



PROJECT INTERIM REPORT

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1. Work progress and achievements during the period

1.1 Work Package 1: Project Management

Regarding Work Package 1 reference is made to section 2 “Project Management” following the individual work package descriptions.

1.2 Work Package 2: User Needs and Requirements

Main objectives of this WP

WP2 elaborates on the user needs and requirements for the proposed technological and clinical research infrastructure to develop an environment that is able to run hypermodels composed of existing and newly developed models by different end users (e.g. clinicians) with the goal to drive common clinical practise to preventive, predictive and participate medicine. This will provide the clinical perspective of the project and will take into account the state of the art, the state of research and the state of practice in the healthcare domains addressed by the project. This WP will address the needs for developing secure and consistent hypermodels and it will address the technological requirements (in conjunction with all other WPs) from a clinical application standpoint facilitating VPH research. The project will take into account existing infrastructures already developed for VPH like the p-medicine and the VPH-share infrastructure dealing with heterogeneous data and models. As requirements might change during the evolution of the project, the specification of user needs and requirements will continuously be updated.

As the VPH vision suggests the creation of repositories where a huge number of models are stored that describe and simulate different physiological processes, interoperability issues between these models are of utmost importance. Knowledge management models are needed to cope with this extreme complexity to build new integrative models. This WP will investigate the following:

1. Which models exist and how they can be accessed and used;
2. Which metadata do exist for these models and for models in general
 - a. regarding annotation and
 - b. interoperability issues;
3. What kind of data are needed to execute models;
4. Which ontologies are available and needed for proposed data, tools and models;
5. Which markup languages do exist that can be used for building hypermodels.

In this WP user requirements and specifications for the interaction with existing infrastructures will be defined and applicable use cases for the system validation will be developed within the clinical domains of the project. In case of usage of hypermodels within clinical trials GCP compliance will be addressed and solutions provided. The certification of tools and hypermodels is beyond the scope of this project. Nevertheless actions will be defined to allow seamless integration in daily clinical practice

Active tasks in this reporting period:

- T2.1, State of the Art Knowledge for Building Hypermodels (M1-8)

- T2.2, Scenario based user needs and requirements (M1-8)
- T2.3, Requirements for enhancing hypermodels beyond the domain of cancer (M1-18)

Summary of progress achieved towards objectives

FORTH initiated the discussion regarding the state of the art knowledge for building hypermodels, which also continued on the plenary meeting that was hosted on FORTH's premises. This process is being documented in the deliverable D2.1, which is due on M8. Use cases and scenarios are under development for the different cancer domains of the project. ICCS created the respective template. Custodix critically followed up the development of scenarios under security issues. It is expected that at the end of M8 deliverable D2.2 will be finalized and submitted by USAAR. Both deliverables are prepared and written by all partners of WP2. All clinical partners did start to collect data from the different cancer domains, including clinical data, imaging data, and molecular data. USAAR started discussions about possible interactions with the *p-medicine* environment. ICCS has had initial discussions with USFD regarding the possible reuse of the hypermodeling infrastructure (approach) by the musculoskeletal modelling community.

Summary of details for each task

- **Task 2.1, State of the art knowledge for building hypermodels:** FORTH lead this task and they have organized a series of discussions through emails and Skype teleconferences for collaboration, interaction and feedback. FORTH is preparing the deliverable D2.1 (due in M8), which focuses on the state of the art knowledge for building hypermodels. Initial discussions with the consortium converge on approaching the SOA through three distinct viewpoints: a) the systems biology/clinical, b) the engineering design and c) the software architecture focusing on semantic interoperability. Critical questions have been defined and were further discussed in the plenary meeting (held on 17, 18 October at FORTH premises). ICCS participated in the discussions related to deliverable D2.1 and its preparation. In this task USAAR started the collaboration with p-medicine including questions of infrastructures, modularity and granularity of tools, the ethical and legal framework as well as interoperability issues and questions regarding the sustainability of CHIC via the proposed Study Trial and Research Centre (STaRC) that is part of the maintenance program of p-medicine.
- **Task 2.2, Scenario based user needs and requirements:** All scenarios and use cases were developed in close interaction between the clinical partners. The scenarios and use cases are clinically driven to guarantee their translation and usage in clinical care. According to results of previous projects all scenarios and use cases are dissected to the finest possible granularity. This results in different modules that can be combined to higher level scenarios and use cases. A list of existing models and new models provided by WP6 is dissected in that way and ranked according to clinical usage. In addition we started to define standardization, open interfaces and functionality descriptions, so that a user can easily build new models as a composition of existing granular tools. Such an approach will guarantee the re-use of already developed tools and models and avoid rebuilding of tools and models from scratch.
- **Task 2.3, Requirements for enhancing hypermodels beyond the domain of cancer:** ICCS has had initial discussions with USFD regarding the possible reuse of the hypermodeling infrastructure (approach) by the musculoskeletal modelling community.

- **Task 2.4, How to get acceptance of hypermodels by patients and physicians:** Initial work has already started in this task. The most important requirement for the validation of models and hypermodels are the availability of data. In this reporting period we started with the collection of data for the different cancer domains. At the moment these data are still locally hosted by the clinical partners as long as the legal and ethical framework is not in place and a user interface is missing for the upload of data to the CHIC platform.

Summary of significant results

The partners involved in WP2 started to collect clinical, imaging and molecular data. Scenarios and use cases are developed by clinical partners and in close interaction with all other partners. They are dissected into granular modules. Interaction and collaboration started with p-medicine and USFD.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

Work has started early in the following task:

T2.4, How to get acceptance of hypermodels by patients and physicians (M12-24).

This will have no effect on the other tasks, available resources and planning.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP2			
Partner	Planned PM Total	Planned PM Period 1	Actual PM Period 1
1-ICCS	2.00	0.60	0.36
3-USAAR	25.00		0.31
7-FORTH	3.00	0.50	1.49
9-UPENN	5.00		0.00
13-CUSTODIX	1.00		0.46
14-PHILIPS	4.00		0.30
Total	40.00		

It should be noted that the person month efforts per partner per reporting period are still being collected and that most tables in this report are therefore incomplete. Completed tables will be available with the first official report due by 30 June 2014.

1.3 Work Package 3: Clinical and Translational Science Scenarios

Main objectives of this WP

The objectives of WP3 are to validate the CHIC environment by focusing on three different cancer types. The selected diseases are Wilms tumor, glioblastoma multiforme (GBM) and non small cell lung cancer (NSCLC). These particular diseases are selected to address different aspects of the project. For all three cancer types, clinically relevant cases are defined. Data from these cases will be stored within the infrastructure of CHIC in a secure and anonymized way according to the legal and ethical framework of CHIC. The data from these concrete clinical scenarios will undergo processing within the environment, and validation of the environment will be based on the clinical and oncologic data produced by the same scenarios.

Active tasks in this reporting period:

- Task 3.1, Wilms tumor (M1-48)
- Task 3.2, Glioblastoma multiforme (M1-48)
- Task 3.3, Non small cell lung cancer (M1-48)

Summary of progress achieved towards objectives

ICCS exploited multiscale data for the different cancer types provided by the other WP members. USAAR provided data from patients with nephroblastoma enrolled in the Wilms Tumor clinical trials as well as data from patients with Non-Small-Lung-Cell Cancer (NSLCC). KU LEUVEN provided prototype data from patients with glioblastoma multiforme enrolled in the HGG-2010 clinical trial. UNITO provided data from patients with prostate cancer to apply in the CHIC infrastructure.

Summary of details for each task

- **Task 3.1, Wilms tumor:** At ICCS, exploitation of Wilms tumor patients' multiscale data, already provided by USAAR in the framework of previous research projects, is in progress. Discussions regarding the provision of micro-RNA data are under way. Within the SIOP Renal Tumor Study Group, that is chaired by Norbert Graf (Task Leader, USAAR) a new clinical trial is under development. This trial will use ObTiMA as the data management system. Corresponding CRFs are developed. Imaging data (DICOM) are collected from patients with nephroblastoma at the time of diagnosis and after 4 weeks of preoperative chemotherapy. Parts of these DICOM data are post-processed by rendering the tumor using DoctorEye. A doctoral thesis is under way building a tool for automatic annotation of Wilms Tumor. This tool is under validation in a feedback loop with the developer. All data that are collected so far are locally stored until the legal and ethical framework is in place for CHIC and a user interface is built for easy upload of the data. Ethical approval for the collection of the data for the CHIC project is given by the Ärztekammer des Saarlandes (No.: 104/10, dated: 19th August 2013).
- **Task 3.2, Glioblastoma multiforme:** Interactions of ICCS with KULeuven and other partners have led to the definition of the specific multiscale data to be provided by KULeuven. The latter will guide the development of the specific glioblastoma multiforme multiscale models. KULeuven has been conducting a trial for immunotherapy in Glioblastoma Multiforme and has carried out a data collection for evaluation and

validation of the Meta- and Hyper Multiscale models. 102 patients have already been included in the clinical trial.

- **Task 3.3, Non small cell lung cancer:** At ICCS, exploitation of lung cancer patients' multiscale data, already provided by USAAR in the framework of previous research projects, is in progress. At USAAR, data collection has started for Non-Small-Lung-Cell-Cancer. These include clinical data, pathology data and molecular data (EGFR, KRAS, BRAF and echinoderm microtubule-associated protein-like 4-ALK (EML4-ALK)). All these data are stored locally up to now until the legal and ethical framework is in place for CHIC and a user interface is built for easy upload of data.
- **Task 3.4, Applying the CHIC infrastructure to other Cancer types:** UNITO has been collecting data and defining models for prostate cancer not applicable in the first reporting period.

Summary of significant results

ICCS: Exploitation of Wilms tumor and lung cancer patients' multiscale data.

Definition of the specific multiscale data to be provided for glioblastoma multiforme modelling.

USAAR: Further development of ObTiMA and starting to collect the first data with ObTiMA.

Collection of data for neuroblastoma and NSCLC has started. Ethical approval for data collection for CHIC is given for neuroblastoma.

KU LEUVEN: There are no results so far (cfr. Point 3), because data sets are still being collected. Ethical approval of HGG-2010 study was already given

UNITO: The Ethical committee approval has already been obtained and the data collection activity is effective since last July.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

Work has started early in the following task:

Task 3.4, Applying the CHIC infrastructure to other cancer types (M12-36).

This will have no effect on the other tasks, available resources and planning.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP3			
Partner	Planned PM Total	Planned PM Period 1	Actual PM Period 1
1-ICCS	2.00	0.40	0.20
3-USAAR	49.00		

4-KULeuven	68.00	9.00	2.50
9-UPENN	2.00		0.00
11-UNITO	14.00	2.00	2.34
Total	135.00		

1.4 Work Package 4: Legal and Ethical Framework

Main objectives of this WP

This workpackage has five objectives:

- To set up an ethical/legal framework to guarantee compliance with existing rules governing the field of patients' medical data. This framework will help partners to process data on valid legal grounds within the project.
- To clearly define who is entitled to do what with existing models and data sets from inside and outside the consortium. Specific attention will be given to the fact that CHIC involves amalgamation of models which adds additional complexity. A deep analysis will be done about the protectability and the pros and cons of copyright protection in the field. Contracts that can be concluded between project partners as well as with interested third parties on copyright protection of the works developed will be provided.
- To help the project to stay compliant with the relevant legislation and jurisdiction and will therefore act as a permanent legal advisor to the other partners.
- To do legal research on the necessary development of the existing European regulatory framework, in order to foster VPH-research initiatives such as CHIC in the areas of data protection, clinical trials regulation and intellectual property. A whitepaper on these issues for the use of the European Commission and other political stakeholders will be produced. Specific focus will be on the amalgamation of models in the field.
- Being legal advisor for all not yet foreseen legal and ethical questions for all partners for the whole duration of the project.

Active tasks in this reporting period:

- Task 4.1, Initial analysis of the ethical and legal requirements on the reuse of pseudonymized and anonymized data within CHIC (M1-6)
- Task 4.2, Initial analysis of the copyright-related legal requirements for the sharing of data and amalgamation of models within CHIC (M1-9)
- Task 4.3, Development of a data protection and copyright framework for CHIC (M1-42)

Summary of progress achieved towards objectives

The initial analysis of the ethical and legal requirements for the sharing of data has been completed as described in Task 4.1. A deliverable (D4.1) has been submitted on time in September 2013 (M6), containing the details of the analysis. LUH led the team on this task. ICCS, CUSTODIX, and USAAR contributed to the discussion on this task as well as in the preparation and review of the corresponding deliverable. USSAR has also obtained Ethical approval for data collection and sharing within CHIC was given by the Ärztekammer des Saarlandes for nephroblastoma.

In task 4.2, information relating to the licences envisaged to be used in the project has been collected by LUH and is under analysis. ICCS, CUSTODIX, and USAAR are involved in the

discussions, and this will result to D4.2 in M9 - the initial discussions on the copyright-related legal requirements for the sharing of data and amalgamation of models within CHIC.

Task 4.3 is ongoing till M42. So far, an initial analysis of the data protection requirements has been carried out and all partners were involved as seen in task 4.1 above.

Summary of details for each task

■ Task 4.1, Initial analysis of the ethical and legal requirements on the reuse of pseudonymized and anonymized data within CHIC:

- a) A questionnaire has been developed and distributed to the project partners in order to gather information on the nature of data to be processed and its flow.

The questionnaire consisted of 14 questions aimed at eliciting details on which partners will provide which kind of data for the project, – personal, pseudonymised, anonymised, whether data will be prospective (collected in the future) or retrospective (already collected), whether informed consent covers the use of the data in CHIC, whether real data will be required to test the tools and models to be developed in the project, and (of relevance to IPR issues in forthcoming deliverables) details of licences under which the tools and models to be used in the project development may be released.

- b) Evaluation of the legal and ethical requirements relating to the use of health data within the CHIC project.

This task evaluated European data protection and data security requirements on the processing of sensitive data. Provisions of the Data Protection Directive 95/46/EC on the processing of sensitive data and the security requirements such as Article 8 and 17 were evaluated, to see the impact of pseudonymisation and anonymisation on the application of the Directive. National transpositions of the Directive and other relevant international and national regulations on data protection also formed part of the evaluation. Other relevant Directives such as the Clinical Trials Directive 2001/20/EC, Good Clinical Practice Directive 2005/28/EC and Medicinal Products Directive 2001/83/EC were also analysed. In addition, due to the consortium's composition, Swiss and US law have been under investigation, to assess the implications of a possible transfer of personal data to and from these countries within the project. Furthermore, ethical requirements that are relevant, in addition to the legal data protection rules, for carrying out medical research using health data were also evaluated such as the Declaration of Helsinki.

- c) Following I and II above, the presentation of an initial data protection and data security schema for the project

On the basis of the overall evaluation of the relevant legal and ethical norms, an initial schema of data exchange was outlined in chapter 7 of deliverable D4.1 (which will be further developed in the first iteration data protection and copyright framework in M14). The schema proposes to establish a network of trust within a community of researchers involved in the CHIC project for data sharing. A core aspect of this, to be further developed in the M14 framework, is of taking care of the project development in two phases – the development/validation phase and the exploitation phase.

In the first phase, data will be used by researchers in anonymous form when developing the tools and models. To achieve the level of anonymity required for the project, the clinical and the research domain will be separated from each other to maintain privacy and the required control mechanism relevant to both domains. Data in the research domain will undergo a second pseudonymisation process. In addition to this double

pseudonymisation the following pillars will be further used to obtain a result that leads to anonymity in a legal sense:

- i. Research data sets will be stripped of any direct identifiers;
- ii. Confidentiality obligation will be imposed on the users by binding contracts;
- iii. A trusted third party will be used for the second pseudonymisation process before data is used within the CHIC research domain;
- iv. A data protection office will be re-used for the project;
- v. Access to the research domain will be limited/restricted to only authorised persons from each partner institution;
- vi. Technical security measures such as traceability/logging capabilities, encryption, etc, will be maintained;
- vii. There will be no publication of personal identifiers in the research results generated.

Towards the end of the development phase (M36) when the tools will be validated and tested with real data (tantamount to personal data in the understanding the Data Protection Directive), this framework will be reviewed, and updated to take care of the validation aspects of the development phase as well as the exploitation phase of the project.

- d) A position paper on the proposed General Data Protection Regulation has been drafted and sent to the VPH Share community.

The position paper shows how data reuse under the proposed General Data Protection Regulation may impact medical research. Three key problems for medical researchers wishing to use health data for non-interventional research were identified, namely terminological and factual difficulties in deciding if some given health data qualify as personal or not; difficulty in deciding when the patient data subject should be approached for consent to data use (and what counts as appropriate consent); and difficulty in deciding when to obtain ethical review of the proposed research using the data. In this regard a closer look was taken at the putative impact of Art 81 and 83 of the Regulation in their original draft form. The paper concluded that, as well as providing specific solutions to the above problems, the rules in the Regulation must also make sense in ethical and professional terms to researchers and other actors in the research community operating on the ground (including ethics review committees)..

- **Task 4.2, Initial analysis of the copyright-related legal requirements for the sharing of data and amalgamation of models within CHIC:** Licenses for the tools to be used in the project have been collected via a questionnaire, and currently being analysed. The examination and assessment of the licenses and other copyright issues that may emerge with the amalgamation of tools and models is currently in progress. This will culminate in a deliverable D4.2, (initial analysis of the copyright-related legal requirements for the sharing of data) in M9 of the project.
- **Task 4.3, Development of a data protection and copyright framework:** An initial analysis of the data protection framework has been carried out. A full framework incorporating the copyright aspect will be completed in M42 of the project. Initial analysis of the data protection framework has been made in M6. A similar analysis of the intellectual property framework will be completed in M9. Task 4.3 will be active till M42 of the project, which give rooms for the necessary updates required in this WP.

Summary of significant results

An initial data protection and data security framework for the project has been developed in compliance with ethical and legal requirements on the reuse of pseudonymized and anonymized data within the EU. A position paper on the current data protection was drafted early on in the project, for further consideration by the VPH initiative, so as allow researcher concerns and experience to be fed directly and in a timely way into the current legislative reform process. Data on the licenses of the tools have been collected and are undergoing legal analysis.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

Not applicable.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP4			
Partner	Planned PM Total	Planned PM Period 1	Actual PM Period 1
1-ICCS	2.00	0.50	0.20
3-USAAR	4.00		
8-LUH	48.00	10.00	5.19
9-UPENN	2.00		0.00
13-Custodix	2.00		1.02
Total	58.00		

1.5 Work Package 5: IT Architecture**Main objectives of this WP**

WP5 will focus on the definition of the architecture for subsequent implementation and integration. The architecture specification will provide the software architecture design patterns to effectively guide and support the construction of a coherent and consistent system. Particular emphasis will be given to the definition of appropriate interfaces among the modules to enable interoperability. This work-package ensures that the legal and ethical restrictions defined on WP4 are met by the system through the definition and implementation of the appropriate policies and security mechanisms. In this work-package also the relevant existing standards with impact on the system will be identified, analyzed and selected. We will also investigate and provide techniques to build a private cloud infrastructure to support data processing by utilizing resources within individual institutions.

This can potentially facilitate a lot of legal and ethical issues concerning data privacy in remote computing.

Active tasks in this reporting period:

- Task 5.1, Reference Architecture (M1-42)
- Task 5.2, Security tools and services (M1-28)
- Task 5.3, Private cloud infrastructure (M1-27)

Summary of progress achieved towards objectives

The specific objective at this initial phase is to identify the components, or building blocks/services, that make up the overall information system, and provide a plan, from which interoperable sub-systems can be developed. In this context an extensive review and evaluation of existing architectures has been performed and the activities towards the definition of the architecture have begun. The evaluation of the private cloud technologies, to be endorsed by the consortium has been done and installation and deployment for productive usage of the most prominent technologies is being carried out. Future steps in order to process data from WP2, WP3 and WP4 have been planned. The participants have collaborated in discussions and explorations in order to exchange knowledge. Finally, the Architecture Board has been established.

Summary of details for each task

- **Task 5.1, Reference Architecture:** Since TEI-C is the leader of WP5, the individual activities have been assigned to the participants in order to perform a review and evaluation of existing architectures and work on the architecture definition. FORTH mainly contributed in the review. The future steps in order to process data from WP2, WP3 and WP4 have been planned. The Architecture Board has been established. In parallel, efforts have been devoted towards the elaboration – through a series of telephone and SKYPE conferences – of the Semantic aspects of the architecture.
- **Task 5.2, Security tools and services:** Initial efforts in defining the security view of the architecture have taken place. The work mainly focused on analysing a variety of scenarios for the elaboration of security related aspects ranging from user authentication, authorization, and auditing, over data integrity and privacy to pseudo anonymization and re-identification of patient data.
- **Task 5.3, Private cloud infrastructure:** FORTH and other involved partners have completed an in depth evaluation of available competing technologies for the implementation of a private or hybrid cloud based infrastructure supporting scientific computation and/or big data management. The selection of the most prominent technologies has been completed and a focused evaluation of their comparative strengths and weaknesses is underway.

Summary of significant results

The Architecture Board has been formed and its operating procedures have been defined. Review of existing architectural styles are prevalent in the Biomedical Informatics and VPH domains. The most appropriate technologies for the implementation of private or hybrid cloud infrastructures for subsequent in depth evaluation have been selected.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

There were no deviations from Annex I. However, one issue for the work of WP5 relates to the fact that – ideally – a number of relevant contributions from other WPs (e.g. analysis of ethico-legal issues) are to be provided at a subsequent point in time. In collaboration with all respective WP leaders, a meeting has taken place and early contributions are being made available to the Architecture Board.

Problems may be encountered if the CHIC reference architecture to be ultimately defined differs significantly from the existing VPH-HF architecture that has already been installed at the location of partner USFD. This issue is taken into consideration by the Architecture Board and efforts to harmonize solutions are being made.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

New staff hired by partner USFD has been included in the Architecture Board and will be strongly included in the upcoming work for Tasks 5.1 and 5.2. Every effort to technically align the CHIC architecture with what already has been developed in the sites of specific partners will be made.

Statement on the use of the resources

Planned versus actual efforts in WP5			
Partner	Planned PM Total	Planned PM Period 1	Actual PM Period 1
1-ICCS	3.00	0.50	0.15
5-BED	19.00		
6-USFD	12.00	2.00	0.00
7-FORTH	10.00	2.00	0.00
12-UBERN	4.00	1.00	0.26
13-Custodix	12.00	3.00	0.00
14-Philips	15.00		0.00
17-TEI-C	15.00	4.00	1.30
Total	90.00		

1.6 Work Package 6: Cancer Models and Hypermodel Design

Main objectives of this WP

Work package 6 aims at achieving the following targets:

a) To develop new multiscale models or to extend and/or adapt already existing ones in order to spatiotemporally simulate the specific clinical trials and studies addressed by the CHIC project. To clinically adapt and partly validate them based on the data available by the clinical partners of the project.

b) To “break down” already developed tumour models, so that models and computer codes of elementary biological processes (biomechanisms) can be provided to the model repository to be developed. Elementary biological processes may include inter alia cell cycling (including e.g. the duration of the various phases of the cell cycle based on the molecular profile of the tumour and interactions among critical molecular entities), the probability of a tumour cell to undergo apoptosis following a particular treatment, such as the administration of a special chemotherapeutic drug or radiotherapy or a targeted therapy agent based on the molecular profile of the tumour (e.g. through the use of molecular networks), the angiogenesis process (e.g. a basic algorithm for creating new blood vessels from existing ones based on the local concentration of TAF) etc.

c) To standardize the inputs, outputs and descriptions of such elementary process modules according to the hypermodelling (or integrated modeling) metalanguage to be developed by workpackage WP7 in collaboration with WP6. The set of parameters that could best describe and make widely usable each one of the elementary process models will have to be identified. In order to end up with a reasonable and hopefully universally acceptable and easily usable description of the basic aspects of all multiscale cancer models (input/output parameters, modelling strategy, mathematical methods used etc.), all cancer modellers participating in the CHIC project will have to make suggestions so that a consensus will be finally reached.

d) For selected tumour types to fit together the standardized elementary tumour bioprocess modules that will have been produced during steps b and c, so as to end up with a modular “re-creation” of existing models referring to the specific cancer type. The resultant hypermodels will be numerically studied and at least partly experimentally and/or clinically adapted and validated using data available from literature and/or collected by collaborating experimentalists and/or clinicians. This step will serve as an initial demonstrator of the analysis and experimental and/or clinical adaptation and validation process applied to modular hypermodels.

e) To contribute to the creation of multi-modeller hypermodels (or integrated models) concerning various tumour types addressed by CHIC by utilizing standardized elementary process modules. The standardized elementary bioprocess models will have to be linked to elementary bioprocess models of complementary mechanisms developed by other modellers according to the model standardization to be achieved by WP7 in collaboration with WP6. Such multi-modeller models will undergo numerical analysis and at least partial clinical adaptation and validation using pertinent multiscale data to be provided by the CHIC clinical partners and/or mined from literature and/or provided by experimental or clinical collaborators of modellers. These hypermodels will serve as demonstrators of the implementation of the concept of hypermodelling in the cancer domain.

Active tasks in this reporting period:

- Task 6.1, Cancer hypomodelling and hypermodelling strategies and elementary models (M1-36)
- Task 6.2, Subcellular cancer modeling (M1-36)
- Task 6.3, Biomechanics enhanced tumour modeling (M1-36)
- Task 6.4, The clinical modeling paradigms of nephroblastoma, glioblastoma and lung cancer (M6-46)
- Task 6.5, The colon cancer modeling paradigm (M6-46)
- Task 6.6, The prostate cancer modeling paradigm (M6-46)

Summary of progress achieved towards objectives

Extensive work has been done by ICCS regarding cancer hypomodelling and hypermodelling strategies, as well suggestions for possible elementary models. FORTH, UNITO, UOXF, UPENN have contributed to the list of models included in the deliverable D6.1 “Cancer hypomodelling and hypermodelling strategies and initial component models.” A molecular-scale methodology and protocol for computational profiling of kinase mutations using molecular dynamics simulations was established by UPENN. As part of the task a multiscale method to combine the molecular studies with signalling network studies was developed.

Discussions were initiated between ICCS, UPENN and USAAR on the linking of the subcellular and the cellular and supercellular levels of biocomplexity. The main components required for the biomechanical modelling have been identified by UBERN. The model behaviour has been defined and requirements to run the model have been defined. Possible extensions of previous work done within the framework of the Contra Cancrum project have been explored by ICCS. ICCS also explored the integration of micro-RNA related mechanisms into the multiscale model developed by ICCS. Moreover, they looked into already available Wilms tumor patients’ multiscale data, provided within the framework of previous projects. The development of an initial machine learning model to be used as the statistical modelling approach has been begun.

ICCS exploited already available data, provided within the framework of the Contra Cancrum project. In tasks T6.5 and T6.6, productive interactions between ICCS, UOXF and UNITO are underway.

Summary of details for each task

- **Task 6.1, Cancer hypomodelling and hypermodelling strategies and elementary models:** Extensive work has been done by ICCS regarding cancer hypomodelling and hypermodelling strategies, as well suggestions for possible elementary models. An extensive outline of this process is included in the deliverable D6.1 “Cancer hypomodelling and hypermodelling strategies and initial component models.” FORTH, UNITO, UOXF, UPENN have contributed to the list of models included in the deliverable.
- **Task 6.2, Subcellular cancer modeling:** UPENN presented a computational modelling and simulation approach to delineate molecular-level mechanisms of activation of protein receptor tyrosine kinases and describe clinical implications of mutations in the Anaplastic Lymphoma Kinase (ALK) receptor tyrosine kinase in pediatric neuroblastoma. What is more, UPENN developed molecular as well as network models of the HER4/ErbB4 activation and signalling, in order to elucidate molecular mechanisms of activation in the wild type kinase and to help rationalize the effects of the clinically identified HER4 somatic mutants on the cell phenotype.
Discussions between ICCS, UPENN and USAAR on the linking of the subcellular and the cellular and supercellular levels of biocomplexity have led to a joint publication.
- **Task 6.3, Biomechanics enhanced tumour modeling:** UBERN identified the main building blocks for the biomechanical simulations. The description of the model has been summarized, including description of the model, the list of input/output components as well as the software requirements. ICCS explored possible extensions of previous work done within the framework of the Contra Cancrum project.
- **Task 6.4, The clinical modeling paradigms of neuroblastoma, glioblastoma and lung cancer**
Subtask 6.4.a, The neuroblastoma paradigm

ICCS explored the integration of micro-RNA related mechanisms into the multiscale model developed by ICCS. Exploitation of already available Wilms tumor patients' multiscale data, provided within the framework of previous projects.

Subtask 6.4.b, The glioblastoma paradigm

ICCS developed an initial machine learning model to be used as the statistical modelling approach. A mechanistic model is envisaged to be developed following the development and evaluation of the statistical one.

Subtask 6.4.c, The lung cancer paradigm

Exploitation of already available data, provided within the framework of the Contra Cancrum project, has triggered improvements on the discrete event based model of lung cancer developed by ICCS.

- **Task 6.5, The colon cancer modelling paradigm:** A productive interaction of ICCS with UOXF took place during the kick-off meeting in Athens and continues to take place.
- **Task 6.6, The prostate cancer modelling paradigm:** A productive interaction of ICCS with UNITO took place during the kick-off meeting in Athens and continues to take place.

Summary of significant results

Extensive work has been carried out regarding cancer hypomodelling and hypermodelling strategies. Suggestions for possible elementary models were made. Components of the biomechanical model have been determined, scientific and technological requirements defined. A computational modelling and simulation approach was developed to delineate molecular-level mechanisms of activation of protein receptor tyrosine kinases and describe clinical implications of mutations in the Anaplastic Lymphoma Kinase (ALK) receptor tyrosine kinase in pediatric neuroblastoma. Molecular as well as network models of the HER4/ErbB4 activation and signalling are in place.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

UBERN and UOXF have had recruitment problems, which are considered by the rest of the partners in this work package to have had minimal impact on the active tasks and the general work plan.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

The recruitment delays at UBERN and UOXF are currently considered to have minimal impact on WP6 tasks, milestones, and the overall planning. As soon as the issue is resolved, the corresponding workplan will be adapted.

Corrective actions

Recruitment efforts are underway at UBERN and UOXF. Both partners have confirmed their commitment to recruit staff for CHIC as soon as possible in order to prevent delays in the workplan.

Statement on the use of the resources

Planned versus actual efforts in WP6			
Partner	Planned PM Total	Planned PM Period 1	Actual PM Period 1
1-ICCS	44.00	10.00	5.79
7-FORTH	9.00	1.50	4.00
9-UPENN	61.00		4.34
10-UOXF	46.00	0.20	0.19
11-UNITO	14.00	0.00	0.00
12-UBERN	20.00	6.00	0.10
14-Philips	1.00		0.00
Total	195.00		

1.7 Work Package 7: Hypermodelling infrastructure

Main objectives of this WP

Develop the ICT hypermodelling infrastructure, intended as a set of services and technologies that make possible to build and execute integrative models, formed by component models and relation models, coherent with the vision of VPH.

Active task in this reporting period:

- Task 7.1, Models execution (M1-27)

Summary of progress achieved towards objectives

In this semester WP7 had only two planned objectives:

1. First draft of the Component Models Generic Stub.
2. VPHOP implementation of the VPH-HF installed on USFD cluster.

They both have been achieved as planned.

Summary of details for each task

- **Task 7.1, Model execution:** USFD have actively engaged in the process of defining the information required (e.g. input/output, flow, resources....) for each of the component models proposed to be implemented on the CHIC hypermodelling architecture. In addition, they replicated on a USFD cluster the VPH-HF software stack that was originally developed in the VPHOP project, and which will be used as starting point for the CHIC hypermodelling framework. Such replication highlighted a number of problems, primarily related to different versions of supporting libraries, and to the limitations of configuration that a large HPC resource typically imposes to its users. All these problems are being dealt with, so to start the development in M7 as planned.
CINECA have worked at preliminary activities for the support of the definition of the model components generic stub. In particular, training activities has been carried out to USFD staff on the hypermodel technology previously developed within the VPHOP project and that will be the base for the CHIC developments. The activities included meeting to introduce the technology and its use and support to the installation of the

hypermodelling framework on the USFD hardware. These activities will be also the base for the start of Task 7.3 and 7.5 activities.

FORTH are working on the definition of a generic stub interface for the execution of models, based on prior experience on the field.

ICCS have ensured that the component models description provided in D6.1 included also the technology specifications of the models, to be used by WP7, include execution time, memory requirements, source code language etc. This list of model descriptions is to be used as a reference basis for the development of specific hypermodeling technologies in WP7.

All partners presented this first semester of activity at the first progress meeting.

Summary of significant results

The first draft of the Component Models Generic Stub is available.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

Partner USFD have elected to engage a PhD student at less cost and more effort in this work package. There will be no net effect on the budget, simply more effort applied to this work package overall. The total effort for partner USFD in WP7, originally planned to be 88 person/month, is now projected to be 118PM.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP7			
Partner	Planned PM Total	Planned PM Period 1	Actual PM Period 1
1-ICCS	6.00	1.20	0.50
3-USAAR	4.00		
5-BED	19.00		
6-USFD	118.00	8.54	9.38
7-FORTH	6.00	0.50	1.92
15-UCL	24.00		
16-CINECA	42.00	10.00	4.50
Total	189.00		

1.8 Work Package 8: Model and Data Repositories

Main objectives of this WP

This work package focuses on the development of various kinds of repositories, including the design and implementation of the corresponding infrastructures and interfaces which will cover the needs of the CHIC project.

This involves the development of:

- a repository of cancer models, spanning from models of generic fundamental biomechanisms involved in cancer progression and treatment response, such as cell cycle and cell metabolism, to complex multiscale models of various types of cancer;
- a repository of multiscale data exploitable by the models, either by physically storing the data in the project's data repository, or by providing links to other, already existing, data repositories or warehouses;
- a repository of in silico trials for various types of cancer;
- a distributed RDF repository to store metadata from each partner, including the corresponding interfaces for annotating and querying.

The aforementioned repositories will be tailored to the needs/clinical scenarios of the project. At the same time they will be generic enough to be reusable by several different medical scenarios.

Active tasks in this reporting period:

- Task 8.1, Development of the model/tool repository (M1-48)
 - SubTask 8.1.a, Development of the model/tool repository
 - SubTask 8.1.b, Development of the data repository
- Task 8.2, Infrastructure for Semantic Metadata Management (M1-48)

Summary of progress achieved towards objectives

ICCS analysed the specifications of the models/tools that will be hosted in models/tools repository. They also analysed the specifications of the clinical data that will be hosted in models/tools repository. UPENN started the development of the data repository. ICCS designed the deliverable D6.1 "Cancer hypomodelling and hypermodelling strategies and initial component models" in such a way as to provide certain initial semantic descriptions of the models. USAAR initiated discussion with p-medicine on collaboration possibilities in the area of semantic interoperability. UCL initiated the articulation and collection of requirements for the knowledge representation for integrative models and associated data, the design of the underlying RICORDO implementation adapted to the project requirements collected above. Moreover, UCL ensured the coherence of the CHIC semantic interoperability framework with metadata frameworks in the pharmaceutical R&D industry. UCL also carried out a first assessment of the applicability of Functional Tissue Unit knowledge in support of multiscale integrative models in cancer and a first assessment of the applicability of the ApiNATOMY knowledge representation in support of flow process metadata management. UBERN identified the data repository framework. An initial version is running and will be available shortly for clinician to store medical image datasets.

Summary of details for each task

■ **Task 8.1, Development of the model/tool repository:**

SubTask 8.1.a

ICCS analysed the specifications of the models/tools that will be hosted in models/tools repository

SubTask 8.1.b

ICCS analysed the specifications of the clinical data that will be hosted in models/tools repository. UBERN selected a database framework as the data repository. The repository can be easily adapted to store the medical image for the CHIC project as well as the results of the image processing steps (i.e. image segmentation). The different datasets can be linked together. An additional object type should be added to enable the system to store other medical information.

- **Task 8.2, Infrastructure for Semantic Metadata Management:** Deliverable D6.1 “Cancer hypomodelling and hypermodelling strategies and initial component models” prepared by ICCS in collaboration with several other partners has been designed in such a way as to provide certain initial semantic descriptions of the models. This is to be used in order to drive the design of the repositories.

The way in which p-medicine is dealing with semantic interoperability was reviewed by USAAR and discussed within the project. Collaboration is proposed. Further discussions are needed.

UCL initiated, at consortium level, the articulation and collection of requirements for the knowledge representation for integrative models and associated data as well as the design of the underlying RICORDO implementation adapted to the project requirements collected above. Moreover, UCL ensured the coherence of the CHIC semantic interoperability framework with metadata frameworks in the pharmaceutical R&D industry and carried out a first assessment of the applicability of Functional Tissue Unit knowledge (see publication in WP12 report for UCL) in support of multiscale integrative models in cancer. UCL also carried out a first assessment of the applicability of the ApiNATOMY knowledge representation in support of flow process metadata management.

Summary of significant results

An analysis of models/tools specifications was carried out as well as an analysis of clinical data specifications.

Knowledge representation requirements for multiscale cancer biology were collected and the design of a semantic interoperability framework based on the above requirements collection that is coherent with developing standards in industry was initiated.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

Not applicable.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP8			
Partner	Planned PM Total	Planned PM Period 1	Actual PM Period 1
1-ICCS	14.00	3.00	1.39
3-USAAR	3.00		
7-FORTH	6.00	0.50	0.00
9-UPENN	3.00		
12-UBERN	15.00	0.00	2.43
13-Custodix	3.00		
14-Philips	7.00		
15-UCL	48.00	3.00	3.03
Total	99.00		

1.9 Work Package 9: Image Processing and Visualization**Main objectives of this WP**

This work package will concentrate on the visualization and image analysis support to the project. The objectives are:

- To provide a set of visualization tools for model and data analysis;
- To provide a set of image analysis tools for image data processing;
- To provide tools for assessing the tumor change from functional tomographic data.

Active tasks in this reporting period:

- Task 9.1, User requirement analysis (M1-6)
- Task 9.2, Scalable visualization techniques (M3-18)
- Task 9.5, A general image processing development toolkit (M6-18)
- Task 9.6, Image registration tools (M3-36)

Summary of progress achieved towards objectives

BED provided the leadership for this task. It is also the leader of Task 9.1 and the main contributor of deliverable D9.1 “User requirements for the visualization toolkit and image analysis toolkits”. In task 9.1, user requirements for the problem of multimodal brain tumor image segmentation have been identified and described by UBERN. In task 9.6, the building blocks of the registration approach to be developed have been initially identified. Within the framework of a close collaboration with BED, ICCS have provided the major requirements regarding image processing and visualization of the multiscale models of WP6 and contributed to the production of the corresponding deliverable D9.1. The content of the deliverable D6.1 “Cancer hypomodelling and hypermodelling strategies and initial component models” also provides useful information for the specific needs of WP9. FORTH

has contributed to D9.1 covering the part of the requirements for the tumor response quantitative platform and analysis tools. Regarding Task 9.8, A software platform for the assessment of tumor treatment response (M8-42), although this task hasn't started officially, there has been a significant preparatory work especially in collaboration with KU Leuven. The FORTH team visited the radiology department and the general analysis framework has been designed. This includes the pharmacokinetic analysis of the MRI data to derive tumor perfusion markers.

Summary of details for each task

- **Task 9.1, User requirement analysis:** This task is completed, and the related deliverable D9.1 has been submitted. Work in this task was to gather user requirement on the visual analysis suite and image analysis tools. Typical approaches and examples that are expected to get benefit from the use of visualization and image analysis have been identified and analysed. The WP9 partners have looked into current problems and needs in the model and data analysis and understand the scales of the model and data repositories. Some questionnaires were developed for collecting information from relevant stakeholders regarding acceptance, user needs and requirements. User requirements for multimodal brain tumor segmentation were identified based on clinical needs and clinical protocols used to diagnose glioma grade III and IV. Documentation of the requirement and analysis have been prepared.
- **Task 9.2, Scalable visualization techniques:** This task has just started. The team is working on literature reviews for a range of latest scalable visualization techniques. In this task, WP9 partners will develop scalable visualization techniques to support the visualization of large scale data. These will include data removal and filtering techniques, which will allow users to focus on their targeted data; aggregation techniques, which will allow users to combine details and create different levels of overviews in hierarchies and will support users to perform “overviews first and details on demand”; dimension reduction techniques (e.g. subspace clustering), which will be able to help identifying the meaningful cohort of data in a subset of relevant dimensions. To allow effective handling of large scale visualization, we will investigate new aggregation techniques based on the traditional approaches, such as binning, abstraction, etc. Hierarchical clustering techniques can be used to create effective aggregation of data at different levels of details. Also, we shall investigate uncertainty-aware aggregation, which creates data aggregation with uncertainty information to enhance user understanding towards the aggregated data. Subspace clustering will be another key area of interest. Given a dataset with high dimensionality, the number of possible sub feature space is exponentially high. Fully automatic machine learning normally does not do a good job in terms of identifying the clusters. A recent trend is to involve human experts, which couples user interaction with the subspace clustering process
- **Task 9.6, Image registration tools:** For rigid registration, tools based on monomodal image intensity based techniques will be integrated, whereas for non-rigid registration fast diffeomorphic demons based registration will be integrated, with a special focus on intra-patient registration for follow-up studies and atlas to patient registration for functional brain mapping. To cope with the presence of varying size tumors in the images (especially for longitudinal studies), landmark-assisted variants of the previous registration algorithms will be also considered. So far, the main components of the image registration pipeline have been identified. The registration metric for monomodal and

multimodal image registration has been selected. The registration model has been selected based on clinical needs and technical specifications.

Summary of significant results

D9.1 “User requirements for the visualization toolkit and image analysis toolkits” has been completed and submitted. This deliverable focusses on the analysis of the requirements for CHIC. The analysis initially reviews related approaches from currently running research projects. Then it specifies the methodology that will be followed and presents the first two phases: i.e. the purpose and scope specification and the knowledge acquisition. In the first phase the description of the work and the use-cases are analyzed to identify the domain of interest whereas in the second phase relevant domains are analyzed and evaluated. In the following months the outcomes of this deliverable will be used to specify the Computational Horizons In Cancer (CHIC).

The main components of the image registration pipeline have been identified. The registration metric for monomodal and multimodal image registration has been selected. The registration model has been selected based on clinical needs and technical specifications.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

Not applicable.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP9			
Partner	Planned PM Total	Planned PM Period 1	Actual PM Period 1
1-ICCS	3.00	0.60	0.23
3-USAAR	15.00		
5-BED	36.00	3.00	2.00
7-FORTH	20.00	3.00	3.71
12-UBERN	12.00	3.00	2.80
17-TEI-C	1.00	0.00	0.00
Total	87.00		

1.10 Work Package 10: Integrated Platform

Main objectives of this WP

This work package will be responsible for the implementation of the system architecture of CHIC and its realization as a distributed software platform. The main challenge of this package is to build an IT infrastructure that is able to support the implementation of the VPH scenarios of the CHIC project in an efficient, well documented, and secure way. The main objectives of this work package are:

- To provide the end user portal application for the CHIC users to enter the platform and use its facilities;
- To define the programmatic interfaces for accessing the model and hypermodel repositories;
- To develop and document the access to the private CHIC cloud infrastructure and its services for the management of the data;
- To support and facilitate the orchestration of the models into the integrative hypermodels by providing the necessary tools for their efficient construction and execution.

Active tasks in this reporting period:

- Task 10.1, Portal (M1-8)
- Task 10.2, Interoperable interfaces for retrieving model and hypermodel descriptions from corresponding repositories (M1-18)

Summary of progress achieved towards objectives

In the current reporting period there are two active tasks.

In Task 10.1 we have selected the portal framework and we have set up a development installation which will be used for the development of the CHIC portal tools/portlets from the appropriate technical WPs of the project. This task has almost fulfilled its objectives.

Task 10.2 depends on the progress of WP7 and WP8 and the development of the corresponding repositories, thus the work conducted so far is mostly preparatory. Work progresses as planned.

Summary of details for each task

- **Task 10.1, Portal:** FORTH have conducted an evaluation of portal frameworks and technologies and have set up a development installation of a portal to be used for CHIC. When preparing deliverable D6.1 "Cancer hypomodelling and hypermodelling strategies and initial component models" ICCS bore in mind the technological integrative needs of WP10. The entire tabulation of the models as well as the provision of specific technical data for each model are to be used as a partial driver by WP10 for the development of the CHIC technological integrated infrastructure. The partners in WP10 are preparing the deliverable D10.1 (due in M8) which will document the process and knowledge gathered from the work described above. In sum, the work in this task progresses as planned.
- **Task 10.2, Interoperable interfaces for retrieving model and hypermodel descriptions from corresponding repositories:** the partners have mainly conducted preparatory work for this task in this reporting period, since this task heavily depends on WP8 and the development of the actual repositories. Initial work which relates also to the objectives of

this task has been partially performed by partner FORTH also in WP7, with the documentation of a draft description of a generic model stub specification.

Summary of significant results

Selection of the Liferay portal framework for the development of the CHIC portal.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

Not applicable.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP10			
Partner	Planned PM Total	Planned PM Period 1	Actual PM Period 1
1-ICCS	7.00	1.50	0.38
3-USAAR	7.00		
7-FORTH	21.00	3.00	4.16
12-UBERN	3.00	0.00	0.00
14-Philips	18.00		
16-CINECA	8.00	1.50	0.00
Total	64.00		

1.11 Work Package 11: Clinical Adaptation and Validation

Main objectives of this WP

According to the different goals and requirements of this project specified in detail in the different WPs and tasks, a clinical adaptation and validation process within the project will be carried as a major part of quality control and guarantee for further usage of tools and models, including the Oncosimulator. The spectrum ranges from testing of tools and models up to their usage in clinical trials. Hence, this WP will identify objectives that need to be specifically tested in each case. For that reason proper evaluation criteria will be defined. This WP is crucial in that it will continuously assess the quality of all services and tasks of the CHIC environment and iteratively gives feedback to all responsible persons. In the first 18 months a set of guidelines and check-lists to support evaluators will be created to standardize the clinical adaptation and validation process including standardized reports. Such reports will suggest possible improvements, modifications and other functionalities to

the technical WPs in a feedback loop. During that period corresponding checklists from other projects will be studied and if possible adapted to the specific requirements of CHIC. Furthermore, workshops are to be held to perform dedicated evaluation sessions engaging both users and developers. Besides these task-specific evaluations, another task is to provide combined evaluations covering the whole integrated CHIC environment and their clinical adaptation and validation. In general, this WP will:

- Formulate criteria for clinical adaptation and validation and feedback report guidelines
- Coordinate validation activities by partners and feedback reports
- Evaluate the developed tools and models by testing functionalities, accessibility, respect of user needs, data integration and execution times
- Verification of GCP (Good Clinical Practice):
 - protection of human rights as a subject in the CHIC environment
 - standards on how data storages, data sharing and hypermodels will be used in clinical care
 - clinical audits: performance will be regularly reviewed to ensure scheduled activities will be properly executed enhancing clinical adaptation of tools and models

Specifically this WP will:

- clinically adapt and partly clinically validate the three Oncosimulator multiscale models (Wilms tumor, glioblastoma, non small cell lung cancer) based on data to be provided by the clinical partners of the consortium (USAAR and KU Leuven)
- clinically check the four cancer multiscale model paradigms (biochemical and molecular interactions, prostate cancer, colon cancer, glioblastoma biomechanics) based on published data and mathematical models
- give a quantitative indication about how safely an active surveillance strategy can be applied
- perform a quantitative validation of the effectiveness of standardized therapies (mainly radiotherapy, chemotherapy and hormonal therapy) versus innovative ones.

Active tasks in this reporting period:

- T11.1, Formulate evaluation and validation criteria for enhancing clinical adaptation of hypermodels (M1-12)
- T11.2, Coordinate evaluation activities by partners (M6-18)

Summary of progress achieved towards objectives

Together with ICCS, USAAR started to define evaluation and validation criteria for enhancing the clinical adaptation of hypermodels. This was done in close collaboration with all partners of WP11. Evaluation and validation criteria from other EU projects (p-medicine and EURECA) are under review. Writing of deliverable D11.1 (Evaluation and validation criteria for clinical adaptation) has been initiated by USAAR. ICCS has contributed to the coordination of the evaluation activities during the kick-off meeting and subsequently on several physical meeting occasions as well as through electronic correspondence. All partners of WP11 were involved in this activity.

Summary of details for each task

- **Task 11.1, Formulate evaluation and validation criteria for enhancing clinical adaptation of hypermodels:** Analysis of evaluation and validation criteria from other EU projects (p-

medicine and EURECA) are under review. The identification of specific application objectives will start as soon as D2.1 is finalized. Adaptation to different stakeholders is under discussion. Writing of deliverable D11.1 (Evaluation and validation criteria for clinical adaptation) has started by USAAR.

- **Task 11.2, Coordinate evaluation activities by partners:** ICCS has contributed to the coordination of the evaluation activities during the kick-off meeting and subsequently on several physical meeting occasions as well as through electronic correspondence. All partners of WP11 were involved in this activity despite the fact that this task starts at month 6.

Summary of significant results

Work in task 11.1 has been started by all partners involved. There is a close interaction with WP2 task 2.1. The collaboration within the consortium and this WP is excellent.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

Not applicable.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP11			
Partner	Planned PM Total	Planned PM Period 1	Actual PM Period 1
1-ICCS	7.00	1.00	0.30
3-USAAR	25.00		
5-BED	8.00		
7-FORTH	3.00	0.50	0.42
9-UPENN	5.00		0.00
11-UNITO	20.00	7.00	1.17
12-UBERN	3.00	0.00	0.00
13-PHILIPS	3.00		0.00
Total	74.00		

1.12 Work Package 12: Dissemination and Exploitation

Main objectives of this WP

The objectives of this work package are the following:

- to coordinate the dissemination of this project's outputs, approaches and results to target groups, new users and communities;
- to coordinate the exploitation of the project results and to guarantee their sustainability;
- to exchange information and establish relationships with current projects and initiatives;
- to coordinate training activities and thereby promote the use of tools and methods created through workshops, conferences and publications.

Active task in this reporting period:

- Task 12.1, Dissemination activities (M1-48)
- Task 12.2, Exploitation and IPR issues (M1-48)

Summary of progress achieved towards objectives

Deliverable D12.1, "Dissemination Plan", which was prepared by CINECA with contribution from Eurice and all partners, was submitted to the EC on 2 October 2013. Eurice was responsible for the layout and set-up of the project website, www.chic-vph.eu, which went online on the 28 June 2013 and has been updated with the latest news ever since. CINECA and Eurice edited and distributed two issues of the CHIC e-mail newsletter. Eurice developed material for a dissemination kit to be used by the project partners, including the poster and the flyer by ICCS. CHIC Partners started to participate to conferences (EMBC'13, CASyM workshop, 2nd Summer School in Computational Oncology). A Computational oncology workshop was held at USFD (11 October 2013) where two other CHIC members were invited as keynote speakers. Moreover, there is ongoing interaction with the following projects: TUMOR, p-medicine, MyHealthAvatar, DrTherapat, and VPH-Share. Regarding IPR issues, a questionnaire was distributed and information from the CHIC partners was collected. There has been frequent interaction with Thomson Reuters, including the initiation of exploration of exploitation scenarios of the CHIC outcomes. USFD has initiated discussion with SCS relating to the IPR associated with the existing hypermodelling MAF source code and future developments that will take place during the CHIC project. Finally, discussion with p-medicine has started about sustainability issues.

Summary of details for each task

■ **Task 12.1 – Dissemination activities**

Subtask 12.1.a: Strategic dissemination planning

During the CHIC project dissemination activities will have a central role in order to foster the widespread awareness as well as strong cooperation and exchange with research communities inside and outside of the EU. The wider dissemination activities will embrace informing all relevant target groups about the project results and the implications that these results might have for clinical, industrial and societal users as well as for the research community. It will also aim for increasing awareness among other target groups, namely "all stakeholders" in general, the scientific community, industry, clinical practice and the public at large.

CINECA has defined the CHIC dissemination strategic plan and, in particular, the communication model, the target groups, the dissemination channels and the associated responsibilities. The outputs of this analysis were reported in deliverable D12.1 "Dissemination Plan" submitted in M6. All partners have contributed to the deliverable with the list of planned dissemination events, target conferences and peer-reviewed journals. Eurice contributed to the section on the project corporate identity, also providing an explanation about the usefulness of a coherent and highly visible design for

dissemination and exploitation purposes. Moreover, Eurice wrote the section about the project website, which will be more thoroughly described in Subtask 12.1.b. Section 5.4.3 of the deliverable deals with the CHIC Newsletters and was written in close cooperation of CINECA and Eurice.

Detailed information on the achieved dissemination events will be collected in every reporting period according to the defined communication model. Consequently the Dissemination Plan will be updated annually throughout the project's lifetime (corresponding deliverables: D12.3, D12.4, D12.5).

SubTask 12.1.b: Web presence

The layout of a professional project website was set up by Eurice, in close cooperation with the coordinator. The design of the website incorporates elements of the CHIC corporate identity such as the defined CHIC colours and the CHIC project logo. As outlined in the Description of Work, the website features an external as well as an internal part. On the external website, users are informed about the project in general, its objectives, strategy and structure, the consortium members and the latest news and events within the VPH community and beyond. Moreover, a download section has been installed to provide newsletters and further material to be defined in the course of the project. Publications originating from the work done in CHIC as well as relating to the project will be listed on the respective section of the website. The textual parts of the website still have to be improved, but Eurice is currently working on this task. The information is to be presented in a lighter and more concise way in order to attract not only scientists but generate interest in the general public as well. The internal part of the website features an online tool for project management which was developed by Eurice specifically for the management of EU funded research projects. The consortium members have access to mailing lists and a large document repository featuring the most important shared project documents, deliverables, publications and other dissemination activities. Moreover, templates for presentations and project reporting are also provided on the internal management tool. More detailed information on the CHIC website can be found in deliverable D12.1 "Dissemination Plan". The progress of the website development will be recorded in the forthcoming deliverables of WP12.

In terms of web presence, CINECA also created a building on the Biomed Town community portal, which will be used during the project to re-post news of general interest to a wider biomedical community. During the next six months, CINECA will create a CHIC presence also on the most important social media websites, like Facebook, Google+, Twitter.

SubTask 12.1.c: Newsletter

Eurice supported CINECA in the collection of material, editing and distribution of two issues of the CHIC e-newsletter. The newsletter is issued every two months and sent out by e-mail to the subscribers. This more frequent communication provides a short and concise overview of news and events related to CHIC, allowing the readers to not only follow the project's immediate progress but also to participate in the "project life". The newsletter accommodates the latest news from the past two months from CHIC as well as the wider VPH community (related projects, initiatives, conferences and other important issues) and a list of noteworthy forthcoming events in which CHIC partners are actively participating or which might be of interest to anybody working in this field. A detailed description of the bi-monthly newsletters is given in deliverable D12.1, "Dissemination Plan". First discussions about the annual newsletter (due after M12) have been initiated.

SubTask 12.1.d: Dissemination Kit

Eurice developed material for a dissemination kit to be used by the project partners. So far, the kit consists of a professional project logo, a consistent corporate design reflected on various templates (ppt template, template for meeting agendas, etc.), an introductory CHIC ppt presentation and the e-mail newsletter, a flyer and various posters for distribution and advertising at various conferences mainly from ICCS. Further dissemination materials will be created in coordination with the rest of the CHIC consortium and the kit will be finalized by the end of March 2014 at the very latest.

SubTask 12.1.e: Conferences, exhibitions, workshops

CHIC partners already started to actively present CHIC-related contents at conferences and workshops.

- IEEE Engineering in Medicine and Biology Society (EMBC'13), 3-7 July 2013, Osaka International Convention Center, Osaka, Japan. ICCS contributed with two oral presentations: 1) a regular IEEE conference paper and 2) an invited special session talk organized by Norbert Graf, USAAR.
- The strategic CASyM (The Coordinating Action Systems Medicine) modelling Workshop in Heidelberg, Germany, 11 June 2013, CHIC presentation given by ICCS.
- The 2nd Summer School in Computational Oncology, 23 - 28.06.2013, Schloss Dagstuhl in Wadern, Germany, CHIC presentation given by ICCS.
- Brain Tumor Segmentation Challenge, MICCAI 2013, Nagoya, Japan (22 Sept 2013). One-day challenge where algorithms for brain tumor segmentation are evaluated and compared. Out of 10 teams, UBERN obtained second place in this competition.
- The USFD Insigneo Institute for In Silico Medicine and the Sheffield Centre for Cancer research organised a one-day workshop on 11 October 2013 with the primary purpose of promoting internal collaboration in the field of computational oncology. Most registrants are from USFD, though there are some with clinical roles associated with Sheffield Teaching Hospitals Trust. The two keynote speakers, Prof Helen Byrne (UOXFD) and Prof Georgios Stamatakis (ICCS) are keynote speakers and Georgios will be talking specifically about the CHIC project.
- UCL organised a cross-industry workshop (30-31 October 2013) for pharmaceutical companies to work towards a communal standard for multiscale anatomy knowledge representation relevant to the semantic interoperability requirements of CHIC.
- KU Leuven - Prof. Dr. Stefaan Van Gool organised the 11th HGG-IMMUNO-Meeting (21 October 2013) in Leuven. The HGG-IMMUNO-Meeting is an annual meeting where international research groups and clinicians who perform experimental and clinical research on immunotherapy are invited to share knowledge and experiences. The clinical research by KU Leuven on immunotherapy will provide the input data of glioblastoma for CHIC (Task 3.2).

With regards to the general audience, ICCS presented the CHIC vision and basics to the wider public in the form of interviews in three Greek newspapers with wide circulation during the kick-off meeting. Further reference is made to the list of dissemination activities in the management section of this report.

SubTask 12.1.f - Scientific & Technical Papers Publications

CHIC partners already started to actively describe CHIC-related outputs on relevant technical and scientific publications. The publications are listed in the respective table in the management section of this report.

SubTask 12.1.g – Interfacing with other projects

ICCS has had continuous interaction with the following projects: TUMOR, p-medicine, MyHealthAvatar, DrTherapat. CINECA is interacting with VPH-Share in order to understand if and how CHIC can become part of the VPH-Share infrastructure beta user programme.

- **Task 12.2, Exploitation and IPR issues:** USFD and SCS have initiated a discussion relating to the IPR for MAF (Multimod Application Framework) – the basis for the hypermodelling framework used in a number of previous projects including VPHOP, which will most likely form the core technology for the CHIC hypermodelling framework.

A discussion about sustainability and maintenance of the CHIC project via the proposed Study Trial and Research Institute that is part of the maintenance programme of p-medicine has started. Further discussions are needed and must be integrated into the exploitation planning report of CHIC.

ICCS, in frequent interaction with Thomson Reuters, has started the exploration of exploitation scenarios of CHIC outcome by the wider biomedical research and clinical community. It is noted that Yuri Nicholsky from Thomson Reuters is a member of the EAB committee of CHIC.

In order to guide and understand CHIC specific IPR issues a questionnaire has been prepared by CINECA with Eurice's support. The questions include expected results, expected stage of development of the results at end of project, plans for securing Intellectual Property Rights, potential for commercial application, licence associated to potential public results, etc. The questionnaire has been distributed to all partners and information is now being collected and categorised. The output of this activity will be reported into the annual periodic reporting.

Summary of significant results

CINECA with the strong support of Eurice and all partners have defined a clear plan and set of tools for the dissemination of the CHIC results (D12.1). A well-defined project identity has been created and a web presence established, together with the sending of the first newsletter issues. Partners have actively started to disseminate CHIC-related content both with presentation at conferences and peer-reviewed journal publications. Concerning exploitation, preliminary activities have started with the identification of IPR issues.

Deviations from Annex I and their impact on other tasks as well as on available resources and planning

Not applicable.

Reasons for failing to achieve critical objectives and/or not being on schedule and the impact on other tasks as well as on available resources and planning

Not applicable.

Corrective actions

Not applicable.

Statement on the use of the resources

Planned versus actual efforts in WP12			
Partner	Planned PM Total	Planned PM Period 1	Actual PM Period 1
1-ICCS	8.00	1.50	1.00
2-Eurice	12.00	3.00	2.17
3-USAAR	3.00		
5-BED	6.00		
6-USFD	6.00	0.00	0.50
7-FORTH	6.00	1.00	0.00
8-LUH	6.00		0.00
9-UPENN	6.00		0.00
10-UOXF	6.00		
11-UNITO	6.00	0.00	0.37
12-UBERN	5.00	0.00	0.00
13-Custodix	6.00	1.50	0.00
14-Philips	6.00		0.00
15-UCL	2.00	0.50	0.17
16-CINECA	6.00	1.50	1.82
17-TEI-C	1.00	0.00	0.00
Total	91.00		

2. Project management

Consortium management tasks and achievements

The consortium management is covered by WP1 and includes

- Task 1.1: Decision making management (M1-48)
- Task 1.2: Administrative coordination (M1-48)
- Task 1.3: Financial management (M1-48)
- Task 1.4: Contractual management (M1-48)
- Task 1.5: Assessment of progress and results (M6-48)

The following achievements were made during the first six months of the project's duration:

The **Grant Agreement** and the Accession Forms were signed by all partners with only a slight delay caused by the 100% acquisition of former consortium partner SCS Srl by the new consortium member CINECA. Further details on this acquisition are given below. A complete copy of the Grant Agreement including Accession Forms was distributed to all partners for their files. The Consortium Agreement, on the other hand, was concluded and signed before the official start of the project on 1 April 2013. On 16 May 2013 CINECA acceded to the Consortium Agreement via Attachment 2, "Accession document".

The **Kick-off Meeting (MS1)** was organized by the coordinator ICCS in cooperation with Eurice and took place on 10-12 April 2013 at the facilities of the Royal Olympic Hotel in Athens, Greece. The meeting laid the foundation for the work of the first six months with thorough and fruitful discussions on how to start and connect the activities in the different work packages.

A **1st Progress Meeting (MS2)** was held on 17-18 October 2013 at FORTH in Heraklion, Greece where the work done so far was presented and the work anticipated for the upcoming months was discussed. Following the 1st Progress Meeting, a first **technical meeting** was held at FORTH on 19 October 2013. Its purpose was to define responsibilities within the technical work packages of CHIC and further coordinate the workplan for the upcoming months. Detailed meeting minutes, attendance lists and ppt presentations are available for all meetings in the internal management tool, which is introduced in the following paragraph.

A web-based password-protected management tool (*ProjectAngel*) was set up within the scope of developing the CHIC website to centrally store templates for presentations and reporting, project relevant information and data. It includes a reporting tool specifically adapted to the latest FP7 reporting guidelines and the partners were asked to use this tool for the preparation of this report (for more information on the website and the features of the internal project management platform, reference is made to deliverable D12.1 "Dissemination Plan").

The first EC payment of 3,703,700€ was received by the coordinator after the start of the project and timely and duly distributed to the partners according to the table below:

Project Number: 600841				Project Title: CHIC		
Participant Number in this project	Participant Short name	Fund. %	Total Costs	Requested EU Contribution	% of Total EU Contribution/ Pre-financing	Pre-financing
1	ICCS	60.0	1.386.800 €	1.128.800 €	10,67%	395.080,00 €
2	EURICE	85.0	645.498 €	645.498 €	6,10%	225.924,30 €
3	USAAR	60.0	1.689.301 €	1.282.996 €	12,12%	449.048,60 €
4	KULeuven	60.0	814.000 €	625.000 €	5,91%	218.750,00 €
5	BED	60.0	857.800 €	659.800 €	6,24%	230.930,00 €
6	USFD	60.0	1.215.675 €	941.825 €	8,90%	329.638,75 €
7	FORTH	87.0	888.106 €	688.031 €	6,50%	240.810,85 €
8	LUH	60.0	608.794 €	474.928 €	4,49%	166.224,80 €
9	UPENN	62.0	742.206 €	573.282 €	5,42%	200.648,70 €
10	UOXF	60.0	561.120 €	446.591 €	4,22%	156.306,85 €
11	UNITO	60.0	597.000 €	462.998 €	4,38%	162.049,30 €
12	UBERN	60.0	844.000 €	651.000 €	6,15%	227.850,00 €
13	CUSTODIX	50.0	303.000 €	245.375 €	2,32%	85.881,25 €
14	PHILIPS	149.0	1.019.116 €	566.120 €	5,35%	198.142,00 €
15	UCL	60.0	1.060.364 €	804.156 €	7,60%	281.454,60 €
16	CINECA	20.0	405.480 €	325.560 €	3,08%	113.946,00 €
17	TEI-C	60.0	78.880 €	60.040 €	0,57%	21.014,00 €
			13.717.140 €	10.582.000 €	100,00%	3.703.700,00 €

Problems which have occurred and how they were solved or envisaged solutions

All in all, no particular problems have occurred during the first six months of the project. This is noteworthy, as the consortium is very large.

Changes in the consortium

None.

List of project meetings, dates and venues

Title	Date	Venue	Local organizer
1 st Progress Meeting	17-18 October 2013	Foundation for Research and Technology Hellas, Heraklion, Greece	FORTH
1 st Technical Meeting	19 October 2013	Foundation for Research and Technology Hellas, Heraklion, Greece	FORTH
D2.1/D2.2, State of the art knowledge for building hypermodels	17 September 2013	Skype conference	USFD, USAAR, ICCS, UCL, FORTH, TEI-C, CINECA
Bilateral meeting (CINECA and USFD)	22-25 July 2013	Consorzio Interuniversitario CINECA, Bologna, Italy	CINECA

ICCS meeting	17 June 2013	UZ Gasthuisberg, Leuven, Belgium	KULeuven
Bilateral meeting (CINECA and USFD)	3-5 June 2013	University of Sheffield, Sheffield, UK	USFD
WP9 meeting	22 May 2013	UZ Gasthuisberg, Leuven, Belgium	KULeuven
Kick-off Meeting	10-12 April 2013	Royal Olympic Hotel, Athens, Greece	ICCS

Related documentation is available in the project management tool.

Cooperation with other projects/programmes

For cooperation with other projects/programmes reference is made to SubTask 12.1.g “Interfacing with other projects” described in the WP12 report.

Project planning and status

In general, the project’s work plan was implemented as foreseen.

Minor deviations from the original work plan are described in the following paragraphs.

Work has started early/is starting late in the following tasks:

- T2.4, How to get acceptance of hypermodels by patients and clinicians (M12-42): Initial work has been done in this task, which includes the discussion of requirements for the validation of hypermodels and the start of data collection for different cancer domains.
- T3.4, Applying the CHIC infrastructure to other cancer types (M12-36): in this task, UNITO has started the collection of data for prostate cancer.

Change of person months:

In work package 7, partner USFD have elected to engage a PhD student at less cost and more effort. There will be no net effect on the budget, simply more effort applied to this work package overall. The total effort for partner USFD in WP7, originally planned to be 88 person/month, is now projected to be 118PM.

For more detail, reference is made to the reports on the work packages. This deviation does not have any negative impact on other tasks and do not influence the resources originally planned.

Impact of possible deviations from the planned milestones and deliverables

In the first six months of the project, deliverables and milestones have been submitted or achieved as foreseen in Annex I.

Any changes to the legal status of any of the beneficiaries

From 1 March 2013 onwards, i.e. shortly before the official start date of the CHIC project, former partner SCS Srl, an SME based in Milano, was taken over by Consorzio Interuniversitario CINECA, a non-profit consortium of 54 Italian universities, the National Institute of Oceanography and Experimental Geophysics, the National Research Council and the Ministry of Education, University and Research. The takeover was organized along the regulations concerning the partial transfer of rights and obligations from one entity to

another. Accordingly, CINECA agreed to perform all of SCS's task and responsibilities in the CHIC project. Following a formal communication between CINECA and the European Commission (dated 15 February 2013), the CHIC budget and Description of Work were adapted to the new partner. CINECA then acceded to the CHIC Grant Agreement as well as the CHIC Consortium Agreement and the project negotiations could be closed.

Development of the Project website

The first version of the CHIC website went online in June 2013 and is available under www.chic-vph.eu. The website has been set up to ensure the smooth information and communication within the consortium as well as with the public. It is therefore divided into a publicly accessible information platform and a password protected internal area for project management. It has been continuously updated over the past months to reflect the progress of the project. Especially the news section has been used significantly to keep the public informed about the on-goings in CHIC. The first attendances at conferences have been announced in the events section to give interested the scientific community the opportunity to meet and connect with CHIC partners. In addition, a Wiki has been installed to provide a feature for the partners where they can share instant information, discuss topics on the spot and create as well as edit documents between the partners. As the project continues over the next 3.5 years, the website will be constantly revised and updated to reflect the project's progress and meet the consortium's requirements.



More detailed information on the features of the website is available in Deliverable D12.1 "Dissemination Plan".

Statement on the use of the resources

Planned versus actual efforts in WP1			
Partner	Planned PM Total	Planned PM Period 1	Actual PM Period 1
1-ICCS	8.00	2.00	0.80
2-Eurice	38.00	9.50	3.13
6-USFD	4.00	0.44	0.25
7-FORTH	2.00	0.50	0.00
10-UOXF	2.00	0.40	0.48
16-CINECA	1.00	0.25	0.40
Total	55.00	13.09	5.06

Dissemination activities and publications

As an overview of the dissemination of foreground, a list of dissemination activities (divided into workshops/conferences and press) as well as a list of publications produced in the current reporting period are provided below.

Workshops and conferences

Title	Type	Main leader/Participants	Event	Venue	Date
Cross-Industry Workshop	Workshop	UCL	Cross-Industry Workshop	London, UK	30-31 October 2013
11th HGG-IMMUNO-Meeting	Conference	KULeuven	11th HGG-IMMUNO-Meeting	Leuven, Belgium	21 October 2013
Computational Methods in Cancer Research	Workshop	USFD	Computational Methods in Cancer Research	Sheffield, UK	11 October 2013
Modelling solid tumour growth: from in vitro to in vivo via in silico	Workshop	UOXF	Computational Methods in Cancer Research	Sheffield, UK	11 October 2013
Brain Tumor Segmentation Challenge	Workshop	UBERN	Brain Tumor Segmentation Challenge, MICCAI 2013, Nagoya, Japan	Nagoya, Japan	22 September 2009
American Chemical Society Annual Meeting	Conference	UPENN	Computational Structural Biology Session	Indianapolis, IN	8-12 September, 2013
Protein Society Meeting	Conference	UPENN	Computational Structural Biology Session	Boston, MA	20-23, July, 2013

Title	Type	Main leader/Participants	Event	Venue	Date
In Silico Oncology: Exploiting Clinical Studies to Clinically Adapt and Validate Multiscale Oncosimulators	Conference	ICCS, FORTH, USAAR, Philips,	EMBC 2013	Osaka, Japan	6 July 2013
Clinical multi-model studies on prostate cancer	Workshop	UNITO	2 nd Summer School in Computational Oncology	Wadern, Germany	25 June 2013
The Continuous Mathematics Based Oncosimulator: A demonstrator for the case of Glioblastoma Multiforme. Clinical validation aspects.	Workshop	ICCS	2 nd Summer School in Computational Oncology	Wadern, Germany	25 June 2013
The Generic Oncosimulator as an integrative platform for In Silico Oncology: The CHIC project paradigm	Workshop	ICCS	2 nd Summer School in Computational Oncology	Wadern, Germany	25 June 2013
Legal and ethical challenges in ICT for health scenarios and how security can help to solve them	Lecture	LUH	2 nd Summer School in Computational Oncology	Wadern, Germany	26 June 2013
Security and privacy challenges for clinical research IT	Lecture	Custodix	2 nd Summer School in Computational Oncology	Wadern, Germany	26 June 2013
CASyM (Coordinating Action Systems Medicine) modelling Workshop	Workshop	ICCS	CASyM 2013	Heidelberg, Germany	11 June 2013
Mathematical modelling: an effective weapon for fighting cancer?	Workshop/ Seminar	UOXF	Centre for Systems Biology, Stuttgart University	Stuttgart, Germany	June 2013

Press activities

Title	Type	Main leader	Reference	Date
Optimising cancer treatment through in-silico oncology	Online article	Eurice	Link: http://eurice.eu/news/details/article/optimising-cancer-treatment-through-in-silico-oncology/	28 May 2013
New Horizons in Cancer Treatment	Newspaper Article	ICCS	http://www.tovima.gr/society/article/?aid=507213	11 April 2013
A Novel Cancer (Related) Project	Newspaper Article	ICCS	http://news.kathimerini.gr/4Dcgi/4Dcgi/_w_articles_columns_2_10/04/2013_516943	10 April 2013
Complex Mathematics Against Cancer	Newspaper Article	ICCS	http://www.enet.gr/?i=news.el.article&id=356570	10 April 2013

Publications

Title	Abstract	Contact person	Involved Institutions	Reference	Category	Publication date	Co-Authors	Status
A Hybrid Model for Multimodal Brain Tumor Segmentation	n/a	Mauricio Reyes	UBERN		Peer-reviewed publication	2013	S. Bauer, J. Slotboom, R. Wiest	Accepted (in press)

In Silico Oncology: Exploiting Clinical Studies to Clinically Adapt and Validate Multiscale Oncosimulators	This paper presents a brief outline of the notion and the system of oncosimulator in conjunction with a high level description of the basics of its core multiscale model simulating clinical tumor response to treatment. The exemplary case of lung cancer preoperatively treated with a combination of chemotherapeutic agents is considered. The core oncosimulator model is based on a primarily top-down, discrete entity - discrete event multiscale simulation approach. The critical process of clinical adaptation of the model by exploiting sets of multiscale data originating from clinical studies/trials is also outlined. Concrete clinical adaptation results are presented. The adaptation process also conveys important aspects of the planned clinical validation procedure since the same type of multiscale data - although not the same data itself- is to be used for clinical validation. By having exploited actual clinical data in conjunction with plausible literature-based values of certain model parameters, a realistic tumor dynamics behavior has been demonstrated. The latter supports the potential of the specific oncosimulator to serve as a personalized treatment optimizer following an eventually successful completion of the clinical adaptation and validation process.	Georgios Stamatakos	ICCS, FORTH, USAAR		Peer-reviewed publication	2013	D Dionysiou, A Lunzer, R Belleman, E Kolokotroni, E Georgiadi, M Erdt, J Pukacki, S Rueping, S Giatili, A d'Onofrio, S Sfakianakis, K Marias, C Desmedt, M Tsiknakis, and N Graf	Accepted (in press)
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The Technologically Integrated Oncosimulator: Combining Multiscale Cancer Modeling with Information Technology in the In Silico Oncology Context	The Oncosimulator is defined as an information technology system simulating in vivo tumor response to therapeutic modalities within the clinical trial context. Chemotherapy in the neoadjuvant setting, according to two real clinical trials concerning nephroblastoma and breast cancer, has been considered. The spatiotemporal simulation module embedded in the Oncosimulator is based on the multiscale, predominantly top-down, discrete entity - discrete event cancer simulation technique developed by the In Silico Oncology Group, National Technical University of Athens. The technology modules include multiscale data handling, image processing, invocation of code execution via a spreadsheet-inspired environment portal, execution of the code on the grid and visualization of the predictions. A refining scenario for the eventual coupling of the Oncosimulator with immunological models is also presented. Parameter values have been adapted to multiscale clinical trial data in a consistent way, thus supporting the predictive potential of the Oncosimulator. Indicative results demonstrating various aspects of the clinical adaptation and validation process are presented. Completion of these processes is expected to pave the way for the clinical translation of the system.	Georgios Stamatakos	ICCS, FORTH, TEI-C, USAAR	IEEE Journal of Biomedical and Health Informatics	Peer-reviewed publication	2013	D Dionysiou, A Lunzer, R Belleman, E Kolokotroni, E Georgiadi, M Erdt, J Pukacki, S Rueping, S Giatili, A d'Onofrio, S Sfakianakis, K Marias, C Desmedt, M Tsiknakis, and N Graf	Accepted (in press)
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<p>Molecular modeling of ErbB4/HER4 kinase in the context of the HER4 signaling network helps rationalize the effects of clinically identified HER4 somatic mutations on the cell phenotype</p>	<p>In the ErbB/HER family of receptor tyrosine kinases, the deregulation of the EGFR/ErbB1/HER1, HER2/ErbB2, and HER3/ErbB3 kinases is associated with several cancers, while the HER4/ErbB4 kinase has been shown to play an anti-carcinogenic role in certain tumors. We present molecular and network models of HER4/ErbB4 activation and signaling in order to elucidate molecular mechanisms of activation and rationalize the effects of the clinically identified HER4 somatic mutants. Our molecular-scale simulations identify the important role played by the interactions within the juxtamembrane region during the activation process. Our results also support the hypothesis that the HER4 mutants may heterodimerize but not activate, resulting in blockage of the HER4-STAT5 differentiation pathway, in favor of the proliferative PI3K/AKT pathway. Translating our molecular simulation results into a cellular pathway model of wild type versus mutant HER4 signaling, we are able to recapitulate the major features of the PI3K/AKT and JAK/STAT activation downstream of HER4. Our model predicts that the signaling downstream of the wild type HER4 is enriched for the JAK-STAT pathway, whereas downstream of the mutant HER4 is enriched for the PI3K/AKT pathway. HER4 mutations may hence constitute a cellular shift from a program of differentiation to that of proliferation.</p>	<p>Ravi Radhakrishnan</p>	<p>UPENN</p>	<p>Biotechnology Journal, 2013, in press. (Published Online)</p> <p>http://doi.wiley.com/10.1002/biot.201300022</p>	<p>Peer-reviewed Article</p>	<p>2013</p>	<p>S.E.Telesco, R. Vadigepalli, R. Radhakrishnan</p>	<p>In Press (Published Online)</p>
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Multiscale Cancer Modeling and In Silico Oncology: Emerging Computational Frontiers in Basic and Translational Cancer Research	n/a	Georgios Stamatakos	ICCS, USAAR, UPENN	J Bioengineer & Biomedical Sci, vol. 3, no. 2	Peer-reviewed publication	2013	N. Graf, R. Radhakrishnan	Published
Functional tissue units and their primary tissue motifs in multi-scale physiology		Bernard de Bono	UCL	Biomed Semant, vol. 4, no. 1 doi:10.1186/2041-1480-4-22	Peer-reviewed publication	2013	P. Grenon, R. Baldock, P. Hunter	Published

3. Deliverables and milestones tables

3.1 Deliverables

Table 1. Deliverables									
No.	Deliverable name	WP no.	Lead participant	Nature	Dissemination level	Due delivery date from Annex I	Delivered Yes/No	Actual / Forecast delivery date	Comments
D2.1	State of the art knowledge for building hypermodels	2	7-FORTH	R	PU	30.11.2013	No		
D2.2	Scenario based user needs and requirements	2	3-USAAR	R	PU	30.11.2013	No		
D2.3	Requirements for enhancing hypermodels beyond the domain of cancer	2	14-PHILIPS	R	CO	30.09.2014	No		
D2.4	Acceptance of hypermodels by patients and physicians	2	3-USAAR	R	PU	30.09.2016	No		
D3.1	Report on Scenarios and data from	3	4-KULEUVEN	R	PU	31.03. 2016	No		

Table 1. Deliverables									
No.	Deliverable name	WP no.	Lead participant	Nature	Dissemination level	Due delivery date from Annex I	Delivered Yes/No	Actual / Forecast delivery date	Comments
	defined patients								
D3.2	Report on Scenarios and data from other cancer types for usage by the CHIC infrastructure	3	11-UNITO	R	PU	31.03.2016	No		
D3.3	Demonstration of the developed Meta- and Hyper-Multiscale Models and Repositories	3	1-ICCS	O	PU	31.03.2017	No		
D4.1	Initial analysis of the ethical and legal requirements for the sharing of data	4	8-LUH	R	PU	30.09.2013	Yes	30.09.2013	
D4.2	Initial analysis of the copyright-related legal requirements for the sharing of data	4	8-LUH	R	PU	31.12.2013	No		

Table 1. Deliverables									
No.	Deliverable name	WP no.	Lead participant	Nature	Dissemination level	Due delivery date from Annex I	Delivered Yes/No	Actual / Forecast delivery date	Comments
D4.3.1	Development of the data protection and copyright framework for CHIC first iteration	4	8-LUH	R	PU	31.05.2014	No		
D4.3.2	Development of the data protection and copyright framework for CHIC - second iteration	4	8-LUH	R	PU	30.09.2016	No		
D4.4	Whitepaper Recommendations for an amended European legal Framework	4	8-LUH	R	PU	31.03.2016	No		
D5.1.1	The CHIC technical architecture – initial version	5	7-FORTH	R	PU	31.03.2014	No		
D5.1.2	The final CHIC technical	5	7-FORTH	R	RE	30.09.2016	No		

Table 1. Deliverables									
No.	Deliverable name	WP no.	Lead participant	Nature	Dissemination level	Due delivery date from Annex I	Delivered Yes/No	Actual / Forecast delivery date	Comments
	architecture (including the security tools and cloud infrastructure)								
D5.2	Security guidelines and initial version of security tools	5	13-CUSTODIX	R	CO	30.09.2014	No		
D5.3	Techniques to build the cloud infrastructure available to the community	5	5-BED	R	PU	31.03.2015	No		
D6.1	Cancer hypomodelling and hypermodelling strategies and initial component models	6	1-ICCS	R	CO	30.09.2013	Yes	22.10.2013	D6.1 is a very extensive report and is expected to serve as the initial scientific basis for the entire project. The coordinator firmly believes that the quality, the extent and the depth of the document will have an important impact on most of the subsequent CHIC work and deliverables. Therefore, D6.1 should be of the highest quality possible and an

Table 1. Deliverables									
No.	Deliverable name	WP no.	Lead participant	Nature	Dissemination level	Due delivery date from Annex I	Delivered Yes/No	Actual / Forecast delivery date	Comments
									extension of the deadline for submission proved to be necessary.
D6.2	CHIC cancer component models: initial tested versions	6	1-ICCS	R	CO	30.11.2014	No		
D6.3	Initial standardized cancer hypermodels	6	1-ICCS	R	CO	31.05.2016	No		
D6.4	Clinical adaptation and partial validation of hypermodels	6	1-ICCS	R	CO	31.01.2017	No		
D7.1	Hypermodelling Specifications	7	1-ICCS	R	PU	31.03.2014	No		
D7.2	First Release Hypermodelling framework deployed on test nodes	7	16-CINECA	P	RE	31.03.2015	No		
D7.3	Hypermodels annotation services	7	15-UCL	P	RE	31.03.2016	No		

Table 1. Deliverables									
No.	Deliverable name	WP no.	Lead participant	Nature	Dissemination level	Due delivery date from Annex I	Delivered Yes/No	Actual / Forecast delivery date	Comments
D7.4	Final Hypermodelling framework deployed on test node	7	16-CINECA	O	RE	31.08.2016	No		
D8.1	Design of the CHIC repositories	8	1-ICCS	R	CO	31.07.2014	No		
D8.2	Prototype implementation of the CHIC repositories	8	12-UBERN	O	CO	31.03.2015	No		
D8.3	Implementation of the interfaces of the CHIC repositories	8	15-UCL	R	PU	30.09.2015	No		
D8.4	Report on the final system	8	1-ICCS	R	PU	30.09.2016	No		
D9.1	User requirements for the visualization toolkit and image analysis toolkits	9	5-BED	R	PU	30.09.2013	Yes	01.10.2013	
D9.2	A model and data visualization	9	5-BED	P	RE	31.01.2017	No		

Table 1. Deliverables									
No.	Deliverable name	WP no.	Lead participant	Nature	Dissemination level	Due delivery date from Annex I	Delivered Yes/No	Actual / Forecast delivery date	Comments
	toolkit								
D9.3	A multimodal and longitudinal brain tumour image analysis tool	9	12-UBERN	P	RE	31.01.2017	No		
D9.4	The tumor response quantitative platform	9	7-FORTH	P	RE	31.03.2016	No		
D10.1	The CHIC portal	10	7-FORTH	O	RE	30.11.2013	No		
D10.2	Design of the orchestration platform, related components and interfaces	10	14-PHILIPS	O	PU	30.09.2014	No		
D10.3	The CHIC Encryption Services	10	13-CUSTODIX	O	CO	31.03.2015	No		
D10.4	The PhysiomSpaceenabled storage on public clouds	10	7-FORTH	R	CO	31.03.2016	No		
D10.5	The CHIC integrated platform	10	7-FORTH	P	RE	30.11.2016	No		
D11.1	Evaluation and validation criteria for clinical	11	3-USAAR	R	PU	31.03.2014	No		

Table 1. Deliverables									
No.	Deliverable name	WP no.	Lead participant	Nature	Dissemination level	Due delivery date from Annex I	Delivered Yes/No	Actual / Forecast delivery date	Comments
	adaptation								
D11.2	Report on the first evaluation workshops round	11	3-USAAR	R	RE	30.09.2014	No		
D11.3	Report on the second evaluation Workshops round	11	3-USAAR	R	RE	31.03.2015	No		
D11.4	Validation of CHIC infrastructure as a whole	11	1-ICCS	R	RE	31.03.2017	No		
D12.1	Dissemination Plan	12	16-CINECA	R	PU	30.09.2013	Yes	01.10.2013	
D12.2	Dissemination Kit available	12	2-EURICE	O	PU	31.03.2014	No		
D12.3	Preliminary Plan for the Use and Dissemination of Foreground	12	16-CINECA	R	CO	31.03.2015	No		
D12.4	Draft Plan for the Use and Dissemination of Foreground	12	16-CINECA	R	CO	31.03.2016	No		
D12.5	Final Plan for the Use and Dissemination of Foreground	12	16-CINECA	R	CO	31.03.2017	No		
D12.6	Periodic	12	2-EURICE	R	PU	31.03.2014	No		

Table 1. Deliverables									
No.	Deliverable name	WP no.	Lead participant	Nature	Dissemination level	Due delivery date from Annex I	Delivered Yes/No	Actual / Forecast delivery date	Comments
	Newsletters					31.03.2015 31.03.2016 31.03.2017			

3.2 Milestones

Table 2. Milestones							
Milestone no.	Milestone name	WP no.	Lead beneficiary	Delivery date from Annex I dd/mm/yyyy	Achieved Yes/No	Actual/ Forecast achievement data dd/mm/yyyy	Comments
MS1	Kick-Off Meeting	1	2-Eurice	01.04.2013	Yes	10-12/04/2013	The Kick-Off Meeting was held at the Royal Olympic Hotel in Athens, Greece from 10-12 April 2013
MS2	Progress meetings	1	2-Eurice	30.09.2013	Yes	17-18/10/2013	The 1 st progress meeting of CHIC was held at FORTH, Heraklion, Greece, from 17-18 October 2013

Table 2. Milestones							
Milestone no.	Milestone name	WP no.	Lead beneficiary	Delivery date from Annex I dd/mm/yyyy	Achieved Yes/No	Actual/ Forecast achievement data dd/mm/yyyy	Comments
MS3	User needs and Requirements are defined	2	3-USAAR	30.11.2013	No		
MS4	Hypermodels are accepted by users	2	3-USAAR	30.09.2016	No		
MS5	Scenarios and data from nephroblastoma, GBM and NSCLC are available	3	4-KULEUVEN	31.03.2015	No		
MS6	Exploitation of the CHIC infrastructure by further cancer types	3	4-KULEUVEN	31.03.2016	No		
MS7	Meta- and Hyper-Multiscale Models can be Demonstrated	3	4-KULEUVEN	31.03.2017	No		
MS8	The CHIC Data protection and intellectual property framework	4	8-LUH	31.05.2014	No		
MS9	Initial CHIC Architecture and security guidelines	5	7-FORTH	30.09.2014	No		

Table 2. Milestones							
Milestone no.	Milestone name	WP no.	Lead beneficiary	Delivery date from Annex I dd/mm/yyyy	Achieved Yes/No	Actual/ Forecast achievement data dd/mm/yyyy	Comments
MS10	Final version of the CHIC Architecture	5	7-FORTH	30.09.2016	No		
MS11	Initial component models available for all cancer modelling branches	6	1-ICCS	30.09.2013	Yes	22.10.2013	D6.1 is available
MS12	Rational, numerical and clinical experience based check of the component models complete	6	1-ICCS	30.11.2014	No		
MS13	Availability of hypermodels for all clinic. scenarios compliant w. the guidelines to be prov. by WP7	6	1-ICCS	31.07.2016	No		
MS14	All hypermodels have been quantitatively clinically adapted	6	1-ICCS	31.01.2017	No		
MS15	First hypermodel infrastructure deployed	7	7-FORTH	31.03.2014	No		
MS16	Folksonomy and	7	5-BED	31.03.2015	No		

Table 2. Milestones							
Milestone no.	Milestone name	WP no.	Lead beneficiary	Delivery date from Annex I dd/mm/yyyy	Achieved Yes/No	Actual/ Forecast achievement data dd/mm/yyyy	Comments
	Ontology annotation and search services deployed						
MS17	Hypermodel editor, development and execution application ready	7	7-FORTH	31.03.2016	No		
MS18	Metahypermodels annotation completed	7	6-	31.03.2017	No		
MS19	Design of the CHIC repositories Completed	8	1-ICCS	31.07.2014	No		
MS20	Deployment of the CHIC repositories	8	15-	31.07.2015	No		
MS21	Integration with security and ethical framework	8	1-ICCS	30.09.2016	No		
MS22	Scalable & uncertainty visualization techniques	9	5-BED	31.03.2015	No		
MS23	Image segmentation	9	12-	30.09.2014	No		

Table 2. Milestones							
Milestone no.	Milestone name	WP no.	Lead beneficiary	Delivery date from Annex I dd/mm/yyyy	Achieved Yes/No	Actual/ Forecast achievement data dd/mm/yyyy	Comments
	& registration Techniques						
MS24	Initial version of the tumor response quantitative platform	9	7-FORTH	31.03.2015	No		
MS25	The CHIC Orchestration Platform and Encrypted Data Services	10	7-FORTH	31.03.2015	No		
MS26	Public cloud Deployment	10	7-FORTH	31.03.2016	No		
MS27	Evaluation and validation criteria for clinical adaptation are ready	11	3-USAAR	31.03.2014	No		
MS28	First evaluation Workshop	11	3-USAAR	30.09.2014	No		
MS29	Second evaluation Workshop	11	3-USAAR	31.03.2016	No		
MS30	Internal collaborative area and external website	12	2-EURICE	30.06.2013	Yes	28.06.2013	Website is online and operational: www.chic-vph.eu
MS31	First CHIC summer School	12	3-USAAR	30.09.2014	No		
MS32	CHIC workshop	12	1-ICCS	30.09.2015	No		

Table 2. Milestones							
Milestone no.	Milestone name	WP no.	Lead beneficiary	Delivery date from Annex I dd/mm/yyyy	Achieved Yes/No	Actual/ Forecast achievement data dd/mm/yyyy	Comments
MS33	Second CHIC summer school	12	3-USAAR	30.09.2016	No		

4. Explanation of the use of the resources

The costs presented in the explanation of the use of the resources in this interim report are based on estimates and serve the purpose of having a good overview on how the budget has been used so far to see problems as early as possible and take corrective action where required.

4.1 Budget Overview

Cost Budget Follow-up Table						
Contract n°	270089	Project acronym				
PARTICIP.	TYPE of EXPENDITURE (as defined by participants)	BUDGET	ACTUAL COSTS (EUR)		Percentage spent	Remaining Budget (EUR)
			Period 1	Total	Total/ Budget	
			M1-M6			
ICCS	Total Person-month	106,00	11,30	11,30	11%	94,70
	Personnel	636.000,00	46.168,11	46.168,11	7%	589.831,89
	Other direct costs	227.000,00	13.654,36	13.654,36	6%	213.345,64
	Subcontracting	6.000,00	0,00	0,00	0%	6.000,00
	Adjustments			0,00	0%	0,00
	Indirect costs	517.800,00	35.893,48	35.893,48	7%	481.906,52
	Total Costs	1.386.800,00	95.715,95	95.715,95	7%	1.291.084,05
Eurice	Total Person-month	50,00	5,30	5,30	11%	44,70
	Personnel	324.500,00	28.223,10	28.223,10	9%	296.276,90
	Other direct costs	39.173,00	1.584,48	1.584,48	4%	37.588,52
	Subcontracting	6.000,00	0,00	0,00	0%	6.000,00
	Adjustments			0,00	0%	0,00
	Indirect costs	275.825,00	23.947,29	23.947,29	9%	251.877,71
	Total Costs	645.498,00	53.754,87	53.754,87	8%	591.743,13
USAAR	Total Person-month	135,00		0,00	0%	135,00
	Personnel	725.498,00	5.851,00	5.851,00	1%	719.647,00
	Other direct costs	326.764,00	2.413,00	2.413,00	1%	324.351,00
	Subcontracting	5.682,00	Due to limited availability of financial data, USAAR's financial efforts, esp. personnel costs remain incomplete for M1-6.			5.682,00
	Adjustments					0,00
	Indirect costs	631.357,00	4.958,40	4.958,40	1%	626.398,60
	Total Costs	1.689.301,00	13.222,40	13.222,40	1%	1.676.078,60
KULeuven	Total Person-month	68,00	2,50	2,50	4%	65,50
	Personnel	340.000,00	12.805,68	12.805,68	4%	327.194,32
	Other direct costs	167.500,00	1.045,85	1.045,85	1%	166.454,15
	Subcontracting	2.000,00	0,00	0,00	0%	2.000,00
	Adjustments			0,00	0%	0,00
	Indirect costs	304.500,00	8.310,92	8.310,92	3%	296.189,08
	Total Costs	814.000,00	22.162,45	22.162,45	3%	791.837,55
BED	Total Person-month	88,00		0,00	0%	88,00
	Personnel	484.000,00	29.966,70	29.966,70	6%	454.033,30
	Other direct costs	49.000,00	2.000,00	2.000,00	4%	47.000,00
	Subcontracting	5.000,00	Due to limited availability of financial data, BED's financial efforts are based on estimates for the period from M1-6.			5.000,00
	Adjustments					0,00
	Indirect costs	319.800,00				319.800,00
	Total Costs	857.800,00	31.966,70	31.966,70	#BEZUG!	825.833,30

Cost Budget Follow-up Table						
Contract n°	270089	Project acronym				
PARTICIP.	TYPE of EXPENDITURE (as defined by participants)	BUDGET	ACTUAL COSTS (EUR)		Percentage spent	Remaining Budget (EUR)
			Period 1	Total	Total/ Budget	
			M1-M6			
USFD	Total Person-month	140,00	10,63	10,63	8%	129,37
	Personnel	679.296,00	34.358,69	34.358,69	5%	644.937,31
	Other direct costs	78.001,00	0,00	0,00	0%	78.001,00
	Subcontracting	4.000,00	0,00	0,00	0%	4.000,00
	Adjustments			0,00	0%	0,00
	Indirect costs	454.378,00	20.615,21	20.615,21	5%	433.762,79
	Total Costs	1.215.675,00	54.973,90	54.973,90	5%	1.160.701,10
FORTH	Total Person-month	86,00	16,71	16,71	19%	69,29
	Personnel	412.800,00	30.849,47	30.849,47	7%	381.950,53
	Other direct costs	110.170,00	0,00	0,00	0%	110.170,00
	Subcontracting	6.000,00	0,00	0,00	0%	6.000,00
	Adjustments			0,00	0%	0,00
	Indirect costs	359.136,00	26.839,04	26.839,04	7%	332.296,96
	Total Costs	888.106,00	57.688,51	57.688,51	6%	830.417,49
LUH	Total Person-month	54,00	5,19	5,19	10%	48,81
	Personnel	350.622,00	25.406,50	25.406,50	7%	325.215,50
	Other direct costs	28.000,00	204,42	204,42	1%	27.795,58
	Subcontracting	3.000,00	0,00	0,00	0%	3.000,00
	Adjustments			0,00	0%	0,00
	Indirect costs	227.173,00	15.366,55	15.366,55	7%	211.806,45
	Total Costs	608.793,00	40.977,47	40.977,47	7%	567.815,53
UPENN	Total Person-month	84,00	4,43	4,43	5%	79,57
	Personnel	391.564,00	13.969,93	13.969,93	4%	377.594,07
	Other direct costs	63.501,00	4.071,55	4.071,55	6%	59.429,45
	Subcontracting	5.000,00	0,00	0,00	0%	5.000,00
	Adjustments			0,00	0%	0,00
	Indirect costs	282.140,00	11.059,87	11.059,87	4%	271.080,13
	Total Costs	742.204,00	29.101,35	29.101,35	4%	713.102,65
UOXF	Total Person-month	54,00	0,67	0,67	1%	53,33
	Personnel	289.077,00	3.073,55	3.073,55	1%	286.003,45
	Other direct costs	59.184,00	537,86	537,86	1%	58.646,14
	Subcontracting	3.902,00	0,00	0,00	0%	3.902,00
	Adjustments			0,00	0%	0,00
	Indirect costs	208.956,00	1.822,61	1.822,61	1%	207.133,39
	Total Costs	561.119,00	5.434,02	5.434,02	1%	555.684,98
UNITO	Total Person-month	54,00	3,88	3,88	7%	50,12
	Personnel	270.000,00	8.114,95	8.114,95	3%	261.885,05
	Other direct costs	100.000,00	264,65	264,65	0%	99.735,35
	Subcontracting	5.000,00	0,00	0,00	0%	5.000,00
	Adjustments			0,00	0%	0,00
	Indirect costs	222.000,00	5.352,38	5.352,38	2%	216.647,62
	Total Costs	597.000,00	13.731,98	13.731,98	2%	583.268,02
UBERN	Total Person-month	62,00	5,58	5,58	9%	56,42
	Personnel	465.000,00	26.817,05	26.817,05	6%	438.182,95
	Other direct costs	60.000,00	5.929,33	5.929,33	10%	54.070,67
	Subcontracting	4.000,00	0,00	0,00	0%	4.000,00
	Adjustments			0,00	0%	0,00
	Indirect costs	315.000,00	19.647,83	19.647,83	6%	295.352,17
	Total Costs	844.000,00	52.394,21	52.394,21	6%	791.605,79

Cost Budget Follow-up Table						
Contract n°	270089	Project acronym				
PARTICIP.	TYPE of EXPENDITURE (as defined by participants)	BUDGET	ACTUAL COSTS (EUR)		Percentage spent	Remaining Budget (EUR)
			Period 1	Total	Total/ Budget	
			M1-M6			
CUSTODIX	Total Person-month	24,00	1,49	1,49	6%	22,51
	Personnel	180.000,00	7.385,06	7.385,06	4%	172.614,94
	Other direct costs	33.000,00	593,16	593,16	2%	32.406,84
	Subcontracting	0,00	0,00	0,00	0%	0,00
	Adjustments			0,00	0%	0,00
	Indirect costs	90.000,00	4.053,66	4.053,66	5%	85.946,34
	Total Costs	303.000,00	12.031,88	12.031,88	4%	290.968,12
PHILIPS	Total Person-month	54,00	0,30	0,30	1%	53,70
	Personnel	398.466,00	3.200,00	3.200,00	1%	395.266,00
	Other direct costs	25.000,00	0,00	0,00	0%	25.000,00
	Subcontracting	3.000,00	0,00	0,00	0%	3.000,00
	Adjustments			0,00	0%	0,00
	Indirect costs	592.650,00	4.768,00	4.768,00	1%	587.882,00
	Total Costs	1.019.116,00	7.968,00	7.968,00	1%	1.011.148,00
UCL	Total Person-month	74,00	10,87	10,87	15%	63,13
	Personnel	497.978,00	14.794,87	14.794,87	3%	483.183,13
	Other direct costs	161.000,00	602,64	602,64	0%	160.397,36
	Subcontracting	6.000,00	0,00	0,00	0%	6.000,00
	Adjustments			0,00	0%	0,00
	Indirect costs	395.386,00	9.238,51	9.238,51	2%	386.147,49
	Total Costs	1.060.364,00	24.636,02	24.636,02	2%	1.035.727,98
CINECA	Total Person-month	57,00	6,71	6,71	12%	50,29
	Personnel	228.000,00	22.527,40	22.527,40	10%	205.472,60
	Other direct costs	54.408,00	1.267,91	1.267,91	2%	53.140,09
	Subcontracting	0,00	0,00	0,00	0%	0,00
	Adjustments			0,00	0%	0,00
	Indirect costs	313.899,00	36.951,98	36.951,98	12%	276.947,02
	Total Costs	596.307,00	60.747,29	60.747,29	10%	535.559,71
TEI-C	Total Person-month	17,00	1,30	1,30	8%	15,70
	Personnel	37.400,00	2.861,04	2.861,04	8%	34.538,96
	Other direct costs	11.900,00	1.555,96	1.555,96	13%	10.344,04
	Subcontracting	0,00	0,00	0,00	0%	0,00
	Adjustments				0%	0,00
	Indirect costs	29.580,00	2.650,20	2.650,20	9%	26.929,80
	Total Costs	78.880,00	7.067,20	7.067,20	9%	71.812,80
Total	Total Person-month	1.207,00	66,27	66,27	5%	1.140,73
	Personnel	6.710.201,00	195.422,87	195.422,87	3%	6.514.778,13
	Other direct costs	1.593.601,00	31.047,52	31.047,52	2%	1.562.553,48
	Subcontracting	64.584,00	0,00	0,00	0%	64.584,00
	Adjustments				0%	0,00
	Indirect costs	5.317.580,00	194.326,11	194.326,11	4%	5.123.253,89
	Total Costs	13.907.963,00	371.248,66	371.248,66	3%	13.536.714,34

4.2 Budget Explanations

Explanation of the use of resources for				ICCS		
Contract n°	600841	Project acronym	CHIC			
Work Package	XXX	Item description	Amount in €	Explanations		
WP1, WP6, WP8, WP12		Personnel	46.168,11	Salaries of 2 senior scientists (3,36PM), 6 PhD Students (6,8 PM), 2 Assistants (1,14 PM)		
WP1, WP6		Travel	4.649,92	CHIC Kick-Off meeting Athens, Greece (EAB members' expenses); Technical meeting ICCS/ KULeuven (16.-18.06.2013)		
		Consumables				
WP6, WP8		Equipment	1.405,06	2 desktop computers and monitors		
		Subcontracting				
WP1, WP12		Other	7.599,38	Banking fees, meeting organization, CHIC poster		
Total Direct Costs			59.822,47			
			INDIRECT COSTS	35.893,48		

Explanation of the use of resources for				EURICE		
Contract n°	600841	Project acronym	CHIC			
Work Package	XXX	Item description	Amount in €	Explanations		
WP1, WP12		Personnel	28.223,09	Salaries of 6 employees (5,31 PM)		
WP1		Travel	1.377,32	CHIC Kick-Off meeting, Athens, Greece		
		Consumables				
		Equipment				
		Subcontracting				
WP1		Other	207,16	Shipping		
Total Direct Costs			29.807,57			
			INDIRECT COSTS	23.947,29		

Explanation of the use of resources for			USAAR		
Contract n°	600841	Project acronym	CHIC		
Work Package	XXX	Item description	Amount in €	Explanations	
		Personnel	5.851,00	Salaries for 3 senior researchers and 2 researchers	
		Travel	2.413,00	CHIC Kick-Off Meeting, Athens, Greece	
		Other			
Total Direct Costs			8.264,00		
INDIRECT COSTS			4.958,40		

Due to limited availability of financial data, USAAR's financial efforts, esp. personnel costs remain incomplete for M1-6.

Explanation of the use of resources for			KULeuven		
Contract n°	600841	Project acronym	CHIC		
Work Package	XXX	Item description	Amount in €	Explanations	
WP3		Personnel	12.805,68	Salary of 1 scientist (2,5 PM)	
WP3		Travel	84,04	Technical meeting ICCS/ KULeuven (16.-18.06.2013)	
WP3		Consumables	961,81	1 laptop solely used for the CHIC project	
		Equipment			
		Subcontracting			
		Other			
Total Direct Costs			13.851,53		
INDIRECT COSTS			8.310,92		

Explanation of the use of resources for			BED		
Contract n°	600841	Project acronym	CHIC		
Work Package	XXX	Item description	Amount in €	Explanations	
		Personnel	29.966,70		
		Travel	2.000,00		
		Consumables			
		Equipment			
		Subcontracting			
		Other			
Total Direct Costs			31.966,70		
INDIRECT COSTS			19.180,02		

Due to limited availability of financial data, BED's financial efforts are based on estimates for the period from M1-6.

Explanation of the use of resources for				USFD		
Contract n°	600841	Project acronym	CHIC			
Work Package	XXX	Item description	Amount in €	Explanations		
WP1, WP7, WP12		Personnel	34.358,69	Salaries of 2 senior scientists (3,08 PM), 1 PhD Student (6 PM), 1 Administrator (1 PM), 1 Research Finance officer (0,05 PM)		
WP7		Travel	2.156,69	CHIC Kick-Off meeting, Athens, Greece		
WP7		Consumables	96,99	Computer equipment (hard drive), travel insurance		
WP7		Equipment	1.033,79	Research workstation		
		Subcontracting				
		Other				
Total Direct Costs			37.646,16			
INDIRECT COSTS			20.615,21			

Explanation of the use of resources for				FORTH		
Contract n°	600841	Project acronym	CHIC			
Work Package	XXX	Item description	Amount in €	Explanations		
WP2, WP6, WP7, WP9, WP10, WP11		Personnel	30.849,47	Salaries of 2 senior scientists (2.4PM); salaries of 7 technicians (13.88PM) and 1 doctor (0,42PM)		
		Travel				
		Consumables				
		Equipment				
		Subcontracting				
		Other				
Total Direct Costs			30.849,47			
INDIRECT COSTS			26.839,04			

Explanation of the use of resources for				LUH		
Contract n°	600841	Project acronym	CHIC			
Work Package	XXX	Item description	Amount in €	Explanations		
WP4		Personnel	25.406,50	salaries of 1 scientist (0,8PM), 2 PhD students (4,1PM) and 1 student assistant (0,29PM)		
WP4		Travel	204,42	CHIC Kick-Off Meeting, Athens, Greece		
		Consumables				
		Equipment				
		Subcontracting				
		Other				
Total Direct Costs			25.610,92			
			INDIRECT COSTS	15.366,55		

Explanation of the use of resources for				UPENN		
Contract n°	600841	Project acronym	CHIC			
Work Package	XXX	Item description	Amount in €	Explanations		
WP6		Personnel	13.969,93	Salaries of 1 senior researcher (0,3 PM) and 2 graduate research assistants (4,04 PM)		
WP6, WP12		Travel	2.627,47	CHIC Kick-Off meeting, Athens, Greece; San Diego Super Computer Center (04.08.2013-09.08.2013); American Chemical Society Meeting (08.-12.09.2013)		
		Consumables				
		Equipment				
		Subcontracting				
	WP6	Other	1.444,08	CHIC poster; Intel Composer XE for Linux OS		
Total Direct Costs			18.041,48			
			INDIRECT COSTS	11.059,87		

Explanation of the use of resources for				UOXF		
Contract n°	600841	Project acronym	CHIC			
Work Package	XXX	Item description	Amount in €	Explanations		
WP1, WP6		Personnel	3.073,55	Senior Scientist: 0.66 PM		
WP1		Travel	537,86	CHIC Kick-Off Meeting		
		Consumables				
		Equipment				
		Subcontracting				
		Other				
Total Direct Costs			3.611,41			
			INDIRECT COSTS	1.822,61		

Explanation of the use of resources for				UNITO		
Contract n°	600841	Project acronym	CHIC			
Work Package	XXX	Item description	Amount in €	Explanations		
WP3, WP11, WP12		Personnel	8.114,95	Salaries of 2 researchers (3,88 PM)		
WP3		Travel	264,65	CHIC Kick-Off Meeting, Athens, Greece		
		Consumables				
		Equipment				
		Subcontracting				
		Other				
Total Direct Costs			8.379,60			
			INDIRECT COSTS	5.027,76		

Explanation of the use of resources for				UBERN		
Contract n°	600841	Project acronym	CHIC			
Work Package	XXX	Item description	Amount in €	Explanations		
WP5, WP6, WP8, WP9		Personnel	26.817,05	Salaries of 2 senior scientists (0,64 PM), 2 PhD students (4,7 PM), 1 assistant (0,24 PM)		
WP6, WP8, WP9		Travel	5.929,33	CHIC Kick-Off meeting, Athens, Greece; bilateral meeting UBERN/ KULeuven in Leuven, Belgium (22.-23.05.2013); MICCAI2013 conference, Nagoya, Japan		
		Consumables				
		Equipment				
		Subcontracting				
		Other				
Total Direct Costs			32.746,38			
			INDIRECT COSTS	19.647,83		

Explanation of the use of resources for				CUSTODIX		
Contract n°	600841	Project acronym	CHIC			
Work Package	XXX	Item description	Amount in €	Explanations		
WP2, WP4		Personnel	7.385,06	Salaries of 2 senior scientists (1,49 PM)		
WP2		Travel	593,16	CHIC Kick-Off meeting, Athens, Greece		
		Consumables				
		Equipment				
		Subcontracting				
		Other				
Total Direct Costs			7.978,22			
INDIRECT COSTS			4.053,66			

Explanation of the use of resources for				PHILIPS		
Contract n°	600841	Project acronym	CHIC			
Work Package	XXX	Item description	Amount in €	Explanations		
WP2		Personnel	3.200,00	1 Senior Researcher (0,3PM)		
		Travel				
		Consumables				
		Equipment				
		Subcontracting				
		Other				
Total Direct Costs			3.200,00			
INDIRECT COSTS			5.100,00			

Explanation of the use of resources for				UCL		
Contract n°	600841	Project acronym	CHIC			
Work Package	XXX	Item description	Amount in €	Explanations		
WP8, WP12		Personnel	14.794,87	Salaries of 2 researchers (3,2 PM)		
WP8		Travel	602,64	CHIC Kick-Off meeting, Athens, Greece		
		Consumables				
		Equipment				
		Subcontracting				
		Other				
Total Direct Costs			15.397,51			
INDIRECT COSTS			9.238,51			

Explanation of the use of resources for				CINECA		
Contract n°	600841	Project acronym	CHIC			
Work Package	XXX	Item description	Amount in €	Explanations		
WP1, WP7, WP12		Personnel	22.527,40	Salaries of 1 senior scientist (0,99 PM), 1 scientist (0,58 PM), 1 technician (3,92 PM), 1 administrator (1,23 PM)		
WP7		Travel	1.267,91	CHIC Kick-Off meeting, Athens, Greece; technical meeting at USFD, Sheffield, UK (03.-05.06.2013)		
		Consumables				
		Equipment				
		Subcontracting				
		Other				
Total Direct Costs			23.795,31			
INDIRECT COSTS			36.951,98			

Explanation of the use of resources for				TEI-C		
Contract n°	600841	Project acronym	CHIC			
Work Package	XXX	Item description	Amount in €	Explanations		
WP5		Personnel	2.861,04	1 PhD student (1,30PM)		
WP5		Travel	1.555,96	CHIC Kick-Off Meeting in Athens, Greece (648,77€); Technical meeting in Leuven, Belgium (907,19€)		
		Consumables				
		Equipment				
		Subcontracting				
		Other				
Total Direct Costs			4.417,00			
INDIRECT COSTS			2.650,20			

4.3 Planned versus actual efforts

Planned versus actual efforts are included in each work package report. An overview of the planned efforts compared to the actual efforts is still in the making as information is still being collected from the consortium members. Therefore, the overview document will be submitted alongside the first official CHIC report due after M12 of the project.