applications and services
- To investigate the evolution of the ACGT integrated platform proposing enhancements to all levels with respect to functionality and performance

During the third year of the project emphasis was given to the following areas:

- Continuous monitoring of the ACGT interoperability requirements and revisiting and evolving them based on the additional feedback that is acquired in the course of the project from the other technical work packages.
- Specification and development of the necessary infrastructure for the semantics aware publication, discovery, and retrieval of the descriptions of services, tools, and workflows in order to facilitate the integration and composition of the different ACGT components and the efficient use of the ACGT platform
- A web based workflow authoring tool integrated in the ACGT portal will be designed and implemented so that the users use a unified interface to gain access to the wealth of functionality offered by the ACGT platform.

Progress towards objectives

In the third year of the project work in WP9 has been focused on the design and implementation of the ACGT web based workflow authoring and execution tool. This workflow editor was demonstrated in the biannual reviews and was also evaluated in the informal ACGT user evaluation and training workshop that was organized by SIB in Vienna in January 2009. In cooperation with WP14 and partner Siveco the workflow editor was integrated in the ACGT portal so that the users use a unified interface to gain access to the wealth of functionality offered by the ACGT platform. To comply with the ethics, legal, and security requirements imposed by WP10 and WP11 it was necessary to design and build the proper security infrastructure so that the workflow execution is seamlessly integrated with the underlying Grid security mechanisms of ACGT. To this end a survey of the available “non-BPEL” enactors and their evaluation with respect to the level of support for Grid Security and credential delegation was undertaken by FORTH. When the results showed that no viable solution exists, after various discussions and study of the available options, the “Proxy Services” infrastructure was designed for achieving the “credential delegation” functionality in the BPEL workflow enactor. This framework provides for the secure, authenticated, and authorized invocation of Grid ACGT Services from within BPEL Workflow Enactors. The generic architecture of proxy services allows the integration of Grid and non-Grid based technologies at the workflow layer and will also permit the incorporation of “third party services” in the future. An initial set of “proxy services” were implemented for the ACGT Semantic Mediator, the GridR, and the Microarray (BASE) Data Access Service by FORTH in close collaboration with UMA, FhG, and Phillips.

On the integration aspect of the work package work has been started for the definition of the data type ontology for the semantic annotation of the ACGT services. In the September’s

consortium meeting in Crete the choice of compliance, to a large extent, to the Biomoby data types was made. For this reason integration with the Biomoby services has begun and will result in the implementation of a generic Biomoby proxy service in the near future. Finally the Deliverable 9.3 “Data and Metadata Management” was prepared and submitted. The second deliverable, D9.4 “Semantic Integration in ACGT”, was decided to be postponed so that enough implementation experience is gained through the integration of Biomoby services and more concrete definition of metadata elements used for service annotation. It will be delivered in time for the first review in 2009. The main activities of the various partners, besides the WP leader, involved in the WP are described below:

Main tasks carried out by Custodix:

Custodix has given assistance to the other partners for integrating their services and tools with the security infrastructure. Additionally work was done on eliminating conflicts between different programs (e.g. registration of users and login) so that the overall function of the infrastructure has improved.

During several teleconferences and a specific integration meeting in Lausanne (18-19/11/2008) Custodix has provided input and helped decision making regarding the review demonstrator. More specifically Custodix has kept the focus on the need of security integration in the demonstrators.

Main tasks carried out by SIB:

SIB was the leading partner for the development of a number of workflows based on the WP2/WP12 scenarios to test integration of ACGT components. It has also actively contributed in the debugging sessions testing the integrated data mining environment.

Main tasks carried out by UMA:

An initial study of related approaches for semantic annotation of workflows was performed. In particular we have studied a few existing ontologies (Feta, INB, emb.net) that can be used to describe service functionality. The purpose is to improve discovery of services/workflows and to facilitate workflow composition.

UMA is also the provider of the metadata repository and its accompanied API. In the reporting period a re-organisation of the API code has taken place so that it provides development and production versions of the metadata repository interface. The aim is that this will provide a more stable interface for components that use the metadata repository.

Main tasks carried out by UVA:

UvA has continued their work on the visualization services. A prototype version of the interactive web based visualization services have been successfully integrated into a number of scenarios, some of which have been demonstrated at the ACGT review in Eindhoven, May 2008. Several performance issues have come up during this integration that have given us pointers to improve performance. The University of Amsterdam has taken part in a user evaluation of the current ACGT portal and modules during the consortium meeting in Vienna. New areas where the visualization modules may be used have been identified.

Deviations from the project work programme, and corrective actions taken/suggested

Deliverable D9.4 “Semantic Integration in ACGT” was decided to be postponed until the first months of 2009 in order to keep its contents inline with the development work that is taking place in the context of metadata.

List of deliverables, including due date and actual/foreseen submission date

Deliverable 9.3 was prepared and made available for submission to the EC on May 2008. Deliverable 9.4 will be ready by the end of March 2009.

List of milestones, including due date and actual/foreseen achievement date

None in the reporting period

WP10 – Ethical, legal and QA issues

Partner Responsible: LUH

Contributing partner(s): UH, Custodix, FUNDP, USAAR, UOXF.BP, IJB, UoC,

Reporting Period: 01/02/2008 – 31/01/2009

Workpackage objectives and starting point of work at beginning of reporting period

One main objective of this WP is to ensure that no barriers regarding data protection (legislation) are in the way of accomplishing the *ACGT* goals. According to the legal requirements identified, technical solutions to safeguard data protection were presented and will be implemented (WP 11). The focus was on the implementation of the proposed ACGT Data Protection Framework, on the negotiation and signing of the produced contracts between ACGT partners, the established Center for Data Protection and on a Risk analysis together with WP11 with regard to data protection. Other objectives of this WP were the most important Intellectual Property-issues resulting from the chosen ACGT architecture. Furthermore, the work on the projected comparative survey on patients' perspectives and needs regarding informed consent and data protection was continued and implemented.

Progress towards objectives

- ⇨ Brecht, Jean-Marc and Nikolaus had a discussion with Corinna Porteri from the 7th FP project NeuGRID on CDP (Custodix, FUNDP, LUH)
- ⇨ A letter to the European Commission was prepared to promote the CDP on the European level. (LUH)
- ⇨ The contracts were finalised. We continued to work on official relations with the Art. 29 Working Group. (LUH)
- ⇨ Meeting with representatives of the Department of the History, Ethics and Philosophy of Medicine of the Hanover Medical School in order to disseminate ACGT and to receive scientific input from different disciplines. (LUH)
- ⇨ D 10.7 Intellectual property issues within ACGT is in progress and will be finalised in time. (LUH, UH)
- ⇨ D10.8 Risk analysis is in progress (CUSTODIX, LUH)
- ⇨ Book on ethical and legal aspects of human genetic research is in progress (UH, LUH)
- ⇨ Analysis of the informed consents used in trails at UOXF (LUH)
- ⇨ Contribution to the second edition of the ACGT newsletter (LUH, UH)
- ⇨ Assessed Oxford inform consent and ACGT requirements (UOXF)
- ⇨ Contributed reading of documents/discussion (UOXF)
- ⇨ Assessed contracts in view of signing (UOXF)
- ⇨ Passed ethical approval of the ethical questionnaire-based study and produced a questionnaire that could be used in oxford (UOXF)
- ⇨ Conduct of a national survey on needs and concerns of parents of minors affected by cancer. (UH, USAAR)
- ⇨ The international and national survey on patients' and parents' perspectives and needs regarding informed consent and data protection was designed and set up. Several co-operations with clinical partners and the German Childhood Cancer Registry were

installed: Jules Bordet Institute (Belgium), Oxford University (UK), University of Crete Hospital (Greece), Westgerman Study Group who coordinates the Mindact-Study (Microarray in Node negative Disease may Avoid Chemo Therapy) in Germany as partner of EORTC/Transbig, University of the Saarland, Rehabilitation Centre Katharinenhöhe, Sylt Clinic, After Care Clinic Tannheim, German Childhood Cancer Registry. (UH)

- ⇨ The questionnaire was developed and pre-tested in a German hospital and translated into English, French and Greece (the latter two by our clinical partners in Brussels and Heraklion). The patient information, the contact information, the consent form, and the letter to ask for assistance by attending physicians and study nurses were developed. The approvals for local ethics committees and institutional review boards were prepared and submitted. The management board of the German Society for Paediatric Oncology was informed about the planned survey and was asked for approval. (UH)
- ⇨ D10.6.1 Status report of the international and national empirical survey on patients' and parents' perspectives and needs is in progress. (UH)
- ⇨ Analysis of the informed consent and its feasibility in research in course at FUNDP (FUNDP)
- ⇨ Contacts with Jules Bordet Institute to finalize the contracts (FUNDP)
- ⇨ Contribution to the production of Deliverable "D10.5 Design of an empirical survey on patients' perspectives and needs-regarding informed consent and data protection in clinical and clinico-genomic trials". In collaboration with FORTH, the permanent staff of the hospital (expert clinicians) reviewed the questionnaire for the patients and gave their feedback. (UoC)
- ⇨ The planned survey on patients' perspectives and attitudes on tissue-based research on breast cancer has been translated and submitted for approval at the Ethics Committee of the University Hospital of Heraklion. After the approval of the Ethics Committee, clinicians have started the distribution of the questionnaires to selected patients. The collection of the questionnaires is expected to be completed until June 2009. (UoC)
- ⇨ IJB discussed internally the contracts regarding data protection, data security and ethical issues. (IJB)
- ⇨ Participation in the implementation of the questionnaire regarding patients' perspectives and attitudes towards clinico-genomic research in the context of D10.5 "Design of an empirical survey on patient's perspectives and needs". This questionnaire has been submitted to the ethics committee of the institute, the necessary insurance has been taken and a strategy has been defined within the institute to submit/retrieve the questionnaire. IJB)

Deviations from the project work programme, and corrective actions taken/suggested

No deviations from the project work programme and no corrective actions taken.

List of deliverables, including due date and actual/foreseen submission date

D10.5 - Design of an empirical survey on patients' perspectives and needs (month 25)

D10.6.1 - Status report of the international and national empirical survey on patients' and parents' perspectives and needs (month 38)

List of milestones, including due date and actual/foreseen achievement date

Non in this period.

WP11 - Trust & Security

Partner Responsible: Custodix

Contributing partner(s): UMA, UPM, FHG, UHANN, PNSC, Custodix, FUNDP, UH

Reporting Period: 01/02/2008 – 31/01/2009

Workpackage objectives and starting point of work at beginning of reporting period

WP11 aims to create a technical environment in which processing of sensitive patient data for research purposes complies to the relevant (data protection) regulations “by default”. The necessary documentation and guidelines will be provided to the developers of the ACGT services to make the ACGT framework live up to the data protection expectations. Finally it is the task of WP11 to continuously monitor the ACGT security and privacy requirements, revisit and evolve them based on additional feedback acquired during the project.

In the reporting period the focus shifted from implementation of services to the evaluation and monitoring of the infrastructure. Initial work was planned for (VO) management tools, documentation of guidelines and requirements and additional evolution of the ACGT anonymisation tool CAT.

Progress towards objectives

- ⇨ A technical workshop was organised to discuss the various requirements and existing solutions regarding VO management
- ⇨ D11.4: Requirements and guidelines for developing secured ACGT services has been finished and made available for internal review
- ⇨ The Custodix Anonymisation Tool (CAT) has reached version 1.0. Further development has been done to make a Command Line Interface (CLI) available.
- ⇨ A workshop organised by WP13 was attended to gather up-to-date security requirements for deploying ACGT infrastructure in a hospital environment
- ⇨ A meeting was attended organised by Jules Bordet Institute to discuss the transfer of new data into ACGT
- ⇨ Modules for the monitoring system were created and deployed to monitor the stability and function of security services.
- ⇨ The Gridge Authorization Service was further developed and improved.
- ⇨ The meta-data repository was extended to support data set identifiers
- ⇨ More services were integrated in the ACGT security framework Amongst those was the metadata repository where changes in services and workflow metadata should be restricted and subject to appropriate permission as specified in GAS.
- ⇨ Specification for the role based secure access to ObTiMA and user roles and rights management (Fraunhofer together with FORTH).
- ⇨ All WP participants were involved in the Technical Parallel Session of the Consortium Meeting (Crete, November 2007) where amongst other topics security was discussed.
- ⇨ October 31st – November 5th 2008, ObTiMA Meeting regarding Trial Outline Builder, Ontology Viewer, Secure access and User Roles and Rights, St. Ingbert, Germany, (participants: USAAR, Fraunhofer IBMT, UHok, FORTH)

Deviations from the project work programme, and corrective actions taken/suggested

Deliverable D11.5: Finalized ACGT security architecture is to be merged with Deliverable D3.3

Deliverable D11.6 will be delayed until the VO management tools are in a stable state

List of deliverables, including due date and actual/foreseen submission date

D11.4 Requirements and guidelines for developing secured ACGT services **T0+33**

D11.5 Finalized ACGT security architecture **Merged with Deliverable** D3.3 "The ACGT technical architecture: Final Specifications" (**T0+36)**

D11.6 ACGT guide for administrative documentation of ACGT security and VO management (**T0+36)**

List of milestones, including due date and actual/foreseen achievement date

MWP11.2 Finalized ACGT security architecture (T0+36) ***Part of Major project milestone M12***

WP12 - Clinical Trials

Partner Responsible: IJB & FORTH – IMBB

Contributing partner(s): UHANN, UH, USAAR, Biovista, EIO, UOXF, UoC, SIB, Custodix, FUNDP, LundU.

Reporting Period: 01/02/2008 – 31/01/2009

Workpackage objectives and starting point of work at beginning of reporting period

The Workpackage has the following major objectives:

- Implement the ACGT post-genomic clinical trials collecting multilevel clinical information for the validation of the ACGT infrastructure.
- Identify and address the various harmonization issues related to cross-platform and multi-centric post-genomic data collection.
- Implement various advanced post-genomic analyses including expression profiling, genotyping, proteome and metabolome profiling methodologies.
- Promote post-genomic medicine according to the ethical, regulatory and technical requirements.

Progress towards objectives

(a) Two clinical trials were previously selected as the ACGT clinical trials:

- The TOP trial: This multi-centric trial, which is coordinated by IJB, investigates pre-operative chemotherapy treatment and responses in order to identify indicative individualized patients' profiles. In the summer of 2008, the team in charge of the TOP trial reviewed thoroughly its status, and after consideration, decided to stop the accrual of patients in this trial. However, patients are still asked to re-consent for their data to be shared in the context of ACGT. However, before data can be shared, the contracts developed by WP10 need to be signed by the legal department of IJB and other partners wishing to access the data. These contracts are now being finalised based on the last requirements of both data holders and data users. Once these contracts are signed, IJB will send real data to Custodix for anonymisation. It has to be noted that UoC submitted the protocol of the TOP trial to the National Organization for Medicines and the National Committee of Ethical Deontology and signed an insurance contract concerning patient's protection for the above clinical trial with AIG Greece Insurance Company. Unfortunately, the TOP trial recruitement was closed during the waiting period for approval and UoC did not have the opportunity to contribute any patients.

- The SIOP trial: The Nephroblastoma study and trial protocol 2001 started accrual in June 2001 and is coordinated by USAAR. In 2006 the first patient did enter the ACGT Nephroblastoma trial after approval of an amendment of the SIOP 2001/GPOH trial by the ethical committee (Landesärztekammer des Saarlandes). This trial is still ongoing, as well as the antigen scenario.

The status of implementation of these two trials is being extensively described in D12.6. These two trials are contributing data for the oncosimulator (for more detail see WP8).

Additionally, IEO carried out the clinical part (and the preliminary electronic duties) of the Trenett study, and started collecting and pre-validating the data as well as planning the statistical analyses to be carried on through the tool GridR .

The clinical partners are also continuously interacting with the other WPs to answer all the questions they may have regarding these trials.

(b) In order investigate the various harmonization issues related to cross-platform and multi-centric post-genomic data collection and analysis, we developed a study which aims to assess the variability in gene expression microarrays, and of the prognostic and predictive profiles obtained from this technology, performed at different sites and using different array methodologies in human breast cancer samples. To this end we are comparing reproducibility of results obtained in two different ACGT partners institutions (IJB and UOXF) using two different but well established technologies for gene expression microarrays; namely, Affymetrix gene expression arrays (processed at IJB) and Illumina arrays (processed at UOXF). A lot of time has been spent to define and agree on the ethical and legal requirements to share clinical and genomic data, to update the clinical database and to formulate research-clinical meaningful data mining scenarios for the review demonstrators.

(d) Different initiatives have been taken to promote post-genomic studies conducted in the context of ACGT as well as to get feed-back from the clinical community. This has been done by interactions with:

1/ **the breast cancer clinical community**: the Breast International Group (BIG). ACGT initiated collaboration with BIG to investigate whether ACGT could help with data-sharing issues linked with their new research program.

2/ **the nephroblastoma clinical community**: USAAR has presented the ACGT Nephroblastoma trial at major international congresses and at the SIOP Nephroblastoma Committee Meeting, which are listed in detail:

1 March 5th 2008, Meeting with I-BFM and discussion about role of ACGT in Leukaemias, Hannover, Germany, (participants: N. Graf)

2 March 12th – 13th 2008, Meeting with the SIOP Nephroblastoma Study Group and basic researchers proposing ObTiMA for SIOP Renal Tumour Study Group (SIOP-RTSG), Chamonix, France (participants: N. Graf, members of SIOP-RTSG)

3 April 11th – 12th 2008, Meeting between physicians and lawyers regarding Genetic data, Ethics and law and personalized medicine, La Petite Pierre, France (participants: N. Graf)

4 April 23rd 2008, Meeting with PD Dr. Langer, chairman of LESS (Long effecting surveillance Study) regarding the use of ACGT and ObTiMA for documentation and querying long lasting side effects across different clinical trials, Homburg, Germany (participants: N. Graf)

5 April 17th – 18th 2008, GPOH Meeting, proposing ObTiMA for Clinical trials within GPOH, Hannover, Germany, (participants: N. Graf)

6 April 27th – 30th 2008, SIOP nephroblastoma Committee Meeting, proposing ObTiMA for the next SIOP Nephroblastoma trial, Milano, Italy, (participants: N. Graf, members of SIOP-RTSG)

7 May, 16th – 17th 2008, Berlin, GPOH Meeting, discussion about ObTiMA with several chairmen of different GPOG trials, Berlin, Germany, (participants: N. Graf)

8 June 17th 2008, Meeting with the Stem Cell Transplantation Group of GPOH, Discussion about the use of ObTiMA for this Group, Frankfurt, Germany, (participants: N. Graf)

9 July 20th – 22nd 2008, Meeting in Lausanne regarding Clinical trials and data exchange between ACGT and Hospital Information Systems, Lausanne, Switzerland (participants, SIB, Custodix, USAAR, Oxford, members of the local hospital)

10 July 28th 2008, Meeting with the 'Deutsche Herzzentrum' to explain ACGT and discuss a possible use of the ACGT IT-Infrastructure for clinical trials outside of Cancer, Homburg, Germany, (participants: N. Graf)

11 September 8th -10th, Meeting with SIOP-RTSG (Renal Tumour Study Group) and radiotherapists proposing ObTiMA for the next SIOP nephroblastoma trial, London, UK, (participants: N. Graf, members of SIOP-RTSG)

12 September 27th 2008, Workshop of the Comprehensive Cancer Center (CCC), proposing ACGT and ObTiMA for CCCs, Freiburg, Germany, (participants: N. Graf)

13 October 20th – 23rd 2008, active participation at the ICT BIO 2008 Conference, Brussels, Belgium, (participants: N. Graf)

14 November 20th – 23rd 2008, Meeting with the Paediatric Oncologists in Moscow regarding improvement of clinical trials for children with cancer in Russia, explaining ACGT and ObTiMA as an IT-Infrastructure facilitating clinical trials and research, Moscow, Russia, (participants: N. Graf)

15 November 29th – 30th 2008, Meeting with the SIOP-RTSG (Renal Tumour Study Group) for further discussing the IT-Infrastructure for the next nephroblastoma trial, Amsterdam, The Netherlands, (participants: N. Graf)

- 3/ the **wider cancer community:** Collaboration has been formalized with the European Organization for Research and Treatment of Cancer (EORTC) through a subcontract with IJB. The main items of the collaboration are: 1/ the review of the security infrastructure of ACGT (ogoing); 2/ the sharing of Case Report Forms of different studies to further improve and validate the Master Ontology (ongoing); 3/ the sharing of data from an EORTC trial which has recently been closed (Tarceva trial by the Brain Tumor Group/ongoing); 4/. the access to the Protocol and Case Report Form of the MINDACT trial (ongoing)and 5/ to attend meetings and events related to the ACGT project (L.Collette from EORTC attended the consortium meeting in Vienna in January 2009).

Deviations from the project work programme, and corrective actions taken/suggested

The sharing of data from the TOP trial is taking more time than initially thought. This is due to the fact that patients need to re-consent. However data from an additional 20 patients are now available.

List of deliverables, including due date and actual/foreseen submission date

- The final version of D12.2 "Bio-bank protocols and regulations"was submitted in May 2008. This deliverable was coordinated by FORTH.
- The deliverable D12.6 **–** Review and extension of the ACGT clinical studies, was submitted in November 2008. This deliverable was coordinated by IJB.
- The deliverable D12.7 Report on the local ACGT trial-specific biobanking activities, initially planned on month 30 has been cancelled since this deliverable would not add significant contribution to the ACGT project in his globality and will be replaced by a future deliverable that will summarize the advancements of the different efforts that have been done in this WP.

List of milestones, including due date and actual/foreseen achievement date

No milestones were foreseen during the reporting period.

WP13 - Evaluation and validation

Partner Responsible: SIB

Contributing partner(s): FORTH, UvA, IJB, UMA, UOC, ICCS, UdS, UOXF.BP, IEO

Reporting Period: 01/02/2008 – 31/01/2009

Workpackage objectives and starting point of work at beginning of reporting period

The aim of WP13 is to formulate evaluation criteria, validation procedures and feedback report guidelines, to coordinate local validation activities and feedback reports and to write a final evaluation report. In the third reporting period, WP13 was to issue an initial series of recommendation as regards the procedures and tools related to software quality assurance in ACGT, and as regards the usability of the software by end-users. Scenarios for evaluation and validation of the software components of the ACGT platform were to be issued, based on the anticipated features of the demonstrator.

Specific focus points were to be addressed e.g. regarding data formats, usability and user-friendliness, speed and robustness of the platform.

Progress towards objectives

Significant progress with regards to the development of the ACGT platform occurred during the reporting period. Two large scenarios (PseudoTOP and MCMP) used to test the data mining infrastructure have been prepared in the context of WP13 and demonstrated during the project reviews.

The demonstrator of the May 2008 review was described in Deliverable D13.3 to which most technical partners contributed.

A first evaluation-and-training session with end users occurred during the plenary meeting in Vienna, in which all technical partners of the project contributed (action coordinated by SIB and FhG).

Specific contributions of partners to WP13 are:

FORTH installed and started conducting administration and maintenance of the “Request Tracker” (RT) system, an open-source feature-request and bug-reporting tool, in the ACGT grid node of FORTH.

UvA extended their unit testing framework with tests for validating the functionality of the visualization modules. New areas where those visualization modules may be used have been identified during the Vienna session with end-users.

Philips cooperated with many technical partners to implement the PseudoTOP and MCMP scenarios. Validating the implementation of data sources included, checking that the retrieved data were correctly passed through the data access service layer of the platform. This activity required the creation of a “dummy” environment with simulated data not subject to legal dissemination limitations (activity **conducted**

jointly with SIB). Public and private versions of both relational and microarray data sources were deployed.

IJB contributed actively to the Vienna evaluation session and to the writing of Deliverable D13.3. IJB established a liaison with the new partner EORTC which initiated a formal evaluation of the security infrastructure of ACGT (to be reported in Deliverable D13.2).

IFOMIS conducted a review of the adequacy of the ACGT Master Ontology with the rules required for publication in the OBO foundry (to be reported in D13.2).

As WP13 leader, SIB coordinated the development of the testing scenarios demonstrated during the reviews of the project and during the Vienna session. SIB collaborates with FhG to define the specifications of the formal evaluation session which are due to take place during the final phase of the project.

UMA developed a web-service-based workflow for two-color gene-expression data processing. UMA made contributions to Deliverable D13.2 with sections on validation of metadata repository and automatic code testing. A unit-testing-based approach was developed to test the ACGT metadata repository API modules. ACGT metadata repository access was developed for the jOrca client, which facilitates testing and benchmarking of repository.

UPM designed and conducted performance tests for the query building and mapping tools. Integration testing with ObTiMA and the data mining environment was also conducted in the context of the review scenarios.

FhG conducted integration tests for the GridR environment. FhG is working in close collaboration with WP13 leader, to address software quality issues. A usability engineer working at FhG conducted a series of interviews addressing in particular the expected level of user-friendliness of the platform. She also proposed formal evaluation procedures for future sessions with end users.

PSNC contributed for the grid and DMS aspects during testing sessions.

Custodix contributed with security aspects of the testing scenarios. Discussions with WP13 partners have lead to the clarification and freeze of a security infrastructure framework for testing. Security needs in the context of real hospital use were identified during the joint meeting at CHUV.

ICCS performed a large number of code executions and studied the numerical behaviour of the models including consistency, convergence and stability in the context of the Oncosimulator development. Clinical data available in ACGT were used to adapt, optimize and validated the Oncosimulator.

UOXF was instrumental in the development of the MCMP scenario. UOXF conducted tests of the ACGT data mining environment through the portal, and contributed to the definition of testing, in collaboration with FhG. UOXF contributed actively in the discussions regarding ACGT validation.

Skype-based technical sessions aiming at identifying and fixing bugs in the platform took place on a regular basis when scenarios had reached a mature state.

Deviations from the project work programme, and corrective actions taken/suggested

.

No significant deviation of the work programme was observed, taking into account the dependency of the activities of WP13 on the availability of software issued by other WPs.

List of deliverables, including due date and actual/foreseen submission date

D13.2 describing the evaluation of some individual ACGT components (e.g. Master Ontology and security infrastructure) has been postponed to Spring 2009

D13.3 describing the scenario implementation used in the context of the demonstration of the first integrated demonstrator (May 2008) has been issued in the reporting period

A new deliverable describing the April 2009 demonstrator is foreseen, due at the beginning of April.

WP14 – Training

Partner Responsible: SIVECO

Contributing partner(s): FORTH, INRIA, IJB, UPM, FHG, UOC, UHANN, Custodix, HealthGrid, ICCS, USAAR, FUNDP, IEO, UMA

Reporting Period: 01/02/2008 – 31/01/2009

Workpackage objectives and starting point of work at beginning of reporting period

The Workpackage has the following major objectives:
- To develop the ACGT Portal, based on the GridSphere Portal platform that provides a grid-enabled integrated, customizable, multi-lingual, and user-friendly interface to end-users.
- To develop a uniform, grid enabled, training platform for biomedical data analysis by providing professional training tools to end-users (physicians, biologists, etc.) as to perform individual and cross-disciplinary data analysis and clinico-genomic trials design, monitoring and evaluation, thereby paving the way towards the advance of Clinico-Genomic Trials in Practice.

Objectives during reporting period
- The integration at the interface level of the ACGT services into the ACGT Portal
- The development of online training modules and other electronic training materials to be integrated in the ACGT Portal.

- **Progress towards objectives**

The main activities corresponding to the reported period were:
- Redesign of the front-end and content contribution in the ACGT Portal (SIVECO, Biovista, HealthGrid, UOXF)
- Redesign of the ACGT Portal back-end from the needs for “evaluation and validation” point of view (SIVECO, SiB)
- Review and test deployment of Gridsphere portal technology (SIVECO, HealthGrid)
- Integration of the workflow environment in the ACGT Portal and the implementation of a simple "single-sign-on" (SSO) seamless access to it (FORTH)
- Initial prototype of new service and workflow search portlet in local portal installation (mango.ac.uma.es). This new search portlet uses Magallanes. (UMA)
- Development of the DMS Portlet v2 (SIVECO)
- Updating of the Metadata Registration Portlet. (SIVECO)
- Development of the GridR Console Portlet (SIVECO, FhG)
- Development of the VO Management Portlet (PSNC, Custodix)
- Research and review of training environment tools (SIVECO, HealthGrid)
- Recommendations for training material creation tools (screencasting tools) (SIVECO, HealthGrid)
- Organization (SiB) and providing technical help and gathering feedback and usability comments from users (SIVECO, HealthGrid) at the internal training session during the consortium meeting in Vienna
- Local training courses for the submission of the clinical trial folder to the National authorities. (UoC)
- Researching interesting events to co-locate with for ACGT trainings (HealthGrid)
- Preparing physical training environments (HealthGrid)

- Preparation of tutorial material: the documentation of MCMP scenario from end-user (biomedical researcher) perspective providing the basis for a “hands-on” training material (SiB) and development of the tutorial (SIVECO)
- Creation of in-tool assistant for the query tool and manual for the mapping tool (UPM)
- Initial work on preparing web-based tutorial for Ontology viewer (Biovista)
- Initial tutorial and user guide for Magallanes (discovery resources and WF composition) deployed as PFD document (available at http://chirimoyo.ac.uma.es/magallanes) (UMA)
- Initial tutorial, getting started and user guides for jORCA (easlying integration) deployed both as PFD document and as on-line resource (formatted in Doc2Help style) for web-based deployment (available at http://chirimoyo.ac.uma.es/jorca) (UMA)
- Production (SIVECO) and review (HealthGrid, FhG-IBMT) of deliverable D14.3
- Production (SIVECO) and review (FORTH, Biovista) of deliverable D14.5bis
- Production (SIVECO) of deliverable D14.

- **Deviations from the project work programme, and corrective actions taken/suggested**

There were several deviations from the project work programme in what concerns the training workshops. The small delay registered with these activities was determined by the need to wait for the ACGT services to reach a certain state of development, in which they are ready to be exposed and demonstrated to the ACGT users.
This delay will be covered in the next 6 months by focusing on the training related activities.

- **List of deliverables, including due date and actual/foreseen submission date**

D14.3 Demonstration and Report of training modules, due and submitted on Month 21, was initially rejected. Resubmitted.
D14.4 Training workshop for end-users on ACGT Technologies & methodologies. Delayed.
D14.5bis Methodology for ACGT service integration in the ACGT portal on the Business Process Layer. Submitted and accepted.
D14.6 First report on ACGT Portal usage, online training modules development and evaluation. Submitted and accepted.

- **List of milestones, including due date and actual/foreseen achievement date**

No milestones due within this reporting period.

WP15 - Dissemination

Partner Responsible: HealthGrid

Contributing partners: ERCIM, FORTH, INRIA, UvA, Philips, IJB, SIB, LundU, UMA, UPM, FHG, BIOVISTA, UOC, UHANN, PSNC, Custodix, ICCS, USAAR, SIVECO, FUNDP, UH, UOXF, UHok, IEO

Reporting Period: 01/02/2008 – 31/01/2009

Workpackage objectives and starting point of work at beginning of reporting period

The workpackage has the following major objectives:

- To raise awareness of the benefits of ACGT to new user communities ensuring an appropriate message is delivered to each of them;

- To ensure new user communities know where and how to get involved in the project so they can be converted to real users;

- To ensure the information tools needed for each target audience are available and support the growth of many, varied, individual user communities;

- To identify and target new user community audiences and applications. The challenge is to reach new communities, such as new research disciplines, new industrial and commercial groups and branches of government. WP 15 will need the assistance of ALL activities to help identify new user communities (see audiences for more detail).

Objectives during reporting period

The main objectives during the reporting period were threefold:

- Disseminate the results of the project widely in Europe using the ACGT website and flyers / leaflets.

- Keep the users informed about the latest developments with newsletters, news in the website, workshop,...

- Provide specific dissemination tools for developing and maintaining a strong community.

Progress towards objectives

ACGT collaborators participated at number of conferences, organized workshop and exhibitions to spread significant developments and results that have been made on training, technical tools and clinical trials.

A general tendency of augmentation in the number of technological march allows to cater for new partner and to reach new targets. That allows maintaining a strong community with specific dissemination tools.

Tasks worked on and achievement made with reference to planned objectives, identify contractors involved.

External website

The external website at www.eu-acgt.org has been updated taking into consideration user's feedbacks as well as recommendations from the consortium's management. It is being updated regularly to better fit the user's point of views.

The ACGT website has been revised, including six different parts corresponding to each target users (medical professionals, researchers, industry, patients, regulatory bodies and general public). HealthGrid's designer has made minor modification to make the ACGT website more attractive.

More and more Internet users are interested to know the ACGT project. The most visited web pages are contact information, newsletter subscription; take action and ACGT for you. The number of unique visitor in the ACGT website in 2008 is 48684. To compare the two first months 2008 and 2009. There were 7785 unique visitors in 2008 and 9066 in 2009.

Over the entire period HealthGrid stayed in contact with all the ACGT partners to obtain events, and news to inform partners and Internet users for further publication on the website.

Events organisation, participation and presentation

-Organizing an ACGT conference would not have been feasible at this stage in the project in the light of the current budget for dissemination and would not have had the expected outcome. We therefore have made the strategic choice to participate in communities conferences with publications, demonstration stands, participating in reaching further the potential users of the community and the cancer communities at large. ACGT partners participated to disseminate the project toward different events, conferences. HealthGrid organized the ACGT for two events:

- EBCC-6 from 15 to 19 April 2008 in Berlin The conference encourages interaction and collaboration between clinicians, scientists and patients in a partnership of equals to talk not just about scientific advances, but also the ethical, social, political, and practical issues associated with caring for patients with breast cancer.

- UICC 08 from 27 to 31 August 2008 in Geneva. The World Cancer Congress brings together the global cancer community (.Clinicians, practitioners, government agencies and NGOs, patient-care providers and advocates, researchers and behavioural scientists and public health)

- For the next event, ACGT would be very interested to participate to a major conference in Japan. The consortium is currently evaluating the possibilities and the outcome of such a conference. Professor Tanaka, who works in Japan, help us to determine the better Japanese event for the project. The consortium may as well try to link the participation to the conference with the EU-Asia Grid project to gather the both project in the future.

Publication production and dissemination

- The ACGT partners have been encouraged to submit papers and publications to promote the research undertaken. The list of publications can be found as Annex, part 2.

- Flyers / leaflets and posters have been designed to introduce the project and to highlight different aspects of the multidisciplinary work carried out in ACGT. The disseminations tools provided were:

- Oncosimulator flyer, 1000 flyers were printed and 500 distributed during UICC conference and Consortium Meeting so that partners disseminate the Oncosimulator solution during their meetings/conferences.

- General leaflet to introduce the ACGT project, 5000 flyers were printed and 4000 distributed during EBCC and UICC conferences and Consortium Meeting so that partners disseminate the ACGT project during their meetings/conferences.
- Poster for Medica 2008
- General poster to Introduce the ACGT project

The three first newsletters have been published on the ACGT website. Each ACGT partner has provided content. The fourth newsletter will be available at the end of March 2009 with the following table of content:

- Editorial
- Clinical trials news: Clinical facilitation group
- Product and service: Obtima: Ontology based trial management for ACGT
- Grid News: Grids for optimizing cancer radiotherapy treatment
- Feature article: The integrated ACGT environment
- Community view: Action Against Cancer / Rare Cancer are widely spread in Europe
- Events: 15th UICC reach to recovery international breast cancer support conference / Impakt / HealthGrid 2009
- Legal and ethical : Center for Data Protection (CDP)
- Life in ACGT: Review in December / Project expansion / Welcome to EORTC
- ACGT people: F.Buffa / T.Sengstag

Deliverables

Deliverables D15.5 and D15.4 were finished. The first introduce the revision regarding the dissemination plan for the ACGT project and the third report on organisation of scientific events and participation in conference since the beginning of the project. Both are available on the BSCW server. Input of these deliverables was given by all participant of WP15.

Deviations from the project work programme, and corrective actions taken/suggested

The idea was to organise an ACGT conference which would gather people (such as scientists, medical professionals, biologist, computer scientist, etc) from many different backgrounds (from medical to technical people) on a same place and same time to discuss about and spread tools and technology. It might have however presented some risks. Therefore it has been decided to better meet professionals in their own conferences, and to be where they expect to meet the project members able to explain and introduce the advances.

Moreover, the “Editorial Board” prepared some content material for some dissemination tools, like the poster, Newsletter or the website. Yet, due to lack of other technical content, some dissemination vectors still lack of content and/or have been slightly delayed.

List of deliverables, including due date and actual/foreseen submission date

D15.4 “Report on organisation of scientific events and participation in conference” Submitted (25th February 2009) The D15-4 was delivered with a consequent delay of 1 month (due date January 2009). We allowed the consortium to have a little more time to provide the information based on the heavy development work they all had at that time

D15.5 “Revised dissemination plan” Re-submitted 28th November 2008 according to the due time in December 2009.

D15.6 “Report and analysis of project dissemination activities “Due to T 0 + 42

WP16 - Market Investigation and Exploitation

Partner Responsible : BIOVISTA

Contributing partner(s): ERCIM, Philips, UPM, FHG, SIVECO, FUNDP, UoH, UdS, Custodix, UOXF-BP, HealthGrid, PSNC, SIB, UMA, IRI

Reporting Period: 01/02/2008 – 31/01/2009

Workpackage objectives and starting point of work at beginning of reporting period

The Work package has the following major objectives for the reporting period:

- To implement the updated exploitation plan defined in year 2 for the ACGT
- To update the exploitation plan for period 4 (1/2/09-31/1/10)
- To create exploitation materials
- To explore exploitation options where applicable

In particular the consortium had decided at the end of the previous period (2) to target other EU efforts (e.g CaBIG and EGEE) in the areas of health-grid services and clinical trials support. A related goal was the opportunistic contacting of potential 3rd parties namely from the end-user stakeholder group.

ACGT makes contributions in three distinct domains: (a) infrastructures (grid oriented) in support of clinical trials (b) tools that support end users (clinicians and biologists) and (c) research in its areas of focus. Each of these domains places different needs and requires the exploitation activities to focus on largely different goals and supporting work. Since these issues and the related options are not obvious, it has been decided for the reporting period to explore these options and report the findings in the next version of the Exploitation Plan (D16.3)

Finally, a goal was set to initiate the preparation of the ACGT video.

Progress towards objectives

During the reporting period most effort has focused on the opportunistic exploration of exploitation opportunities with third parties, namely potential end user groups and consortia.

EORTC officially joined the consortium and a plan of action agreed upon (see further details below). In addition two meetings have been organised with the Breast International Group (BIG) with a view to exploring the suitability of ACGT resources and tools by that consortium. Certain partners (e.g Custodix, Biovista and NTUA) have also been promoting their individual modules as end user tools that answer specific needs. While fragmented, these efforts are considered to be in line with project objectives since compatibility with the ACGT infrastructure is an added end user benefit once their individual utility is established.

On the generation of exploitation related materials, the following developments occurred in the reporting period:

i) having launched the first two versions of the Newsletter, the task was handed over to WP15. Collaboration aims to ensure a consistent message and developing 'story' that reflects the evolving ACGT-platform capabilities

ii) new materials that can be used for training purposes have been developed (e.g. tutorial on Ontology Viewer as a video to be accessible via the ACGT portal)

The ACGT Video

During the Consortium meeting (Iraklio, 22-24 September 2008) a meeting was held with CAID, an organization that specializes in the popularization of science and the production of amongst others scientific documentaries. CAID was introduced to the consortium and a discussion on the ACGT Video goals and requirements was held. Additional technical meetings have been held with CAID in order to define the basic parameters of the video. It has been decided to create one 15-20 minute introductory video that will target the general public and also as an option a shorter 5-10 minute video that will target potential end users (probably clinicians). There has also been some progress on the content of the video. Currently the consortium is looking into the administrative details that will allow CAID to begin the work officially and in earnest.

Lessons learned

It has become increasingly obvious that for a complex undertaking such as ACGT, there is a significant number of difficult issues that arise and need to be addressed, often breaking new ground. Solutions as well as the issues themselves are not obvious, and so capturing and disseminating the acquired experiences becomes a valuable outcome of this work. These 'lessons learned' are reported in the current version of the Exploitation Plan deliverable (16.3).

Deviations from the project work programme, and corrective actions taken/suggested

The latest edition of the Exploitation Plan (D16.3) reports on the new focus of the consortium for the remaining period. The main changes from v2 are the following:

The consortium decided to drop the *ACGT Ready* Initiative. Partners agreed that the materials required to support this, namely extensive technical documents at various levels of detail that would allow the uninitiated IT developer to prepare ACGT compatible modules, would not be able to be prepared in time and with the given resources.

On the other hand the ACGT Competition is still believed to be feasible. A final decision has been deferred for early Q3 of 2009 when the basic infrastructure will be in place and stable enough to support the competition. At that point the necessary materials and effort required will be discussed in detail and a decision to proceed or not will be taken by the PMB on the basis of the expected relative merits/benefits for the project.

The potential collaboration with BIG was not foreseen in the previous edition of the exploitation plan. It is seen though as a major test of the project as a whole and also as a major opportunity given that it is an experiment for the future with serious backing from some important industry players (both Jules Bordet and major pharma companies). Like some other already known to the consortium user needs (namely the assurance that the main parts of the ACGT infrastructure will be available and supported post project-end) however, this opportunity poses some challenges that the consortium will need to discuss and decide

whether it is capable of addressing and undertaking at this point in time. Some effort will be allocated to this issue in 2009 with a view to making its final decision.

IT is also felt that as the project is entering its final stage all partners will need to invest more time in supporting the exploitation objectives and also some tighter collaboration with WPs 14 and 15 will need to happen.

.

List of deliverables, including due date and actual/foreseen submission date

Deliverable 16.3 was prepared during this period. The final version will be delivered by end March 2009.

List of milestones, including due date and actual/foreseen achievement date

No intermediate milestones existed for this period.

Consortium Management

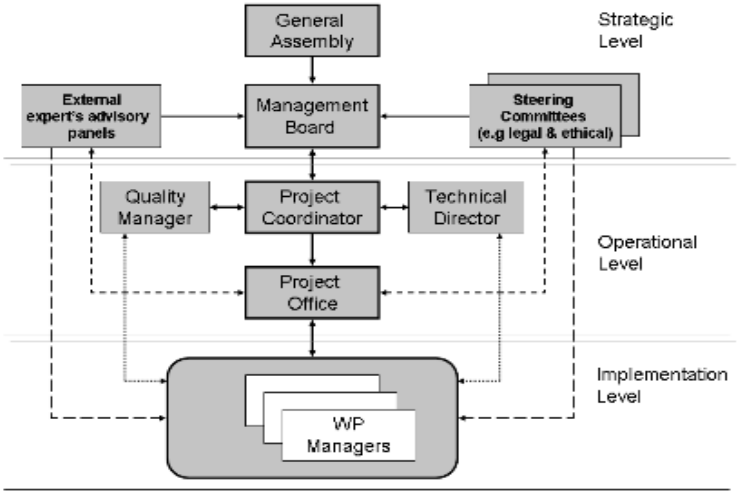
Main tasks completed or started in the reporting period

The permanent and continuous tasks accomplished by the project Management were:

- Implementation of the project's general organization and of the management architecture;
- Assistance and support to Scientific Management;
- Preparation of the internal working documents (templates);
- Definition of procedures and guidelines (reimbursement, costs claims, votes and communication protocol);
- Validation of partners financial figures and coordinates;
- Reception and transfer to all partners of the advance payment;
- Validation and monitoring of partners efforts and contributions to the project
- Implementation of the ACGT partner database;
- Integration and delivery of the bi-monthly activity reports
- Preparation of the six-monthly activity Report. Regular efforts were devoted to the collection of every partner's contribution to the periodic report (work description and effort figures in person-months).
- Definition of the dissemination strategy
- Preparation of dissemination material: ACGT poster, leaflet and give away material
- Supervision of the information flow within the project and support of collaborative tool (BSCW)
- Interaction with related initiatives to lay a grounds for cooperation (e.g EGEE, caBIG, Cancer Grid, @nurist FP6 project, etc)

Project Organisation and Scientific Management

Among the first priorities was the implementation of the Integrated Project's general organisation and governing boards, whose roles and responsibilities were defined in the consortium agreement. The Scientific Management of ACGT is composed of several yet complementing bodies: Management Board, General Assembly, Workpackage Steering Committees and the Advisory Board. This report presents the people involved and composing managerial organ:



Management Board

The Management Board is the ACGT executive and coordinating body. The MB is comprised of the Technical Director; Administrative and Financial Coordinator; Quality Manager; and the Workpackage Leaders. In order, these roles are currently occupied by:

- Rémi Ronchaud, ERCIM – Project Coordinator
- Manolis Tsiknakis, FORTH – Technical Director
- Norbert Graf, Uds – Quality Manager and WP2 Leader
- Jarek Nabrzyski, WP3 & 4 Leader
- Anca Bucur, WP5 leader
- Stefan Rüping, WP6 Leader
- Luis Martín, WP7 Leader
- Georgios Stamatakos, WP8 Leader
- Stelios Sfakianakis, WP9 Leader
- Nikolaus Forgo, WP10 Leader
- Brecht Claerhout, WP11 Leader
- Christine Desmedt and Dimitris Kafetzopouls, WP12 Leaders
- Thierry Sengstag, WP13 Leader
- Radu Gramatovic, WP14 Leader
- Yannick Legre, WP15 Leader
- Andreas Persidis, WP16 Leader

Steering Committees

The Executive Committees are the ACGT technical workpackage coordination bodies. Headed by their respective WP leaders, each Executive Committee pilots and monitors the activities in their Workpackages. Involving all the WP actors and sub-tasks leaders, the steering committees drive WP activities and monitor progress, achievements and the quality of work delivered.

WPn	WP Name	WP Leaders	Institute
WP2	User Needs Analysis & Specifications	Norbert Graf	UdS
WP3	Architecture and Standards	Jarek Nabrzyski	PSNC
WP4	Biomedical GRID technology Layer	Jarek Nabrzyski	PSNC
WP5	Distributed Data Access, Tools and Applications	Anca Bucur	Philips
WP6	Knowledge Management & Discovery Tools	Stefan Rüping	FhG
WP7	Ontologies and Semantic Mediation Tools	Luis Martin	UPM

WP8	Technologies and Tools for in-silico Oncology	Georgios Stamatakos	ICCS
WP9	The Integrated *ACGT* Environment	Stelios Sfakianakis	FORTH
WP10	Ethical, Legal and QA Issues	Nikolaus Forgo	LUH
WP11	Trust and Security	Brecht Claerhout	Custodix
WP12	Clinical Trials	Christine Desmedt & Dimitris Kafetzopoulos	IJB
WP13	Evaluation and Validation	Thierry Sengstag	SIB
WP14	Training	Radu Gramatovici	Siveco
WP15	Dissemination	Yannick Legre	Healthgrid
WP16	Market Investigation & Exploitation	Andreas Persidis	Biovista

In addition to these managerial bodies, additional organs have been established to address particular aspects of the project coordination, in particular:

- Editorial Board: Headed by the WP15 Leader, Yannick Legré, this board is in charge of gathering the information and elements that will fuel the ACGT dissemination effort.

- Technical Management Committee: Headed by WP6 Leader, Stephan Rüping, this committee is in charge of assisting the technical Director by ensuring a close monitoring of all technical achievements and of all interoperability issues across Workpackages.

External Advisory Board

The ACGT Management Board has the authority to establish panels to advise it and support it in the proper management of and co-ordination of the project. These panels have an advisory role only. The Panels will be responsible for the exchange of technical views on the development of the components between industry partners, providing advice to the work packages.

At this stage, the ACGT overall Advisory Board has been implemented and is composed of:

1. Prof. Dr. Dr. h.c. Spiros Simitis
   Institute of Labour Law
   University of Frankfurt
   Senckenberganlage 31
   D – 60054 Frankfurt/Main
   Tel: (+49) 69 79 82 21 87

2. Thomas S. Deisboeck, M.D.
   Principal Investigator, CViT
   Assistant Professor of Radiology (HMS, MGH, HST),
   Director, Complex Biosystems Modeling Laboratory, Harvard-MIT (HST)
   Athinoula A. Martinos Center for Biomedical Imaging
   Massachusetts General Hospital-East Bldg. 149, 13th Street Charlestown, MA 02129
   http://biosystems.mit.edu/
   and
   Director of the Center for the development of a Virtual Tumor
   http://www.cvit.org
3. Niilo Saranummi
   Research Professor
   VTT Techical Research center of Finland
   Pervasive Health Technologies
   Tampere, FINLAND
   and
   Editor-In-Chief, IEEE Transactions on Information Technology in Biomedicine (TITB)
   TITB web site: http://www.vtt.fi/virtual/proj2/titb/
   TITB paper submission: http://embs-ieee.manuscriptcentral.com/,
   Chairman, HL7 Finland: http://www.hl7.fi
4. Dr. Peter Maccallum,
   Department of Oncology
   University of Cambridge,
   Wilberforce Road, Cambridge, CB3 0WA
   and
   CancerGrid Project Manager

Mailing lists

In addition, dedicated mailing lists were created to support each managerial body and for intra-project communication purposes. The Sympa software was chosen for managing the mailing lists, which currently include:

acgt@inria.fr	All partners
acgt-mb@inria.fr	Management board
acgt-tmc@inria.fr	Technical Management Committee
acgt-eb@inria.fr	Editorial Board
acgt-qa@inria.fr	Quality Assurance
acgt- eab@inria.fr	External Advisory Board
acgt-reporting@inria.fr	ACGT reporting
acgt-wp1@inria.fr	acgtWP1
acgt-wp2@inria.fr	acgtWP2
---	
acgt-wp16@inria.fr	acgtWP16

Following the kick-off meeting that was organized in Juan les Pins; an electronic directory illustrating the project was established on the private section of the project's web site, allowing partners to get the office and mobile phones of other ACGT Partners, in particular members of the Management Board, as well as the key individuals (e.g., work package leaders).

BSCW server

Opened during the negotiation phase of the project, this virtual workspace is used to store both working documents and archives. Several folders have been created, ranking from templates to dedicated section for every Workpackage.

In addition, a Wiki has been implemented to allow the fast exchange of information and views on on-going work across Work packages.

Meetings and Audio conferencing

The Management has been preparing and organising the plenary project meetings during the reporting period. Additional Management board and technical meetings have also been organised to support the scientific coordination effort across disseminated teams and workpackages.

The two ACGT Plenary meetings are detailed hereafter:

- ACGT Kick off Meeting in Juan les Pins, France, 27-28 February and 1rst of March 2006

- ACGT Plenary and Technical Meeting in Malaga, Spain, 23 to 26 January 2007

In addition, a periodic audio conferencing services has been implemented to support monthly exchanges among ACGT Participants. Audio conferences are jointly chaired by the Project coordinator and the Technical Director. If necessary to address a particular issue, additional audio conferences can be organised. Specific agenda and actions are defined for every audio conference, hence avoiding other costly and time consuming meetings.

Monitoring of the Report Management Procedure

Every deliverable undergoes a rigorous control process in which the report is first submitted to assigned "reviewers" (partner institutes with the relevant technical/managerial expertise) and then must be validated by the Management Board before submission to the Commission by the Coordinator.

This has been further detailed in D1.2 Quality Assurance Plan.

Definition of financial procedures and guidelines

Prior to the internal education and training of the different ACGT teams, guidelines on project reporting in FP6 were produced by the Coordinator to present the Commission's financial guidelines and project reporting documents in a more "readable" manner. The kick off meeting and the plenary meeting in Malaga has both dedicated sessions to present project researchers and administrative contacts the European Commission's rules and the periodic reporting procedures.

Preparation of internal six-monthly progress reports and Periodic Management Report

Six monthly progress reports:

The six monthly report has been produced to present the activities and achievements of every Workpackage.

Moreover, the report also presents every partners' efforts in terms of person-months during the first six months. This is essential to keep a clear monitoring of partner effort and

commitment in the project, and proves a valuable asset to measure the quality of work against the effort spent by every team.

An online reporting tool was created to facilitate the collection of reporting contributions.

In addition, internal ACGT reporting is being conducted in-house through short statement of the WP leaders to present their activities and identify any potential issue.

Periodic Management Report and Periodic Activity Report:

All necessary documentation was uploaded on the BSCW server in order to help ACGT Partners proceed with this annual reporting comprising multiple documents:

Pre-filled Appendices and Forms C, templates for the audit certificate, ERCIM and European Commission Guidelines, Commission check-list, FAQs, guidelines for the PAR, Preparation of summary report on distribution of funding, financial report and consolidated Appendices.

Preparation of the next Detailed Implementation Plan

The Project Coordinator and the Technical Director have invited all Workpackage Leaders to prepare the work plan of their workpackage activities over the next 18 months, including information about deliverables, effort dispatch among partners and describing the main subtasks their WP encompasses.The activity is still under preparation and the new workplan will be submitted to the European Commission before the first Annual Review.

Financial Coordination

The third advance payment of the Community financial contribution was received by the Coordinator. The full amount was distributed to the contractors immediately.In the preparation of the financial statement composing the PMR, the coordination has prepared detailed guidelines and checklist to assist all the partner prepare the budget claims. ERCIM has carried out a permanent and final validation of each financial statement produced by the partners.

Monitoring of Partners efforts

The Project Coordinator will collect every six months the actual consumption of **person-months** of every partner institute across the different Workpackages. The person months tables are presented in a dedicated section of the **six-monthly reports**. These figures are analyzed and **compared against the expected (planned) person-months** declared in the work plan. The Project coordinator and the Technical Director will assess the relevance of the person months declared against the work done during the corresponding reporting period. The Management Board is informed of any major discrepancy between planned and declared effort allocation, which must systematically be justified by the partners and for every Workpackage concerned.

Follow up and validation of deliverables to be submitted

The ACGT project Management will ensure a continuous watch and monitoring of Deliverable preparation, to make sure that their submission are not delayed and that the contractual engagement of the project vis-à-vis the European Commission are respected.

	Deliverables in Chronological order		

Deliverable	Deliverable title	Delivery date	Status
D10.5	Design of an empirical survey on patients' perspectives and needs	T0+25	Submitted
D13.3	Specification of scenarios for the first integrated demonstrator of the ACGT platform	T0+27	Submitted
D1.1.4	Six-Monthly Progress Reports	T0+30	Submitted
D2.4	Report on additional user-driven scenarios in post-genomic clinical trials on Cancer	T0+30	Submitted
D5.4	Conceptual specification and a prototype for an ontology-based Clinical Data Management System and for the Trial Builder	T0+30	Submitted
D8.3	Report on the refinement and optimization of the algorithms and codes, and the initial clinical validation and adaptation of the "Oncosimulator".	T0+30	Submitted
D9.4	Semantic Integration in ACGT	T0+30	Submitted
D12.6	Review and extension of the ACGT clinical studies	T0+30	Submitted
D13.2	Intermediate evaluation report	T0+30	Pending
D14.4	First Workshop Training for end-users on ACGT Technologies & Methodologies (moved to month 30)	T0+30	Pending
D14.6	First Report on *ACGT* Portal usage, online training modules development and evaluation.	T0+30	Pending
D5.5	Initial model definition of an ACGT-specific Clinico-Genomic EHR	T0+32	Submitted
D6.4	The integrated ACGT analysis environment	T0+32	Submitted
D7.5	Demonstration of final mediation access tools and services	T0+32	Submitted
D4.4	Gridge-GridR integration	T0+33	Submitted
D11.4	Requirements and guidelines for developing secured ACGT services	T0+33	Pending
D12.7	Report on the local ACGT trial-specific biobanking activities	T0+34	Pending
D1.1.5	Six-Monthly Progress Reports	T0+36	Submitted
D1.1.6	Annual Progress Report	T0+36	Pending
D2.5	Report on requirements for an ontology submission system and for the selection of tools, software and	T0+36	Pending

	data within ACGT		
D3.2	The ACGT technical architecture: Final Specifications	T0+36	Pending
D6.5	Demonstrator of analytical services	T0+36	Submitted
D9.5	The final Workflow editing and enactment tools	T0+36	Pending
D11.5	Finalized ACGT security architecture	T0+36	Pending
D11.6	ACGT guide for administrative documentation of ACGT security and VO management	T0+36	Pending
D14.5	First Training Workshop for service providers on ACGT Technologies & Methodologies (moved to month 36)	T0+36	Pending
D15.4	Report on organisation of scientific events and participation in conferences	T0+36	Submitted
D16.4	Exploitation Plan v3 – this is an update report discussing the changes and additions, if any, made to the original exploitation plan (D16.1).	T0+36	Submitted
D3.3	Grid Interoperability report	T0+38	Pending
D7.6	Prototype of the Ontology Submission sub-system	T0+38	Submitted
D7.8	Introduction of a new CT in ACGT: A Case study	T0+38	Pending
D8.4	Report on the integration of the simulation services into the ACGT architectural framework	T0+38	Pending
D10.6.1	Draft of the results of the international empirical survey on parents of minor patients' perspectives and needs	T0+38	Submitted
D12.8	Report on the ACGT simulated trials	T0+38	Pending
D5.6	Guidelines and recommendations for open source database management systems to be used with the ACGT integration platform	T0+40	Pending
D10.7	Analysis of the most important Intellectual Property issues resulting from the chosen ACGT architecture	T0+40	Pending
D1.1.7	Six-Monthly Progress Reports	T0+42	Pending
D3.5	Final report on standards	T0+42	Pending
D4.5	ACGT Service Development and Deployment Framework.	T0+42	Pending

D6.6	Final specifications of service and workflow semantic data definitions	T0+42	Pending
D7.7	The ACGT Master Ontology (Updated MO based on new trials)	T0+42	Submitted
D8.5	Demonstration of the final version and validation of the ACGT Oncosimulator	T0+42	Pending
D10.6.2	Results of the international and national empirical survey on patients' and parents of minor patients' perspectives and needs	T0+42	Pending
D10.8	Risk analysis concerning the data security and data protection framework	T0+42	Pending
D13.4	Intermediate evaluation report	T0+42	Pending
D14.7	Second Training Workshop for end-users on ACGT Technologies & Methodologies	T0+42	Pending
D14.8	Second Report on ACGT Portal usage, online training modules development and evaluation.	T0+42	Pending
D15.5	Report and analysis of project dissemination activities	T0+42	Pending

Project Meetings (including WP technical meetings)

Regular meetings, either at a consortium level, or focus technical meetings and requirement gathering meetings were held regularly. This, we believe, has helped in creating the required "team spirit" for the successful implementation of the project. The list of events below shows the meetings held, their scope and a summary of results achieved.

Overview of the ACGT plenary technical project meetings:

- ACGT technical meeting, MILANO – BASEL, 5-10/2/08
- ACGT PMB meeting, IRAKLIO, 21-24/9/08
- ACGT PMB meeting, LAUSANNE, 17-19/11/08
- ACGT PMB meeting, BRUXELLES, 9-11/12/08
- ACGT consortium meeting, VIENNA, 26-29/1/09

In addition the following meetings were organized:

European Breast Cancer Conference-06 (Berlin 14/4/08)

ACGT hosted a workshop addressed at EBCC attendees. Approximately 80 delegates attended the various sessions with circa 50 of them providing their contact details and subsequently receiving the ACGT Newsletter. One observation was that while the medical/biology oriented presentations maintained audience interest, the technical/IT oriented ones did not fair so well, reflecting more the synthesis of the audience than the quality/content of the technical presentations themselves. Future efforts will need to match more closely the message with the expected audience.

ACGT – EORTC meeting, Brussels, 21/11/08

The contract with EORTC is now signed and the main points of the collaboration are as follows:

1. A review of the security infrastructure of ACGT by EORTC staff with a view to provide appropriate comments from an experienced group of end users (included in deliverable 13.2)
2. Provision of CRF from EORTC with the aim of improving the ACGT Master Ontology
3. Provision of data from a recently closed EORTC trial which has extensive clinical, imaging and biological data.
4. Provision of access to the protocol and CRF of the MINDACT trial so as to see the degree to which ACGT infrastructure meets the needs of this trial.

Presentation of ACGT infrastructure and project to the Thalassaemia International Foundation (TIF) in Nicosia (25-26/9/08).

TIF is interested in deploying a simple patient record system at 4-8 collaborating hospitals in Cyprus (to start with) and later on in other countries with which it has ties. The domain area of interest is of course beta-thalassaemia but the management of patient records is along the lines envisaged by ACGT. The presentation generated keen interest – in a recent

communication TIF have said that they want to move ahead but are short on funds and are currently looking at national and other funding options. We expect to have a clear position in Q3-Q4 of 2009.

ACGT-NeoBIG meeting

Partner JB arranged a meeting with the NeoBIG consortium to explore the potential for ACGT to be the platform of choice that will support BIG in its future work. Due to the confidential nature of this work, involved partners (ERCIM, FORTH, Custodix, Biovista, Lausanne, Saarland, Phillips, FHG) were requested to sign a NDA. Following the first meeting, an internal ACGT meeting was also held during the latest consortium meeting in Vienna (26-29/1/09). While in theory partners agreed that the ACGT platform is capable of providing the necessary solution, long term support and other requirements of BIG mean that an unequivocal 'Yes' at this point in time is not possible. ACGT members have decided to explore this internally and deliver an official position in due time.

Project Timetable and status

Although, there has been an initial delay in the start of the project of approximately 1-2 months, we can safely say that overall the project is running as scheduled. The management has asked for many activities to start even earlier than planned (provided there was adequate input from the activities they depend on). This has allowed the project to "catch-up". Today the only noticeable "problem" is the fact that we are pressed time-wise for the production, and internal review, of some Deliverables. In this perspective, the project will ask for a 6 months extension, without any additional funding, in order to finalise the project under optimal conditions.

As a general remark, we observe that quite a few activities are ahead of schedule (e.g. the biomedical grid layer, Workflow Editor, GridR, etc). On the other hand some other activities are slightly behind schedule, mainly in the timely production of the Deliverables rather than performing the work itself.

We are aware of the criticality of the ObTiMA related activities to the success of the whole project. At the consortium meeting in Milan (Feb. 2008) we have discussed alternatives and possibilities for putting more resources into this task. Additional resources have already been put into the task by the main developers (FhG/IBMT) who withdrew their participation in other activities of WP5 (i.e. post-genomic EHR). The decision was taken to review the situation after the annual review meeting.

The following barchart represents the project timetable, with indications of tasks running ahead of schedule and tasks behind schedule.

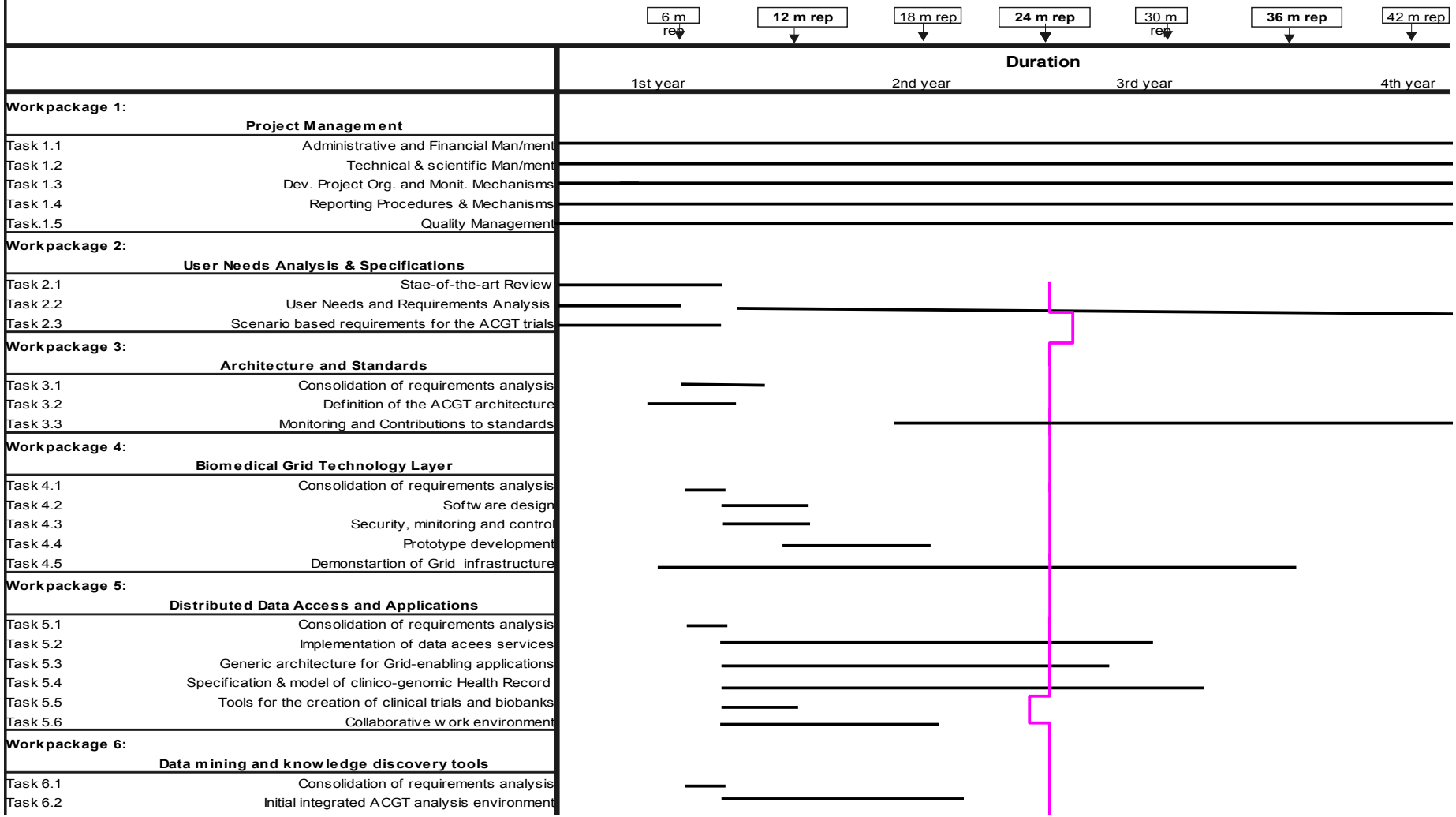
PROJECT BARCHART and STATUS

Acronym: ACGT

Contract Nº: FP6-026996

(to be frontlined to show status at project reviews)

(any previous revisions to be attached if original plans are revised)



Coordination activities

A number of coordination activities have been undertaken during the reporting period. Specifically:

- The most important coordination activities of the period relate to discussion with user organizations with respect to their involvement and/or adoption of the ACGT set of tools and technologies. These included both EORTC and SIOP. We have concluded a formal collaboration with EORTC, which we believe will result in significant benefits for the project.
- We continue to monitoring of developments in EGEE, and are constantly exploring possibilities for utilizing EGEE's infrastructure as its biomedical grid layer and other forms of concertation. We regularly participate in EGEE scientific and concertation events.
- Met with various technical contributors (imaging workspace) to the caBIG initiative, discussing their architectural choices and exploring possibilities of collaboration.
- Discussed, through email and phone calls, with the UK's Cancer Grid. Have reached initial agreement wrt to potential concertation. The first physical meeting with its technical director is planned to take place in April 2008 and a technical concertation workshop is planned for July 2008, in Oxford.
- Held a meeting with the "sister project" @nurist. Have jointly organized a scientific session during the Healthinf 2008 conference, in Madeira, January 2008. Reached initial agreement to collaborate on the domain of ontology development, with an ultimate objective to exhibit interoperable ontologies in their two domains of work.
- Met, discussed and formed a strategic alliance with the Center for the development of a virtual tumour (CViT, www.cvit.org) with the objective to collaborate on the domain of developing coherent "in-silico models" of tumor growth and its response to theatment.
- We have also planned joint scientific events with other projects, such as the (a) HARTFAID Specific Targeted Project - (Full Title: A Knowledge based platform of services for supporting medical-clinical management of Heart Failure within elderly population), (b) SMARTHEALTH Integrated Project – (Full Title: Smart Integrated Biodiagnostic Healthcare), and (c) the "LOCCANDIA" Targeted Research Project - (Full Title: Lab – On – Chip profiling for CANcer DIAgnosis). Common areas for potential concertation and exchange of experiences have been identified (i.e. semantic services and metadata (SMARTHEALTH), re-use of IS (Proteiomics IS with LOCCANDIA) and ontology engineering (HARTFAID)).
- Through ERCIM, ACGT remains an "observing participant" of the Virtual Physiological Human Network of Excellence (VPH NoE) under FP7 and the wider VPH Initiative.
- ACGT is also getting involved (through its partner PSNC) in the GIN initiative (Grid Interoperability Now), an activity held in the framework of the OGF work, under the umbrella of the GIN working group.

Other Issues

Ethical issues are of paramount importance for the project, since it will be handling sensitive personal, including genetic, data.

The project is devoting substantial resources for the analysis of the legal requirements to be fulfilled for lawfully establishing an integrated Clinico-Genomic ICT environment employing data extracted from human tissues. Special emphasis is laid on the issues of data protection and privacy.

The starting point of the analysis is the European Data Protection Directive 95/46 EC, which introduces rules applicable to every processing of personal data and sensitive data on a European level. As every EU Member State has to implement the regulations of the Data Protection Directive into national law, for an EU- wide project like ACGT, this Directive is the common legal basis for all participating states. Furthermore, the relevant sections of the Directive on Electronic Commerce 2000/31/EC are analysed.

As genetic data is very sensitive data, which holds information not only about the data subject itself but also about his or her relatives, possible diseases, etc., the processing of this kind of data is only possible under special requirements.

An elaborate data protection framework has been set up for ACGT, which consists mainly of three parts. First, an ACGT Data Protection Board, which is the central data controller within ACGT as well as a legal body able to conduct contracts regarding data protection on behalf of ACGT. Second, a Trusted Third Party, which is responsible for the pseudonymization of the patient's genetic data and which will also be the keeper of the pseudonymization key to re-identify the patient concerned. Therefore the patient's genetic data is de-facto anonymous for users and participants of ACGT not having the link. Third, contracts between all participating hospitals, research units or other users of the genetic data and ACGT have bben developed and must be concluded in order to ensure confidentiality, data security and compliance with data protection legislation.

Annex: Plan for using and disseminating the knowledge

Exploitable knowledge and its Use

The project, at its current stage of implementation, has produced a number of results that as an integrated platform (which is the central objective of the project) or as individual tools, systems or services could be exploited.

Detailed plans for potential commercial or otherwise exploitation have not been drafted. Nevertheless, the project is seriously focusing on this issue and is devoting significant efforts in the activities of the corresponding Workpackage.

Dissemination of knowledge

A significant number of dissemination activities have taken place. These are listed in the sections that follow.

Detailed list of ACGT dissemination and technical meetings

Title	Place and Date	Main conclusions
ACGT Consortium Meeting	Milan, Italy 5-7 February 2008	Discussions about the next review meeting and its end-to-end demonstrators. Additional management related issues were discussed, such as the next description of work, budget modifications, etc.
RIRAAF Kickoff Meeting	Spain (Malaga), 1st February 2008	Plenary meeting. Presentation of the web-services and repositories strategies to manage clinical and medical data. Speaker: Oswaldo Trelles. http://www.bitlab-es.con/riraaf
ObTiMA and Trial Outline Builder	Homburg, 1st-3rdFebruary 2008	Meeting with Micke Kuwahara and Jun Fujima from Hokaido University and Norbert Graf, Alexander Hoppe from UdS and Fatima Schera and Gabriele Weiler from Fraunhofer St. Ingbert to coordinate the work for the Trial Outline Builder
Ontology meeting	February 14th2008	Local meeting with IFOMIS regarding ObTiMA and Master Ontology, Homburg, Germany, (participants:

Title	Place and Date	Main conclusions
		USAAR, IFOMIS)
VIII Jornadas de BioinformÃ¡tica	Spain (Valencia), 13-15th February 2008	Developments in bioinformatics towards biomedical applications or systems biology and workshop on training of Bioinformatics. Speaker: Johan Karlsson. http://cbbl.imim.es:8080/RNB/events-1/jornadas/home
BioHackathon	Japan (Tokyo), 11-15th February 2008	This BioHackathon is focused in web services in different domains (providers, developers and clients) Speaker: Oswaldo Trelles. http://hackathon.dbcls.jp/
Meeting with I-BFM	March 5th2008	Discussion about role of ACGT in Leukaemias, Hannover, Germany, (participants: N. Graf)
Meeting with the SIOP Nephroblastoma Study Group and basic researchers proposing ObTiMA for SIOP Renal Tumour Study Group (SIOP-RTSG)	March 12th – 13th 2008 Chamonix, France	, (participants: N. Graf, members of SIOP-RTSG)
Integration of Hokkaido recipesheet with UvA Visualization services	Amsterdam, March 17 to 21 2008	People involved: Aran Lunzer, Paul Melis, Robert Belleman.
VO Management Workshop	Merelbeke, 27th March	Requirements and needs for VO management in ACGT
ACGT Technical Meeting	Berlin, Germany, 14 April 2008	Organization and preparation for the next reviewâ€™s demonstrator. The minutes are available at https://bscw.ercim.org/bscw/bscw.cgi/d421856/ACGT_Berlin_TM_Minutes.doc
GPOH Strukturtagung	Hannover, 17th-18th of April 2008	Presentation of ObTiMA to the German Paediatric

Title	Place and Date	Main conclusions
		Oncologists, dissemination activity, great interest in ObTiMA, new clinico-genomic trials in the German Paediatric Oncology want to use ObTiMA for future trials (e.g. Rhabdoid tumour Registry 2008, Stem cell transplantation Registry)
MultiVis meeting,	Twente University, April 22 th 2008.	People involved: Robert Belleman.
Workshop with LESS (Long Effect surveillance Study)	Homburg, 23rdof April 2008	Discussion about the use of ObTiMA for analysing cardiotoxicity in the SIOP Wilms Tumour trial of GPOH
SIOP Nephroblastoma Study conference	Milano, 28th 29th of April 2008	Part of the meeting was the discussion of the IT infrastructure for the upcoming nephroblastoma trials of SIOP. Presentation of ObTiMA and ACGT by Norbert Graf, great interest for using ObTiMA, if maintenance is guaranteed
German Syrian Medical Conference	4th-7thof May 2008 in Aleppo, Syria	Presentation of ACGT and ObTiMA by Norbert Graf as an IT infrastructure that will facilitate clinico-genomic trials in cancer
ACGT Technical Meeting	Eindhoven, Netherlands, 8-9 May 2008	Integration meeting for the next review demonstrator
GPOH Meeting	16th-17thof May 2008, Berlin	Multiple discussions with Paediatric Oncologists and chairmen of clinical trials regarding ObTiMA for upcoming clinical trials in Paediatric Oncology in Germany; dissemination activity done by Norbert Graf
ACGT Review Meeting	Eindhoven, Netherlands, 26 (preparation), 27-28 May 2008	Review

Title	Place and Date	Main conclusions
OncoSimulator meeting, May 29th, Amsterdam	Amsterdam, May 29th2008	People involved: Georgios Stamatakos, Andrea Sottoriva, Peter Sloot, Robert Belleman.
Meeting of the IT Group for Stem cell transplantation of the German Paediatric Oncology Society (GPOH)	17thof June 2008, Frankfurt	Discussion of ACGT and ObTiMA for the use in clinical trials regarding Stem cell transplantation in childhood in Germany
Computer Based Medical Systems (CBMS) 2008	Finland , 17-19th June 2008	International forum for discussing the latest results in the field of computational medicine. Speaker: Johan Karlsson. http://cbms2008.it.jyu.fi/
Further development of ObTiMA	3rdof July 2008, Homburg	Coordination in the development of the Ontology for ObTiMA, Meeting between UdS (Norbert Graf, Alexander Hoppe, Jochen BÃ¶hm) and Fraunhofer St. Ingbert (Gabriele Weiler, Fatima Schera)
International Conference on Telecommunications and Multimedia (TEMU-08)	Greece , 16-18th July, 2008	International conference to present new and original research results and the latest state-of-the-art in Telecommunications and Multimedia. Speaker: Oswaldo Trelles. http://www.temu.gr/2008/
ACGT and ObTiMA for Cardiology	28thof July 2008, Homburg	Meeting between the Competence Centre for Paediatric Cardiology, Berlin and ACGT people of UdS. The IT-Infrastructure and ObTiMA was presented by Norbert Graf. The Competence Centre for Paediatric Cardiology has great interest to use this infrastructure for their clinical research. They do not want to build an IT Infrastructure by their own, if an existing one

Title	Place and Date	Main conclusions
		fulfils all their requirements.
WP 15 meeting Spanish National Institute for BioInformatics (INB)	July 2008, Valencia	
Working on the specification of the Trial Builder of ObTiMA	August 11th-21st 2008, Sapporo, Japan	Meeting with Prof. Tanaka, Dr. Fujima, Dr. Lunzer, Mike Kuwahara from University of Hokkaido
"Distributed Data Analysis using R" at 2008 UserR conference	12 August 2008, Dortmund, Germany.	http://www.statistik.uni-dortmund.de/useR-2008/tutorials/rueping.html
Meeting with SIOP-RTSG and radiotherapists	September 8th -10th, 2008, London, UK	Proposing ObTiMA for the next SIOP nephroblastoma trial
ACGT Consortium Meeting	Heraklion, Crete, 22-24 September 2008	Discussions on the various implementation sides of the Project. Review of the status and problems of all â€œcurrentâ€ ▪ trials and discussions about the opportunities for new ones.
Obtima security meeting	October 31st- November 5th 2008,	ObTiMA Meeting regarding Trial Outline Builder, Ontology Viewer, Secure access and User Roles and Rights, St. Ingbert, Germany,
ACGT Technical Meeting	Lausanne, Switzerland, 18-19 November 2008	Organization and preparation for the next reviewâ€™s demonstrator.
ObTiMA Meeting	October 31st November 5th2008, St. Ingbert, Germany,	Technical meeting to introduce the technical action regarding ObTiMa
WP11 meeting with Jules Bordet	21th November, Brussels	EORTC will review the security architecture
Meeting with the SIOP-RTSG	November 29th30th2008, Amsterdam, The Netherlands	Group for further discussing the IT-Infrastructure for the next nephroblastoma trial

Title	Place and Date	Main conclusions
ACGT Review Meeting	Brussels, Belgium, 8-9 (preparation), 10 December 2008	Review
ObTiMA Meeting	January 21st2009, Homburg/ St. Ingbert, Germany	participants: USAAR, Fraunhofer IBMT, University of Madrid
ACGT Consortium Meeting	Vienna, Austria 28-29 January 2009	Discussions about the next (and final) implementation period. ACGT User training and informal evaluation ▪ workshop.

Publications:

1. Kaste SC, Dome JS, Babyn PS, Graf N, Grundy P, Godzinski J, Levitt GA, Jenkinson H: Wilms Tumor: Prognostic factors, Staging, Therapy and Late Effects, Ped Radiology 38:2-17, 2008

2. Reinhard H, Reinert J, Beier R, Furtwängler R, Alkassar M, Rutkowski S, Frühwald M, Koscielniak E, Leuschner I, Kaatsch P, Graf N: Rhabdoid tumors in children: Prognostic factors in 70 patients diagnosed in Germany. Oncology Reports 19: 819-823, 2008

3. Graf N, Desmedt C, Buffa F, Kafetzopoulos D, Forgó N, Kollek R, Hoppe A, Stamatakos G, Tsiknakis M: Post-genomic clinical trials – the perspective of ACGT. Ecancermedicalscience 1: DOI: 10.3332/eCMS.2007.66, 2008

4. M. Zervakis, M.E. Blazadonakis, V. Danilatou, G. Tsiliki, M. Tsiknakis, D. Kafetzopoulos, Outcome Prediction Based on Microarray Analysis: A Critical Perspective on Methods, BMC Bioinformatics 2009, 10:53.

5. S. Sfakianakis, M. Blazantonakis, I. Dimou, M. Zervakis, M. Tsiknakis, G. Potamias, D. Kafetzopoulos, D. Lowe, Decision Support Based on Genomics: Integration of Data and Knowledge Driven Reasoning, International Journal of Biomedical Engineering and Technology, Special Issue on Decision Support in Medicine (accepted).

6. M. Brochhausen, G. Weiler, L. Martin, C. Cocos, H. Stenzhorn, N. Graf, M. Doerr, M. Tsiknakis, B. Smith, Applications of the ACGT Master Ontology on Cancer, 4th International Workshop On Semantic Web & Web Semantics (SWWS '08), 9-14th November 2008, Monterrey, Mexico.

7. A. Bucur, A. Persidis, D. Kafetzopoulos, M. Tsiknakis, L. Koumakis, V. Danilatou, The need for integration of genomic information in a future EHR: An ACGT case study. In proceedings of the 9th International HL7 Interoperability Conference (IHIC 2008), Heraklion, Crete, 8-11 October 2008.

8. M. Zervakis, ME. Blazadonakis, A. Banti, D. Kafetzopoulos, V. Danilatou, M. Tsiknakis, Performance Validation of Microarray Analysis Methods. In proceedings of the 8th IEEE

International Conference on Bioinformatics and BioEngineering (IEEE BIBE 2008), Athens, Greece, 8-10 October 2008.

9. A. Analyti, E. Christodoulou, V. danilatou, M. Iannou, D. Kafetzopoulos, M. Kafousi, A. Kanterakis, H. Kondylakis, L. Koumakis, D. Manakanatas, T. Margaritis, G. Papaginnakis, G. Potamias, E. Sanidas, E. Stathopoulos, D. Tsiftis, M. Tsiknakis, G. Tsiliki, S. Vassilaros, A new gene expression signature related to breast cancer estrogen receptor status. In proceedings of the 8th IEEE International Conference on BioInformatics and BioEngineering (IEEE BIBE 2008), Athens, Greece, 8-10 October 2008.

10. A. Anguita, L. Martín, J. Crespo, M Tsiknakis, An Ontology Based Method to Solve Query Identifier Heterogeneity in Post-Genomic Clinical Trials, Proceedings of MIE2008 – The XXIst International Congress of the European, Federation for Medical Informatics, Studies in Health Technology and Informatics, Volume 136, pp 3-8, 2008, S. K. Andersen, et al (Eds), IOS Press, 2008.

11. Wittmann S, Wunder C, Zirn B, Furtwängler R, Graf N, Gessler M: Wilms Tumors: New prognostic markers revealed by evaluation of genes correlated with clinical parameters in Wilms tumors. Genes Chromosomes Cancer 47:386-395, 2008

12. Fuchs J, Szavay P, Luithle T, Furtwangler R, Graf N: Surgical implications for liver metastases in nephroblastoma-Data from the SIOP/GPOH study.Surg Oncol 17:33-40, 2008

13. Schenk JP, Graf N, Günther P, Ley S, Göppl M, Kulozik A, Rohrschneider WK, Tröger J.: Role of MRI in the management of patients with nephroblastoma. Eur Radiol 18:683-691, 2008

14. van den Heuvel-Eibrink MM, Grundy P, Graf N, Pritchard-Jones K, Bergeron C, Patte C, Peter E, van Tinteren H, Rey A, Hutton C, Anderson JR, de Kraker J: Characteristics and Survival of 750 Children with a Renal Tumour in Infancy (0-6 months). A collaborative retrospective Study of the SIOP/GPOH/SFOP, NWTSG, and UK-CCSG. Pediatr Blood & Cancer 50:1130-1134, 2008

15. Zils K, Furtwänler R, Reinhard H, Alkassar M, Graf N: Consultation within SIOP 2001/ GPOH as part of the competence centre for nephroblastoma. Klin Pädiatr 220:183-188, 2008

16. Wetli SC, Leuschner I, Harms D, Rufle A, Foerster A, Bihl M, Graf N, Furtwaengler R, Paulussen M, Briner J, Tornillo L, Mihatsch MJ, Zlobec I, Bruder E: KIT, PDGFR ▪ and EGFR Analysis in Nephroblastoma. Virchow Archiv 452:637-650, 2008

17. Furtwängler R, Schenk JP, Alkassar M, Leuschner I, Rübe C, von Schweinitz D, Gessler M, Graf N: Das Nephroblastom und andere pädiatrische Nierentumoren. Pädiat Prax 72:59-77, 2008

18. Reinhard H, Schmidt A, Furtwängler R, Leuschner I, Rübe C, von Schweinitz D, Zoubek A, Niggli F, Graf N: Outcome of relapses of nephroblastoma in patients registered in the SIOP/GPOH trials and studies. Oncology Reports 20:463-467, 2008

19. Royer-Pokora B, Weirich A, Schumacher V, Uschkereit C, Beier M, Leuschner I, Graf N, Autschbach F, Schneider D, von Harrach M: Clinical relevance of mutations in the Wilms tumor suppressor 1 gene WT1 and the cadherin-associated protein ß1 gene CTNNB1 for patients with Wilms tumors. Results of long-term surveillance of 71 patients from

International Society of Pediatric Oncology Study 9/Society for Pediatric Oncology. Cancer 113:1080-1089, 2008

20. Brochhausen M, Weiler G, Cocos C, Stenzhorn H, Graf N, Doerr M, Tsiknakis M: The ACGT Master Ontology on Cancer - a New Terminology Source for Oncological Practice, In: Puuronen S, Pechenizkiy M, Tsymbal A, Lee DJ (eds.): Proceedings of the 21st IEEE International Symposium on Computer-Based Medical Systems, IEEE Computer Society, Los Alamitos, pp324-329, 2008, DOI Bookmark: http://doi.ieeecomputersociety.org/10.1109/CBMS.2008.17

21. Kolokotroni EA, Stamatakos GS, Dionysiou D, Georgiadi ECh, Desmedt C, Graf N: Translating Multiscale Cancer Models into Clinical Trials: Simulating Breast Cancer Tumor Dynamics within the Framework of the "Trial of Principle" Clinical Trial and the ACGT Project. Proceedings of the 8th IEEE International Conference on Bioinformatics and Bioengineering (BIBE 2008), Athens, Greece, 8-10 October 2008. IEEE Catalog Number: CFP08266, ISBN: 978-1-4244-2845-8, Library of Congress: 2008907441, Paper No. BE-2.1.1, length: 8 pages (in electronic format)

22. Georgiadi ECh, Kolokotroni EA, Dionysiou DD, Graf N, Hoppe A, Uzunoglu NK, Stamatakos GS: Simulating the response of Nephroblastoma Tumor to chemotherapy in the clinical context. Proceedings of the 3rd International Advanced Research Workshop on In Silico Oncology, Istanbul, Turkey. Sept. 23-24, 2008: pp 27-30

23. Georgiadi ECh, Stamatakos GS, Graf N, Kolokotroni EA, Dionysiou DD, Hoppe A, Uzunoglu NK: Multilevel Cancer Modeling in the Clinical Environment: Simulating the Behavior of Wilms Tumor in the Context of the SIOP 2001/GPOH Clinical Trial and the ACGT Project. Proceedings of the 8th IEEE International Conference on Bioinformatics and Bioengineering (BIBE 2008), Athens, Greece, 8-10 October 2008. IEEE Catalog Number: CFP08266, ISBN: 978-1-4244-2845-8, Library of Congress: 2008907441, Paper No. BE-2.1.2, length: 8 pages (in electronic format).

24. Brochhausen M, Weiler G, Martin L, Cocos C, Stenzhorn H, Graf N, Dörr M, Smith B, Tsiknakis M: Applications of the ACGT Master Ontology on Cancer. In: R. Meersman, Z. Tari, P. Herrero (eds.): OTM 2008 Workshops, LNCS 5333, 1046-1055, 2008

25. Fuchs J, Kienecker K, Furtwängler R, Bürger D, Thüroff JW, Hager J, Graf N: Surgical Aspects in the treatment of patients with unilateral Wilms´tumor – a report by the SIOP 93-01/ German Society of Pediatric Oncology and Hematology, Ann Surg accepted 2008

26. Brochhausen M, Dörr M, Smith B, Weiler, G, Graf N, Tsiknakis M: Implementation of an Ontology-Based Clinical Information System: A case study. 9th International HL7 Interoperability Conference on Friday, October 10, 11:00 – 11:30 & 16:00 – 16:30 and Saturday, October 11, 11:00 – 11:30 at the Poster Session, Crete October 2008

27. Graf N, Hoppe A, Desmedt Ch, Lunzer A, Belleman R, Jacques J, Tsiknakis M, Stamatakos G : The impact of 'in silico' oncology on clinical decision-making in the context of nephroblastoma. Klin Pädiatr submitted 2009

28. Monnier Y, Farmer P, Bieler G, Imaizumi N, Sengstag T, Alghisi GC, Stehle JC, Ciarloni L, Andrejevic-Blant S, Moeckli R, Mirimanoff RO, Goodman SL, Delorenzi M, Rüegg C. "CYR61 and alphaVbeta5 integrin cooperate to promote invasion and metastasis of tumors growing in preirradiated stroma.", Cancer Res. 2008 Sep 15;68(18):7323-31.

29. 22. Wirapati P, Sotiriou C, Kunkel S, Farmer P, Pradervand S, Haibe-Kains B, Desmedt C, Ignatiadis M, Sengstag T, Schütz F, Goldstein DR, Piccart M, Delorenzi M. "Meta-analysis of gene expression profiles in breast cancer: toward a unified understanding of breast cancer subtyping and prognosis signatures." Breast Cancer Res. 2008;10(4):R65. Epub 2008 Jul 28.

Key Note Addresses in International Conferences

1. M. Tsiknakis, *The European Cancer Informatics Landscape: Challenges for the biomedical informatics community*. The 8th IEEE International Conference on Bioinformatics and Bioengineering (BIBE 2008), Athens, Greece, 8-10 October 2008.

Talks

1. Graf N: Clinical requirements regarding In Silico Oncology. Lecture from the European Union ICT BIO 2008 Conference (Oct. 23-24, 2008). Ecancermedicalscience; ecancer.tv 2009; Video: http://www.ecancermedicalscience.com/tv/?play=120

2. Brochhausen M (2008) Ontologie-basierte IT-Systeme für die klinische Forschung. Institut für Pathologie, Johannes Gutenberg-Universität, Mainz, 28 October, 2008, 5 pm.

3. Brochhausen M (2008) Exploiting Ontologies in Clinical Research and Practice. Nation Center for Electronic Patient Records (NSEP), Trondheim, Norway.

4. Brochhausen M (2008) How Can We Utilise Ontologies to Maximise Our Data/Knowledge Base? 3rd Annual DKI (Discovery Knowledge & Informatics), Brussels, Belgium, 15-17 September, 2008.

5. Brochhausen M, Brochhausen C, Kirkpatrick CJ (2008) Using Formal Ontology in Analyzing Complex Systems in Pathology - Data Integration and Standardization. 92. Jahrestagung der Deutschen Gesellschaft für Pathologie e.V., May 16, Berlin, Germany.

6. Brochhausen M (2008) Biomedical Ontologies: Principles and Perspectives of Exploitation – A critical review. Special Session on Personalised Medicine: Current Trends and Scientific Challenges, TEMU 2008, International Conference on Telecommunications and Mutlimedia, Ierapetra, Greece, 16.07.2008.

7. Brochhausen M, Weiler G, Cocos C, Stenzhorn H, Graf N, Doerr M, Tsiknakis M (2008) The ACGT Master Ontology on Cancer - a New Terminology Source for Oncological Practice, IEEE CBMS 2008: 21st IEEE International Symposium on Computer-Based Medical Systems, Jyväskylä, Finland, June 17-19, 2008.

8. Georgios Stamatakos "Fundamentals of multiscale modelling"Introductory talk in ICT BIO17/12/2008. D 2008-First transatlantic workshop on multiscale cancer modelling.rgios Stamatakos "Fundamentals of multiscale modelling" Introductory talk in ICT BIO Third International Advanced Research Workshop on In Silico Oncology: Advances and Challenges (3rd IARWISO), September 23-24, 2008 Istanbul, Turkey.O17/12/2008
9. 1st Transatlantic Workshop on Multiscale Cancer Modelling: an ICT BIO event coorganized by NCI and EC, October 23-24, 2008 Brussels, Belgium
10. D.D.Dionysiou,G. S.Stamatakos, D. Gintides, N. Uzunoglou, K. Kyriaki. "Critical parameters determining standard radiotherapy treatment outcome for glioblastoma multiforme: a computer simulation", Open Biomedical Engineering 2, 43-51, 2008.

11. E. A. Kolokotroni, G. S. Stamatakos, D. D. Dionysiou, E. Ch. Georgiadi, Ch. Desmedt, N. M. Graf, "Translating Multiscale Cancer Models into Clinical Trials: Simulating Breast Cancer Tumor Dynamics within the Framework of the "Trial of Principle" Clinical Trial and the ACGT Project.," Proc. 8th IEEE International Conference on Bioinformatics and Bioengineering (BIBE 2008), Athens, Greece, 8-10 Oct. 2008. IEEE Catalog Number: CFP08266, ISBN: 978-1-4244-2845-8, Library of Congress: 2008907441, Paper No. BE-2.1.1, length: 8 pages (in electronic format) 2008.
12. E. Ch. Georgiadi, G. S. Stamatakos, N. M. Graf, E. A. Kolokotroni, D. D. Dionysiou, A. Hoppe, N. K. Uzunoglu, "Multilevel Cancer Modeling in the Clinical Environment: Simulating the Behavior of Wilms Tumor in the Context of the SIOP 2001/GPOH Clinical Trial and the ACGT Project," Proc. 8th IEEE International Conference on Bioinformatics and Bioengineering (BIBE 2008), Athens, Greece, 8-10 Oct. 2008. IEEE Catalog Number: CFP08266, ISBN: 978-1-4244-2845-8, Library of Congress: 2008907441, Paper No. BE-2.1.2, length: 8 pages (in electronic format) 2008.
13. D. Kyriazis, A. Menychtas, D. Dionysiou, G. Stamatakos,T. Varvarigou, "Clinical Trial Simulation in Grid Environments," Proc. 8th IEEE International Conference on Bioinformatics and Bioengineering (BIBE 2008), Athens, Greece, 8-10 Oct. 2008. IEEE Catalog Number: CFP08266, ISBN: 978-1-4244-2845-8, Library of Congress: 2008907441, Paper No. BI-1.2.1, length: 6 pages (in electronic format) 2008.
14. D. D. Dionysiou and G. S. Stamatakos, "Glioblastoma Multiforme Response to Radiotherapy: Critical Parameters and In Silico Trials," Proceedings of the 3rd International Advanced Research Workshop on In Silico Oncology, Istanbul, Turkey, Sept. 23-24, 2008.Edited by G. Stamatakos and D. Dionysiou, pp.13-16, 2008
15. E. Ch. Georgiadi, E. A. Kolokotroni, D. D. Dionysiou, N. M. Graf, A. Hoppe, N. K. Uzunoglu and G. S. Stamatakos, "Simulating the Response of Nephroblastoma Tumor to Chemotherapy in the Clinical Context," Proceedings of the 3rd International Advanced Research Workshop on In Silico Oncology, Istanbul, Turkey, Sept. 23-24, 2008. Edited by G.Stamatakos and D. Dionysiou pp.27-30, 2008.
16. E. A. Kolokotroni, E. Ch. Georgiadi, D. D. Dionysiou and G. S. Stamatakos, "A 4-D Simulation Model of Tumor Free Growth and Response to Chemotherapy in Vivo: The Breast Cancer Case," Proceedings of the 3rd International Advanced Research Workshop on In Silico Oncology, Istanbul, Turkey. Sept. 23-24, 2008. Edited by G.Stamatakos and D. Dionysiou pp. 31-34, 2008.
17. S. G. Giatili, G. S. Stamatakos, D. D. Dionysiou, E. A. Kolokotroni, E. Ch. Georgiadi, "Geometrical and Mechanical Aspects of Tumor Growth and Response to Chemotherapeutic Schemes in the Context of the ACGT Oncosimulator," Proceedings of the 3rd International Advanced Research Workshop on In Silico Oncology, Istanbul, Turkey, Sept. 23-24, 2008. Edited by G. Stamatakos and D. Dionysiou pp.35-37, 2008
18. T.Athanaileas, A. Menychtas, D.Dionysiou, G. Stamatakos, D. Kaklamani, T.Varvarigou, I. Venieris and N. Uzunoglu "Applying Grid Computing Technologies to In Silico Oncology," Proceedings of the 3rd International Advanced Research Workshop on In Silico Oncology,Istanbul, Turkey. Sept. 23-24, 2008,Edited by G. Stamatakos and D. Dionysiou pp. 41-43, 2008
19. D.D.Dionysiou, G.S.Stamatakos, T.Athanaileas, A.Menyxtas, D.Kaklamani, T.Varvarigou, N.K.Uzunoglu “In silico simulation of a clinical trial concerning tumour response to radiotherapy”, in American Institute of Physics Conference Proceedings 1060, pp.94-97, 2008.

Publishable results

A number of publishable results are available at the current implementation phase of the project.

These include:

- ACGT Master Ontology on Cancer.
- The GridR platfrm
- ObTiMA, the Ontology based Trial Management System
- The Workflow editor and workflow enactment services
- The Oncosimulatror platform
- The Ontology Viewer application
- The ACGT Semantic Mediator
- CAT (The Custodix Anonymization Tool)

Exploitable Knowledge Overview table

Exploitable Knowledge (description)	Exploitable product(s) or measure(s)	Sector(s) of application	Timetable for commercial use	Owner & Other Partner(s) involved
Novel algorithms for the cytokinetic and mitotic potential initialization of an imageable real tumour.	Corresponding simulation code	Basic science. Clinical sector.	Following completion of the clinical adaptation, optimization and validation procedure.	ICCS (up to now)
The entire simulation module	Corresponding simulation code	Basic science. Clinical sector.	Following completion of the clinical adaptation, optimization and validation procedure.	ICCS (up to now)
Clinical methodologies for in silico oncology.	Corresponding protocols for model validation etc.	Clinical sector	Following completion of the clinical adaptation, optimization and validation procedure.	USAAR (up to now)
Technological modules and integration.	Corresponding codes	Clinical sector.	Following completion of the clinical adaptation, optimization and validation procedure.	UvA, PSNC, UoH, FhG, INRIA, ICCS

Project Logo and public Web Site

The public web site of the project can be found at: http://eu-acgt.org/

The project logo is as shown below: