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GEMSS

Grid-enabled Medical Simulation Services

http://www.gemss.de

Deliverable D6.2c
Third (Final) Project Progress Report

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1.0	16.01.2005	Preview for ATR2005
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The GEMSS Consortium:

NEC Europe Ltd. – UK
ISS – Austria
CRID – Belgium
ASD – Germany
IT-Innovation – UK
MPI of Cognitive Neuroscience – Germany
IBMTP – Austria
ANSYS – UK
IDAC – Ireland
Sheffield University – UK

Executive Summary:

The final project progress report covers project months 25-30 (September 1st, 2004 - February 28st, 2005) of the GEMSS project and provides a summary of technical progress made and a consolidated management overview of final 6 months of the GEMSS project. Activities reported are in line with the project workplan as covered by the GEMSS Contract IST-2001-37153. The Final Project Progress Report will be available as a public document.

This report builds on the Second Annual Project Progress Report (D6.2b), to which the reader is conferred for additional context information.

Table of Contents:

1 Project Overview

GEMSS developed an interoperable, innovative Grid middleware for medical service applications building on common Grid standards. The focus is on innovative extensions that support medical applications including security models compliant with European legal issues, fail-over and recovery from errors as well as workflow and service orchestration techniques for time-critical processes. GEMSS is a two and a half year project which started in September 2002.

For more details, see the Second Progress Report, D6.2b, or for a comprehensive overview the Final Project Report, D6.3a.

2 Consortium

The Consortium consists of 10 partners, with three experienced in the GRID, two software developers, two University medical departments, and three end users, two of whom are specialist SME's in the area of bio-medical simulation. The Consortium thus represents a well balanced mixture of private and public partners whose activities range from basic research to industrial/commercial development and sales. The heterogeneous character of the Consortium has been designed to form a critical mass to best address the scientific requirements imposed by the problems to be solved.

No	Partner	Country	Specific Expertise, Role in the project
1	NEC	UK	Finite element simulation, mesh generation, GRID-middleware, HPC software & hardware, Project Management.
2	MPI	Germany	Medical image processing, Model validation, Acquisition of scan-data, medical end-users.
3	ISS	Austria	Programming environments, software tools, HPC tools and hardware, GRID technology.
4	USFD	UK	FSI modelling, cardiovascular and respiratory applications. Provision of validation datasets, scan data. Clinical test site for radiosurgery application. Medical end user.
5	ANSYS (CFX)	UK	Software and applications.
6	IT-Innovation	UK	GRID technology and know-how, technology transfer.
7	CRID	Belgium	Consultant in legal issues
8	ASD	Germany	FE and CFD consultancy for artificial organs and biomedical devices.
9	IDAC	Ireland	Stress-analysis consultancy, Consultancy, ANSYS re-sellers, GUIs
10	IBMTP	Austria	Image reconstruction software, acquisition of scan data, clinical end users

The following table shows the involvement of partners in work packages. Work package and sub-task leaders are marked by a red L.

Partner	ST1.1	ST1.2	ST1.3	ST2.1	ST2.2	ST3.1	ST3.2	ST3.3	ST4.1	ST4.2	ST4.3	ST4.4	ST4.5	ST4.6	WP5	WP6
NEC	x	x	x	x	x	L	L	x	L						x	L
MPI	x		L						x	L					x	
ISS	x	x	x	L	x	x	x	x						x	x	
USFD	L		x								L	L	L		x	
CFX/ANSYS	x		x	x		x	x					x	x		L	
IT-Innov.	L	L	x	L	L		x				x				x	
CRID	x		x		L										x	
ASD	x		x									x	x		x	
IDAC	x		x	x		x	x	L					x		x	
IBMTP	x		x											L	x	

3 Progress Report

3.1 Workpackage 1: System Design and Evaluation

This workpackage has three main responsibilities:

- to capture the system and end-user requirements,
- to produce a global design for GEMSS including the medical service applications and
- to evaluate the testbeds and the medical service applications within the testbeds produced during the course of this project.

3.1.1 Sub-task 1.1: Requirements Capture

Completed in a previous reporting period.

3.1.2 Sub-task 1.2: System Design

Completed in previous reporting period.

3.1.3 System Development

The final status of development work to date is shown in figures 3.1 and 3.2. The blue (light) modules have been developed and the red (dark) modules are technology demonstrators. Technology demonstrator modules will not be released as part of the main software release, but have been worked on until the end of the project and form the basis of a proof of concept development.

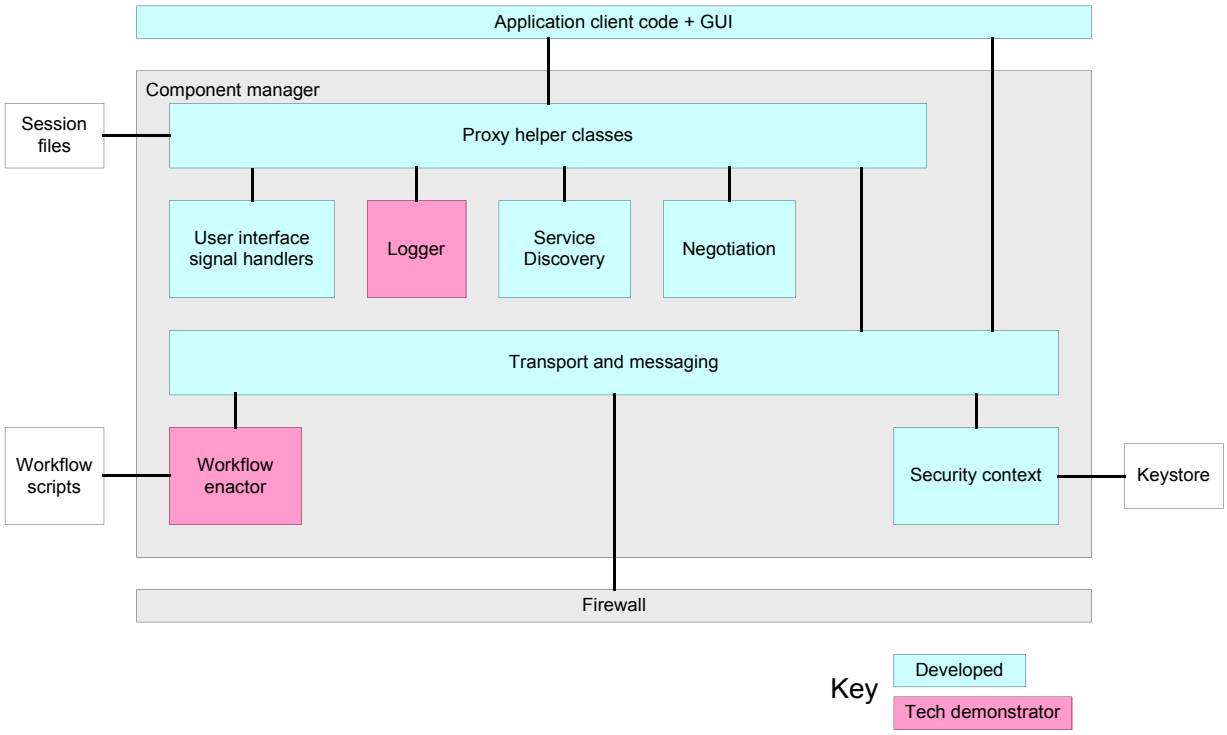

Figure 3.1: Client module development summary.

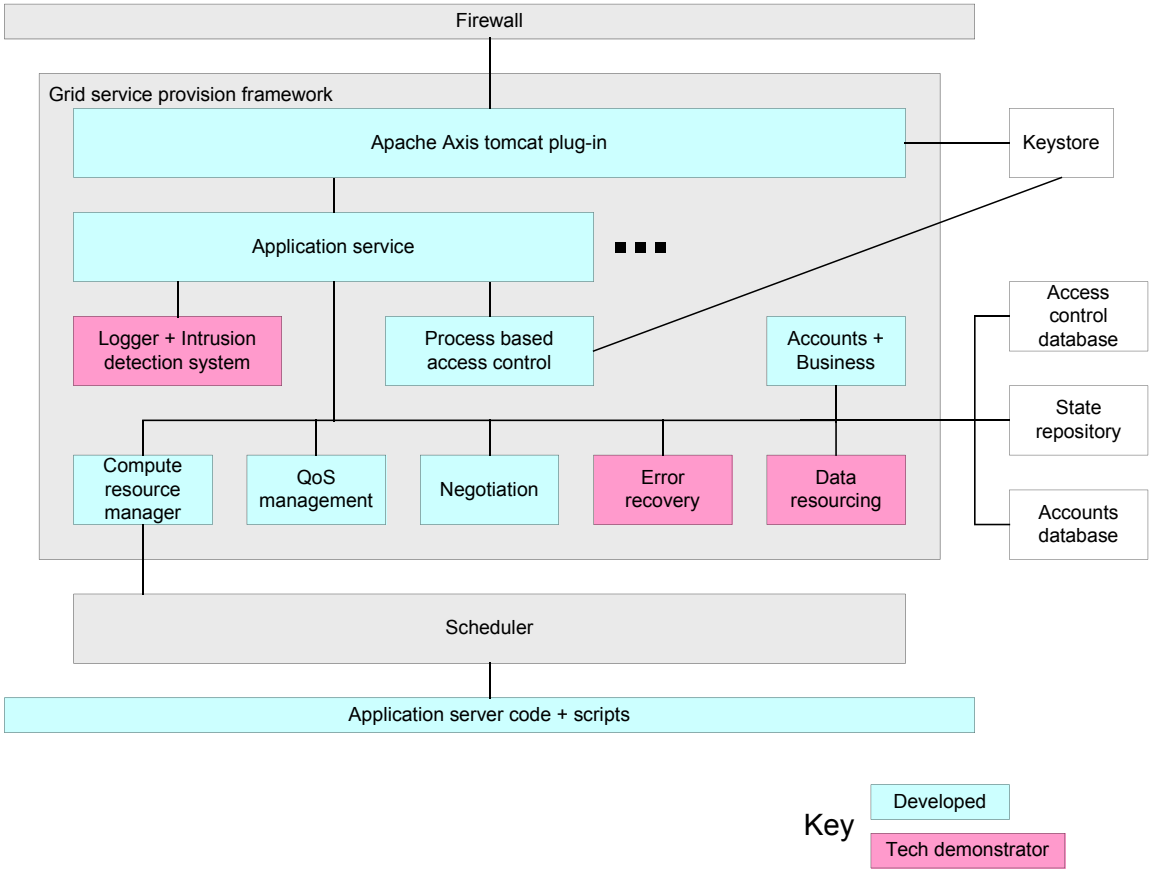

Figure 3.2: Service provider module development summary.

3.1.4 Sub-task 1.3: Evaluation

The final evaluation report D1.3b includes an evaluation of the final GEMSS system, a survey regarding the application developer experience, and a test of the performance of the GEMSS system.

The results of the evaluation can be summarised as follows:

- All six medical applications are now Grid-enabled, using the final phase I3 version of the GEMSS middleware. Five of the six GEMSS applications have been ported to the phase I4 technology demonstrator.
- Multiple stress tests were conducted to burden the middleware with a high load sufficient to break it, with tests lasting from a couple of days to a whole week. These tests revealed bugs within the server side parts of the middleware and after fixing, performance and robustness tests validated the middleware design and demonstrated the quality of the infrastructure.
- A long term test of the middleware provided information about the standard usage of the GEMSS middleware, lasting several months. Negotiation and file transfer overhead were measured and showed that the middleware is most suited for applications with a relatively

long run-time. This is consistent with the testbed applications implemented by the GEMSS consortium since they normally require such long runtimes.

Important feedback from the application developers identifed a few problems regarding the middleware:

- The certification process and Java keystore setup could be optimised further.
- The Client installation of the middleware could be supported by a cross-platform GUI installer in order to hide the complexity of the installation process.
- A server side standardisation of the execution environment would help the application developers to easily distribute applications to different service providers.
- A tutorial describing the steps necessary to port a high performance application to the GEMSS infrastructure could be part of the final release.

3.2 Workpackage 2: Grid Services & Security

3.2.1 Sub-task 2.1: Workflow and Quality of Service

3.2.1.1 Quality of Service

The work on this task was completed in a previous report period. Only minor bug fixes had to be provided after this date.

3.2.1.2 Workflow

The GEMSS workflow enactor is a technology demonstrator, and this work has continued until the end of the project. An internal report will be written to summarize all findings from this work.

Workflow related work in the last reporting period includes:

- Implementation of negotiation code
- Implementation of business / accounts code
- Integration of newly coded workflow with job handling code
- Internal report on how best to encode and enact GEMSS workflows

Hard-coded GEMSS workflow:

The initial workflow has been hardcoded in the phase I3 & I4 prototype, with job handling and negotiation workflow encoded into proxy components. Full details of the proxy components are available in the design deliverable D1.2b.

The GEMSSProxy provides an easy to use Java interface representing the GEMSS application service. As a proxy it provides java method wrappers for each of the application services functions, hiding the transport component invocation calls that are required behind the scenes. The GEMSSProxy component thus provides everything the application developers need to run jobs.

The GEMSSNegotiator provides all the functionality of the GEMSSProxy, but with additional support for negotiation workflow. This class will automatically conduct an auction with a number of service providers and agree the best WSLA contract with one of them.

Shipped with the phase I3 and I4 prototypes is an example application that demonstrates how to use the proxy classes and run Grid jobs. The workflow to run GEMSS jobs is very simple, consisting of the series of steps shown in figure 3.3. The negotiation workflow is more complicated, but from the interface screen shot of the example application's GUI it can be seen "in action" represented at a high level.

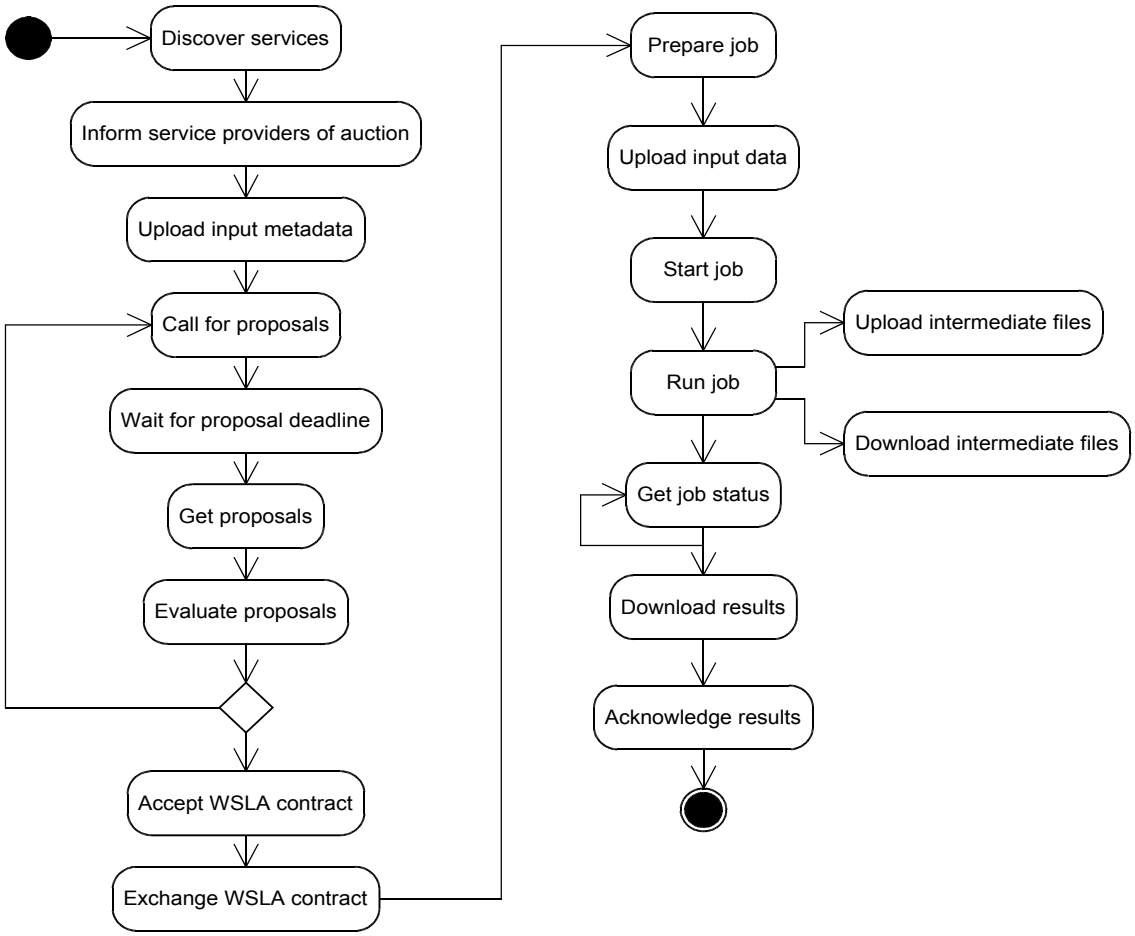

Figure 3.3. GEMSS workflow

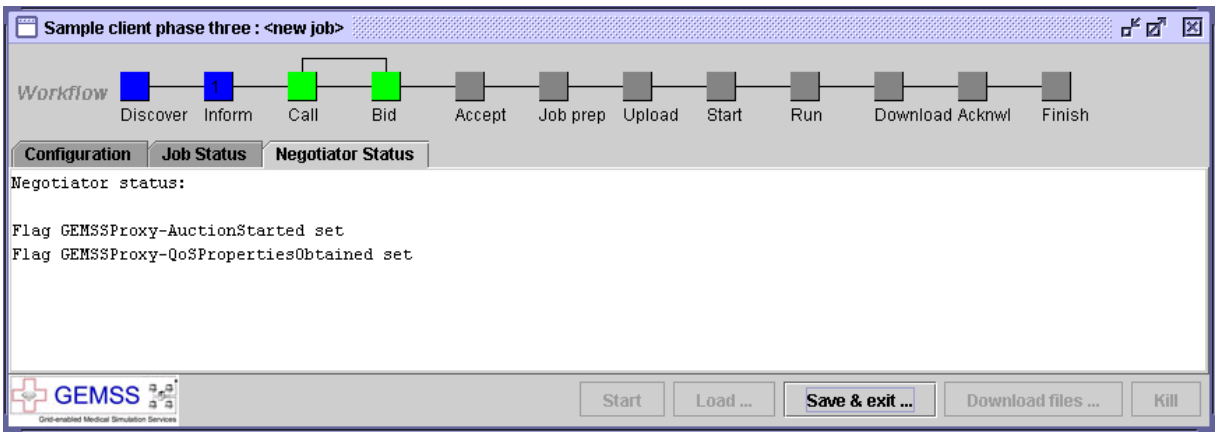

Figure 3.4 Screen shot of the example application shipped with the phase I4 prototype

3.2.2 Sub-task 2.2: Security and Legal Issues

3.2.2.1 Security Issues

All security deliverables have previously been released. Security work has continued until the end of the project with the following activities:

- Monitoring and investigation of the latest security issues, and provision of alerts to partners where appropriate (e.g. notification of security patches in third party code)
- Periodic upgrades to the GEMSS security software to keep in line with best practice
- Security advise to technical partners when developing the GEMSS infrastructure
- Security advise to end users when installing the GEMSS software and integrating thier applications
- Integration of the process-based access control software into the phase 4 infrastructure (see previous section on ST1.2 for more details)

3.2.2.2 Legal Issues

3.2.2.2.1 Privacy approach

This work has been completed in a previous reporting period.

3.2.2.2.2 Contractual approach

This work has been completed in a previous reporting period.

3.2.2.2.3 Liability approach

The legal work considers the liability aspects when using such HealthGRID tools regarding European Law.

It aimed at :

1° presenting the European rules interesting the liability aspects of the provision of GEMSS services;
2° giving a global view on the liability aspects for the provision of GEMSS services regarding European Law;
3° providing a conclusion and suggesting possible remedies.

Several legal instruments may concern the liability aspects when providing Grid-enabled Medical simulation services :

1° The European Convention on products liability in regard to personal injury and death;
2° The Council Directive 85/374/EEC of 25 July 1985 on the approximation of the laws, regulations and administrative provisions of the Member States concerning liability for defective products;
3° The Directive 2001/95/EC of the European Parliament and of the Council of 3 December 2001 on general products safety.

The producer is liable for damage caused by a defect in his product regarding Directive 85/374.

1. This assertion focuses on industrially produced movables.

2. The injured person has to prove:

1. the damage;
2. the defect;
3. the causal relationship between the defect and the damage.

3. When several persons are liable for the same damage, the injured person is entitled to full compensation for the damage from any of them.

4. The defect has to be determined by reference to the lack of the safety which the public at large is entitled to expect.

5. The producer is not liable in several cases as, by example, when he did not put the product into circulation or when the objective state of scientific and technical knowledge, including the most advanced level of such knowledge, at the time when the product in question was put into circulation was not such as to enable the existence of the defect to be discovered. The knowledge must have been accessible at the time when the product was put into circulation.

6. Compensation may be asked for:

4. death;
5. personal injury;
6. damage to property – limited to goods for private use or consumption.

Under directive 85/372 there is no compensation for pain and suffering and other no material damages payable where appropriate under the law applicable to the case.

7. There is a limitation period under Directive 85/374 for the recovery of damages from the day on which the plaintiff became aware or should reasonably have become aware of the damage, the defect and the identity of the producer.

The right of the plaintiff to compensation is extinguished ten years from the date on which the product was put into circulation.

In conclusion there is harmonization in European Law concerning the liability aspects for the provision of the GEMSS services regarding defective product – even if this harmonization does not include compensation for pain and suffering and other no material damages.

This harmonization does no more cover the liability relative to the provision of the services provided notably to the patient.

In order to fully appreciate the liability issue regarding the provision of the GEMSS services, the partners should consider all the legal possibilities to be attacked in case of damage. It requires to study first the international jurisdiction of the States where the suit could be introduced (forum convenience) and then to analyze the law applicable to the suit. This kind of legal consultancy is very expensive and takes a lot of time.

On this other hand if the funding of this kind of legal consultancy may be considered for simple situation inducing huge financial return, it seems to be inappropriate for the provision of the GEMSS services on a day-to-day and low cost basis.

Numerous works have already been conducted to study the problem related to the disharmonies between national Tort Laws in Europe, notably by the European Centre of Tort and Insurance Law (www.ectil.org).

ECTIL edits the serie of PRINCIPLES OF EUROPEAN TORT LAW comprising today the following studies :

- Vol. 1: J. Spier (ed.), *The Limits of Liability: Keeping the Floodgates Shut* (1996);
- Vol. 2: J. Spier (ed.), The *Limits of Expanding Liability: Eight Fundamental Cases in a Comparative Perspective* (1998);
- Vol. 3: H. Koziol (ed.), *Unification of Tort Law: Wrongfulness* (1998);
- Vol. 4: J. Spier (ed.), *Unification of Tort Law: Causation* (2000);
- Vol. 5: U. Magnus (ed.), *Unification of Tort Law: Damages* (2001);
- Vol. 6: B.A. Koch/H. Koziol (eds.), *Unification of Tort Law: Strict Liability* (2002);
- Vol. 7: J. Spier (ed.), *Unification of Tort Law: Liability for Damage Caused by Others* (2003);
- Vol. 8: U. Magnus/M. Martín-Casals (eds.), *Unification of Tort Law: Contributory Negligence* (2004);
- Vol. 9: W.V.H. Rogers (ed.), *Unification of Tort Law: Multiple Tortfeasors* (2004).

ECTIL also edits the results of research projects:

- Vol. 1: M. Faure/H. Koziol (eds.), Cases on Medical Malpractice in a Comparative Perspective (2001);
- Vol. 2: W.V.H. Rogers (ed.), Damages for Non-Pecuniary Loss in a Comparative Perspective (2001);
- Vol. 3: U. Magnus (ed.), The Impact of Social Security Law on Tort Law (2003);
- Vol. 4: B.A. Koch/H. Koziol (eds.), Compensation for Personal Injury in a Comparative Perspective (2002);
- Vol. 5: M. Faure (ed.), Deterrence, Insurability and Compensation in Environmental Liability. Future Developments in the European Union (2003);
- Vol. 6: T. Schobel, Der Ersatz frustrierter Aufwendungen. Vermögens- und Nichtvermögensschaden im österreichischen und deutschen Recht (2002);

- Vol. 7: Jos Dute, Michael G. Faure & Helmut Koziol (eds.), Liability for and Insurability of Biomedical Research with Human Subjects in a Comparative Perspective (2004);

- Vol. 8: Jos Dute, Michael G. Faure & Helmut Koziol (eds.), No-Fault Compensation in the Health Care Sector (2004);

- Vol. 9: W. van Boom, H. Koziol & Ch. A. Witting (eds.), Pure Economic Loss (2004);

- Vol. 10:H. Koziol/J. Spier (eds.), Liber Amicorum Pierre Widmer (2003);

- Vol. 11:B.A. Koch (ed.), Terrorism, Tort Law and Insurance (2004);

- Vol. 12:H. Koziol/W. Doralt (eds.), Abschlussprüfer. Haftung und Versicherung (2004).

Considering the special characteristics of the provision of GEMSS services only the adoption of a Regulation dedicated to HealthGRID is of nature to solve this important problem.

3.2.2.2.4 Ethical considerations

This study aims to introduce the ethical considerations relative to the introduction of new technologies in Healthcare.

The patient has the right:

1° to have an health education to be able to make informed choices. It's important for the patient to have the sufficient knowledge to understand all the information received from the medias or other sources. It's a way to reach the auto-determination of the patient who, without an adequate information, is unable to point out his needs.

2° to have access to healthcare. The right covers both transportation and financial capacity. It looks important that patients - poor or rich, physically/mentally disabled or not - have an equal access to the health. By introducing the Internet in healthcare, we have to be aware to the problem of its accessibility. In fact, the Internet connection is not available everywhere. The gap between rich and poor population is growing up by the cost of such connection. The problem is the same about the physically/mentally disabled who can encounter huge problems in the access to information accessible through the Internet.

3° to be informed about his health, the therapy, etc. This right is already reminded in several legislations in Europe but has to be repeated in the ethical approach. The delivered information must be given in an understandable way and understood by the patient, otherwise it's useless. This right is, naturally, connected with the first one.

4° to give or not his consent after having received all the needed information (cfr. supra). Corollary, he has the right to withdraw his consent at any time without motivation while conserving his right to the health care. This last point is fundamental in the following up.

5° to have a pertinent and secure record containing his health data.

6° to have his dignity respected. In such way, dignity covers also the respect of the religious believe.

7° To have high-grade healthcare regarding the state of the art.

3.3 Workpackage 3: Medical Simulation System

This workpackage has the main task of providing access mechanisms for the GEMSS end users and integrating all the components together into a single system. Before launching into the construction of GEMSS, this workpackage is investigating the different means of providing ergonomic end-user access.

3.3.1 Sub-task 3.1: Portals and Access

This subtask was completed in a previous report period.

3.3.2 Sub-task 3.2: System Integration and Testbed Deployment

Phase 4: The phase 4 technology demonstrator has been developed until the end of the project. It now contains the advanced negotiation, process-based access control, accounts service and business module software components. The phase 4 client has been integrated with all the applications, and the server environment installed at both NEC (using the COSY scheduler) and ISS (using the MAUI scheduler). Modifications for the QUARTS application (ST4.2) have been introduced, allowing an interactive batch mode to be setup to support this applications use case requirements. Testing will continue until the end of the project.

3.3.3 Sub-task 3.3: Grid-based Support and Consulting

IDAC continue to use some of the tools evaluated during the course of this subtask on an ongoing basis. This cooperation is both with project partners and external companies. The tools most used are:

- GoToMyPC – Remote access for PC's in various locations.
- GoToMeeting – Meetings with other members of the consortium (e.g. University of Sheffield)
- WebEx – Used for meetings with clients.
- EASA – Used for testing the GEMSS infrastructure and deploying and demonstrating vertical applications to clients and potential clients.

One area where IDAC did not succeed to find a satisfactory product during the course of the subtask was Voice Over IP (VOIP). Products tested suffered from latency, poor sound quality and often required elaborate firewall configuration to work at all.

Since the end of the task, IDAC have discovered and started using Skype (www.skype.com) for communications between offices. We find this an excellent protocol, call clarity is very good, no noticeable latency and it works over a standard HTTP connection.

3.4 Workpackage 4: Medical Service Applications

This workpackage is responsible for the adaptation and integration of the medical simulation and image processing software into the GEMSS testbed. It includes a variety of medical service applications which

- have different GRID requirements concerning computation time (near real-time requirements vs. standard batch processing), memory usage, encryption, etc. and
- address different medical areas (cranial, pulmonary, cardio-vascular system) to address an end-users group of sufficient size for service provision.

Name	Domain	Class	Users
Maxillo-facial surgery simulation	Medicine – pre-surgical planning	Distributed supercomputing / On demand	Medical doctors, researchers
Neurosurgery support	Medicine – intra-operative planning	On demand	Medical doctors, researchers
Radiotherapy planning	Medicine – Monte Carlo treatment simulation	On demand / distributed supercomputing	Medical end-users; Doctors, researchers
Inhaled drug delivery simulation	Medicine – air flow dynamics	On demand / distributed supercomputing	Medical end-users; Doctors, researchers
Cardio-vascular system simulation	Medicine – blood flow dynamics	On demand	Medical end-users; Doctors, researchers
Advanced image reconstruction	Medicine – nuclear / in vivo diagnostics	On demand	Medical end-users; Doctors, researchers

Figure 3.5 Classification of the 6 GEMSS Medical Service Applications

3.4.1 Sub-task 4.1: Maxillo-facial Surgery Simulation

Medical background In patients suffering from severe maxillary hypoplasia and retrognathia, conventional therapeutic surgery often fails to guarantee long-term stability. Using a rigid external distraction system for midfacial distraction osteogenesis is a new method to correct the underdevelopment of the midface, surpassing traditional orthognathic surgical approaches for these patients. Currently surgical planning is only based on CT images. The treatment consists of a midfacial osteotomy (bone cutting) followed by a halo-based distraction (pulling) step. The goal of this sub-task is the modeling of the distraction process to allow predictions on its outcome.

Tool chain outline See D6.2b for a detailed description. To summarise, the toolchain consists of image processing (conversion, filtering, segmentation, registration), interactive tools (virtual

osteotomy, landmark picking), mesh generation (surface and volume meshes), mesh filters, remote FEM simulation, and result visualisation.

Grid enabling The application has been fully integrated into the final versions of the GEMSS middleware, including support for service negociation (phase4). In particular, a performance prediction model has been implemented and tested. During the remote execution of the job, status data and estimates of completion time are transferred to the client, where they can be processed further. Extensive testing has been performed with the integrated application.

Evaluation and Test cases For making quantitative evaluation possible, landmarks have been employed to perform a rigid registration, using a truncated Newton method for nonlinear fitting of a rigid motion. By selecting a subset of landmarks on the non-moved part of the skull, pre- and postoperative data could be rigidly registered. Additional landmarks on the maxilla permit to measure the actual displacement, which can be used as boundary condition for the simulation. Landmarks on the soft tissue are used to compare simulation and real surgery.
The evaluation showed that at some points in the toolchain, manual intervention may be necessary, because for arbitrary input data, it cannot be guaranteed that the resulting models are always topologically correct. For instance, upper and lower teeth may be not separated due to segmentation artifacts, or the maxilla may not be complete separated from the skull due to other small bridges. A manual separation requires artificial cuts which are tedious to create. In order to increase the ergonomy of the toolchain, additional tools have been implemented which ensure separation of components selected by landmarks.
In order to complement the nonlinear registration approach with a faster alternative for removing metal artifacts, a heuristic algorithm based on morphological image processing for reducing these artifacts has been designed and implemented.
Also, the non-linear simulation poses much higher requirements on the meshes used. We identified several necessary conditions of meshes for successful nonlinear simulations. Filters have been implemented to guarantee that meshes meet these requirements, which greatly improves convergence and paves the road towards a robust nonlinear simulation.

End user evaluation End-user evaluation was done by our cooperation partner at the University Clinic of Leipzig. Surgeon Dr. Dr. Th. Hierl was provided with a desk-top computer running the GEMSS client software for usage in his maxillo-facial surgery planning. Several improvements were implemented according to his advice and Dr. Hierl expressed his satisfaction with the resulting planning tool. A VNC server with access to the root window has been installed on his client computer to permit easy consultancy.

Status summary A complete version of the toolchain is running at several sites, including a clinical one. New developments in the last half year of the project were focused on support for evaluation and increasing robustness and user friendlyness.
In detail, these developments include:

- Integration into GEMSS middleware
- Extensive tests of middleware (both phase I3 and phase I4), with about 200 jobs submitted
- Tool for reduction/removal of metal artifacts
- Landmark-based rigid registration for quantative evaluation
- Tools for helping topologically correct segmentation
- Tools for segmenting (and removing) the brain, reducing model size
- Derivation of criteria for meshes to be used for non-linear simulation
- Implementation of corresponding mesh filters for improving nonlinear robustness

Summary The maxillo-facial surgery application is fully functional. Feedback from our clinical partner Dr. Hierl has resulted into substantial improvements to the toolchain. additional minor modifications can be expected during the evaluation period. The appliciation has been fully integrated into the final version of the GEMSS framework.
Regarding routine use, evaluation has shown that certain input data require additional, sometimes tedious, manual work due to topologically incorrect segmentations and models. Tools helping to deal automatically with these situations have been implemented.

Achieving a fully robust (i.e. automatic) toolchain is a goal for future developments beyond the project. Although this goal is ambitious (especially for the non-linear case, according to our experience in GEMSS), we are confident that we will be able to reach this stage. We firmly believe that the superior modeling capabilities and accuracy of nonlinear approaches are worth the additional effort.

3.4.2 Sub-task 4.2: Neuro-surgery Support

Medical background The major shortcoming of image-guided surgical planning based on pre-surgically acquired functional MRI (fMRI) data is the brain shift phenomenon. The occurrence of surgically induced deformations invalidates positional information about functionally relevant areas. This problem is addressed by non-linear registration of pre-operative fMR images to intra-operative MRI acquired by an Open-MR scanner.

Tool chain outline See D6.2b for a detailed description. To summarise, the toolchain consists of image processing (intensity inhomogeneity correction, rigid registration, non-rigid registration, intensity adjustment and deformation field application to fMRI data), interactive result visualisation tools (client GUI, Vistafile viewer).

Grid enabling The application has been fully integrated into the final versions of the GEMSS middleware, including support for service negotiation (phase I4) and multiple data uploads during one job session. During the remote execution of the job, status data and temporary computation results are transferred to the client.

The neuro-surgery support server software has been installed at NEC and ISS.

Evaluation and Test cases Due to the absence of the Open-MR scanner – which has been available at the beginning of the project – only 2 real patient datasets are available. Evaluation was performed with these 2 datasets. During evaluation it has been noticed that the chain is quite robust, but – as expected – runtime varies for each job run. The runtime of the toolchain never exceeded a time frame of 10 minutes when it was run remotely on an eight processor AthlonMP (2,2 GHz) cluster by utilising the GEMSS middleware phase I3.

Status summary A complete version of the toolchain is installed at several sites (NEC, ISS) and the application is ready for evaluation in a clinical environment. The development in the report time frame was focused on support for evaluation and increasing robustness and user friendliness.
In detail, this includes:

- Completed integration into GEMSS middleware, and performed tests
- Implemented and tested new multiple upload feature

Summary The neuro-surgery support application is fully functional. The appliciation has been fully integrated into the final version of the GEMSS framework.

3.4.3 Sub-task 4.3: Cranial Radio-surgery Simulation

Application Scenario Gamma Knife® Radiosurgery is a non-invasive medical procedure that uses beams of ionising photons from 201 ^{60}Co sources to treat intra-cranial lesions. The Gamma Knife® unit comes with a treatment planning system, GammaPlan® that uses an approximate description of the photon interactions within the head of the patient to calculate the energy dose deposited by these photons in the region of the tumour. There is significant benefit to be obtained from improving the fidelity of these calculations, particularly in cases where photons traverse regions of widely differing electron densities (e.g. soft tissue and bone). Monte Carlo modeling can accommodate these complexities and can play a useful role in complementing the GammaPlan solution (with the potential to eventually supersede it in the event of short enough calculation times). The goal of this sub-task is to adapt and Grid-enable a Monte Carlo code (RAPT/EGS4) written for conventional radiotherapy to that of stereotactic radiosurgery. The presence of the Grid enables calculation of the energy dose delivered to the brain from a Gamma Knife® treatment unit to be obtained in clinically useful timescales (less than one hour).

Workflow The Grid-enabled radiosurgery application uses RAPT as a front end to the EGS Monte Carlo engine to model ionising radiation transport through the head of the patient. It requires:

- Definition of patient geometry
- Specification and distribution of material types contained within the geometry
- Position of beam isocentre
- Beam properties – intensity profile, spectrum
- Beam distribution – number of beams and their arrangement
- Quality of simulation parameters – total number of photons, interaction types

A simulation with approximately 0.5×10^9 photons takes under an hour with 30 or more processors. The result is a variable resolution voxel grid that is a map of the dose distribution within the defined skull geometry. Tools have been written that enable:

- 2D and 3D visualisation of dose data
- quantitative comparison of different dose distributions using established metrics

Evaluation and Test Cases RAPT is now fully compliant with the Phase 3 GEMSS middleware, and it has participated in numerous Grid evaluation tests over the past 6 months. After correction of inital errors, the reliability of the Grid during the month of January 2005 has shown very encouraging performance with over 90% of jobs submitted under the Phase 3 middleware being successful. Recently RAPT has been coupled to the Phase 4 technology demonstrator.

Evaluation of the quality of solution provided by RAPT has involved comparison with GammaPlan (the gold standard planning application). Correlation between the two is excellent in situations in which the assumptions of GammaPlan are valid. However, recent efforts have explored the differences introduced by the presence of a bony skull shell. This can not be accounted for by GammaPlan but is easily accommodated within RAPT. In such cases, the dose distributions can be strikingly different and the work has generated much interest within the clinical department of Radiosurgery at the Royal Hallamshire Hospital. It is the first real evidence that RAPT has the capacity to influence management of the patient. This work will continue beyond the conclusion of GEMSS and publications will undoubtedly follow.

Status Summary This summary outlines key features of the work of the last 6 months:

- RAPT has been deployed with the Phase 3 middleware.

- Grid enabled RAPT accommodates all aspects of a clinical treatment plan through an intuitive user friendly interface and supports…
  - 201 beams with support for beam plugging
  - Multi-shot treatments
  - Bubble head geometry
- The RAPT solver continues to prove accurate and robust
- Extensive evaluation of RAPT has been undertaken, involving:
  - Analysis of multi-shot clinical plans
  - Feedback from the clinical environment
  - Evaluation of the influence of bony shells on the computed dose distribution
  - Continued documenting of Grid performance

Summary Grid-enabled RAPT is operating successfully on the GEMSS Grid. It is apparent that the large Monte Carlo problems encountered in Gamma Knife radiosurgery can be solved effectively through the computing resources provided by GEMSS. The accuracy of the simulation results is a strong function of computation time and resources, and the Grid offers a significant advantage in this respect. Extensive evaluation exercises have demonstrated the utility of Grid enabled RAPT in a clinical environment, and implications for patient management are emerging in cases involving significant tissue inhomogeneity (eg. bony skull shell). The tentative acceptance of the RAPT Grid-enabled radiosurgery application within the hospital environment at Sheffield is early vindication of many of the concepts embedded within the GEMSS infrastructure

Our dissemination programme includes publications, conference presentations, and demonstrations and representation at the GammaKnife users conferences. RAPT can have clinical impact in the radiosurgery environment and therefore continued funding beyond the end of the GEMSS project is being pursued.

3.4.4 Sub-task 4.4: Inhaled Drug Delivery Simulation

Application Scenario The inhaled drug delivery simulation uses the acronym 'COPHIT' – '**C**omputer **O**ptimised **P**ulmonary delivery in **H**umans of **I**nhaled **T**herapies'. This is an application that optimises delivery of medication to the lungs by modelling the drug delivery process. The software allows drug designers or manufacturers of inhalation devices to experiment *in silico* with device geometry, delivery timing, pharmacokinetics or physical formulation of the medication, and thereby maximise anticipated dose to the desired region of the respiratory tract.

The complexity of the drug delivery simulation process requires that GEMSS offers an Inhaled Drug Delivery Simulation *service*. The ethos of such a service is that the expertise required for the application resides with the developer (e.g. University of Sheffield Medical Physics, or consultancies such as IDAC and ASD). The developer, with the availability of additional tools, creates a bespoke application tailored to the needs of the customer. This is made possible through the creation of an interface (using EASA) that is able to hide the complexity of the simulation behind a simple point-and-click GUI, *but it does require that the problem can be expressed in parametric form.*

Workflow The parametric approach makes the respiratory simulation accessible to the end user, but its disadvantage is loss of flexibility. The application guides the user through relevant data entry, spread over eight data entry screens. This includes selection of mesh geometry, timestep information and material properties, properties of the coupled compartments and other boundary conditions etc. Submission of job input files to the Grid server is protected (X.509), and the computationally intensive fluids problem is solved remotely on the Grid platform. The results

data is encrypted and returned to the client, presented in numerical and graphical form. Tools are available for visualisation of flow data, systemic drug uptake and drug deposition. All data is saved in tabulated ASCII format for direct import and manipulation in packages such as EXCEL.

Grid enabling The EASA client is a customised interface that accepts numerical data entry from the user for the purposes of defining and submitting a Cophit job. This approach simplifies interaction with the simulation environment. Note that the purpose of the inhaled drug delivery simulation service of GEMSS is to embed the user's requirements of Cophit in parametric form, as an application residing on the EASA server. At the point of job submission, the parameters are passed from the EASA client to the EASA server hosted on the Grid client, which uses the Phase 3 middleware. All executable files reside on the Grid server and none are transmitted to it, and therefore a malicious user at the EASA client has little opportunity to cause mischief. The Grid server performs the computationally intensive fluids solution step during which job status can be obtained. Because this software is most likely to be used as a research tool, solution is not time-critical. A large job might take of the order of a week to run, but it is anticipated that Grid resources would be used at periods of low demand in order to reduce costs.

Evaluation For the end users within GEMSS (represented by ASD and IDAC), a typical respiratory simulation scenario has been constructed. The application has been installed on the Web server at IDAC's headquarters in Ireland.
ASD has solved numerous example problems using all available examples, including both steady-state and transient, to exercise the Grid and middleware and evaluate the EASA user interface. In a time frame of several weeks, extensive tests were performed at ASD considering both the simple and the complex EASA examples on the GEMSS server. They were performed to assess the performance and availability of the Grid service.
In summary, all tests were successful except for obvious cases when the GRID infrastructure was down for maintenance. Variation in the upload and download times was also apparent. It is clear that speed increases by a factor of 5 or more are achievable with 15-20 processors, but the benefits diminish rapidly beyond this. This is a non-linear simulation tool and consequently accurate prediction of job run time has proven very difficult. The current model is based on a simplistic calculation based on the size of the mesh, the number of iterations/timesteps required and machine-specific factors such as the number of processors. Predicted compute time is rarely exceeded because of large margins for error incorporated within the calculation, but this tends to impair the effectiveness of the business model.
For the application developer (represented by the University of Sheffield in GEMSS) it is important to imbue confidence in the application by establishing that Cophit can provide credible solutions. Therefore, effort has been directed at numerical simulation of experimental studies performed within the Medical Physics department at Sheffield, and also scenarios discussed in the scientific literature. Validation studies have compared the flow through an 'idealised lung' with data from physical experiments, the literature and a clinical study. This work has resulted in presentations at the European Respiratory Society Annual Congress and the Aerosol Society. Visits and demonstration of the software to industry have continued (Boehringer Ingelheim) and feedback continues to indicate that the Grid-enabled Cophit software is easy to use. A recurring appeal is for demonstrable evidence that Cophit can deliver what it claims, underlining the need for the kind of validation exercises discussed above. The emphasis that GEMSS places on security is commended, and in general the provision of a Grid computing platform is viewed positively – provided that it is accompanied by a clear and well-defined business model.

Status Summary This summary outlines key features of the GEMSS inhaled drug delivery service accomplished within the last 6 months:

- The inhaled drug delivery service is implemented as a bespoke application negotiated between an expert developer (typically the portal provider) and the end-user
- The application has been made accessible to, and tested by, our end users by providing a user-friendly interface through EASA.
- The application has been partitioned into local-client and Grid-server sections, operating in conjunction with the Phase 3 middleware.
- Cophit has been presented to industry and at scientific conferences
- A series of extensive evaluation exercises has been undertaken and include
  - End users (ASD/IDAC) running simple and complex EASA jobs
  - Validation with respect to the literature
  - Validation with respect to experimentation

Conclusion A Grid-enabled COPHIT application is now operating successfully on the GEMSS Grid. It is apparent that large problems (i.e. ones that exceed the computational capacity of small business PC networks) can be solved securely through the computing resources provided by GEMSS. The accuracy of the simulation results is a strong function of computation time and resources, and the Grid offers a significant advantage in this respect. The latter assertion has been explored through a suitable period of evaluation. Validation exercises are instilling confidence in the ability of the Grid to deliver effective computing and the ability of the software to deliver effective and accessible respiratory simulation. The dissemination programme has continued contact with industry and also includes conference presentations, demonstrations etc. It is only by such efforts that the profile of the Grid can be raised and the fulfillment of its promise promulgated.

3.4.5 Sub-task 4.5: Cardiovascular System Simulation

Application Scenario Modelling of blood flow in arteries requires the use of sophisticated three-dimensional computational fluid dynamics (CFD) software. Flow through isolated vessel sections can be simulated to provide insight into pathologies of the heart and vasculature. The software reduces global 3D simulation of the vasculature to simulation of a local segment with peripheral vascular properties encapsulated as 1D compartment models. The application couples the full three-dimensional CFD model of a vessel section to terminating compartments, building on principles developed in ST4.4. The software has been designed to be extensible so that new types of compartment system can be added if required. Whereas ST4.4 was EASA-driven, MatLab has been chosen for the cardiovascular application (CARDIO) because of its flexibility and its ability to cope with the sophisticated mathematical calculations required by the compartment systems.

Workflow The specification of the three-dimensional model involves CFX. Software developed in MatLab couples compartments representing the remainder of the circulatory system to this 3D model. The interface is very flexible and permits expert users to add their own compartment types. This gives great freedom in the types of problem that can be modelled, as befits research use or novel consultancy applications. Once the problem has been defined, input files are generated and submitted to the GEMSS client middleware, which authenticates the user to the Grid and encrypts the input data for transmission to the Grid server. The Grid server performs the computationally intensive fluid dynamics simulation step, and solution progress is monitored using a job management utility. The results data is returned to the client, where 3D flow and compartment system results are visualised.

Grid Enabling The cardiovascular simulation application has been split into two parts - the client GUI and pre-processing code, and the server-side simulation code (installed at the service provider site). The client GUI is written in MatLab and connects to the GEMSS infrastructure through a loose coupling, where calls to batch script files are made to perform grid actions (upload/start job, status enquiry, abort, and download results). The client GUI consists of three interlinked parts – pre-processing, solution control, and post-processing. The pre-processing GUI allows the problem to be set up and then submitted for processing on the GEMSS Grid. A session file is created once a job has been uploaded so that the client does not have to remain connected for the entire duration of the job. The job-management GUI allows the users to see the job status, abort jobs, and download results. Once results have been downloaded, a post-processing GUI facilitates visualisation of both the 3D flow results and the compartment system results.
This application runs reliably with the Phase 3 client, but is also an early adopter of the Phase 4 middleware, which offers features such as advanced negotiation with multiple compute servers and incorporation of a business model. This application shares the same performance model as ST4.4, and again, the non-linear aspects of this application make accurate prediction of job run time difficult. The current model uses a simplistic calculation based on the size of the mesh, the number of iterations/timesteps required and machine-specific factors such as the number of processors. Predicted compute time includes a large margin for error so that few jobs over-run. However, inaccurate estimates of compute time can compromise the effectiveness of the business model. All executable code is pre-installed on the grid server, and therefore the user is denied the possibility of running arbitrary code of their choosing on the server.

Evaluation The evaluation phase of ST4.5 has involved the submission of hundreds of jobs over the last 6 months (with both the Phase 3 and Phase 4 clients), investigating not only the capability of the Grid resource, but also the ability of the software to solve complex cardiovascular problems. The purpose of the compartment system is to impose physiologically realistic boundary conditions on flow through the 3D element. A great deal of effort has been expended on validating the behaviour of the compartment system against the literature and all results to date indicate satisfactory and robust behaviour. The cardiovascular software has been applied to idealised geometries (for testing purposes) but has also been applied to computing the flow in the aortic arch and the root of the mesenteric artery. This work has recently been publicised in the medical scientific domain and further publications will follow. End users have used the software to perform their own simulations (see below).
The evaluation exercises have clarified the gains to be obtained by use of the Grid. Large complex models arising from anatomical geometries benefit from the large amount of memory that the Grid can supply. Furthermore, up to a 9-fold increase in compute speed is achievable with 16 processors. However, this class of application does not scale well and recruitment of further processors is not worthwhile. The cardiovascular software is an early adopter of the Phase 4 client middleware, and approximately 100 jobs have been submitted. The solution step can be run locally as well as on the grid, using the same user interface. This allows approximate solutions to be obtained for a coarse mesh (and tested for convergence) before a computationally intensive high-accuracy Grid run is submitted.

End-user testing Our end users have tested the software during the formal evaluation phase. Furthermore, ASD extended the software to include a new compartment type, in close cooperation with the software developer (USFD). ASD ran several example problems to test the CARDIO software.
Additionally, the cardiovascular software was used to couple a CFD stenosis model of ASD to the Westerhof model to get the time-dependent velocity and pressure distribution in the artery with a stenosis. In a further step, this flow field can then be used for the CFD-based prediction

of the thrombosis risk of such a stenosis. This stenosis model was also used to test the performance and availability of CARDIO on the GEMSS server. These tests were performed successfully showing good solution stability and performance.
In summary, the developed cardiovascular software proved to be a useful tool for end-users working in the cardiovascular field. It has a very good graphical user interface which makes it easy for the end user to apply the Westerhof model to his applications and run the jobs locally or on the GEMSS Grid.

Status Summary This summary outlines key features of the GEMSS Cardiovascular simulation service accomplished within the last 6 months.

- The cardiovascular simulation service provides coupled compartment tools for researchers or consultancy companies. These tools allow a 3D CFD model to be coupled to compartments which represent the arterial system both upstream and downstream of the model.
- The Cardiovascular software is flexible and can accommodate a wide range of flow boundary conditions peripheral to the 3D component.
- The software has been successfully integrated with Phase 3 and Phase 4 versions of the GEMSS middleware.
- A series of extensive evaluation exercises have been undertaken that include...
  - Our end users running simple and complex cardiovascular simulations
  - Validation with respect to the literature
  - End user development and integration of a custom compartment model

Conclusion A Grid-enabled Cardiovascular application is now operating successfully on the GEMSS Grid and has been used by end-users at USFD and within GEMSS. It is apparent that large problems (i.e. ones that exceed the computational capacity of small business PC networks) can be solved securely through the computing resources provided by GEMSS. The accuracy of the simulation results is a strong function of computation time and resources, and the Grid offers a significant advantage in this respect. The evaluation period has demonstrated the efficacy of the Grid, and the ability of the software to deliver effective and accessible cardiovascular simulation. The recent release of the software has led to numerous collaborations and it will continue to be promoted through dissemination activities, highlighting the potential of the Grid for solving cardiovascular simulation problems.

3.4.6 Sub-task 4.6: Advanced Image Reconstruction

Since ST4.6 has ended in May 2004 and is documented in deliverable D4.6 (Final Software Deliverable and Documentation), 6.2a (1st Project Progress Report), 6.2b (2nd Project Progress Report) and 6.3a (Final report) we refer to these reports for an extensive description of the ST4.6 Advanced 3D Image Reconstruction. In this report we forbear from replicating the content of the above mentioned documents and only point out additional tasks, minor changes and improvements done during the last 6 months of the project.

Application Scenario Tumour diagnosis and monitoring of metabolism are the main tasks of in vivo diagnosis in nuclear medicine by visualization of distribution of radioactive tracer in the human body. Although SPECT reconstruction suffers from low spatial resolution and poor signal-to-noise ratio compared to modern x-ray CT and MRI, it provides complimentary functional information, and is indispensable in modern clinical diagnosis. The diagnostic procedure requires the patient to receive an ionising radiation dose which provides the radiation necessary for acquisition of multiple projections by the gamma camera. The projection data is

computationally reconstructed for subsequent reporting and diagnosis. A large variety of reconstruction algorithms exists, many of them based on standard filtered back-projection (FBP). This method finds extensive use in current clinical practice but it is only applicable to single slices. The modern iterative algorithms available within GEMSS offer benefits because they encompass technical and physical constraints of the imaging process and are easily extendable to 3D, but this comes at the expense of high computational effort. The Grid is well suited to the task in addition to which an implementation of image reconstruction as a Grid service could also bring access to highly sophisticated image processing resources for better diagnosis.

Workflow Diagnostic SPECT images are reconstructed from projection data, (ie. the sum of emitted photons along a linear manifold). In practice this manifold is a cone-like sub-volume of the object, from which photons are recorded by surrounding detectors. A rectangular detector array is rotated around the patient and a series of projection data is acquired. Iterative reconstruction repeatedly modifies a postulated image matrix through comparison of pseudo-projection and measured projection data. By this method a succession of intermediate images is generated until a convergence criterion is fulfilled. The weighted contribution of each voxel of the image to a specific projection value permits accurate modelling of collimator geometry and photon scatter, and all weights for all projection values define the system matrix which characterises the system response. If N is the length of the image cube, then the number of calculations is of order N^6 for full 3D reconstruction compared to order N^4 with slice reconstruction.

Grid-enabling As a portal to the GEMSS Grid a Graphical User Interface was implemented (described in D4.6). During the last 6 months minor changes have been implemented and bugs have been removed. The phase I4 sample client provided by IT Innovation was adapted to fit the SPECT client needs to perform middleware evaluation (phase I4).

Quality-of-Service, Performance Model:
The measured reference times for the performance model have been incrementally improved resulting in a performance model accuracy of 95-97% during GEMSS middleware evaluation.

Test Case In addition to the two test cases mentioned in D6.2b and D6.3a more general data sets have been acquired and reconstructed.

Status Summary In addition to the key features listed in D4.6 following tasks have been performed:

- User manuals have been revised and completed.
- Source codes have been revised and bugs removed.
- A CD containing a demo version of the GEMSS Vienna SPECT client, a tutorial and an extended user manual, etc. has been compiled.
- A small folder presenting the key features of the GEMSS Vienna SPECT client has been produced.

Conclusion With the release of the GEMSS SPECT reconstruction service, fully 3D image reconstruction is accessible for a greater medical community. This meets one of the main EU R&D efforts for establishing and improving networks of experts on a European level, aided by modern IT infrastructure.
With GEMSS a framework for a secure middleware, especially addressing the issues of patient data privacy and legal issues of healthcare at an international level, was developed. Cost control

is a major issue for most health services. In GEMSS billing procedures based on detailed Quality of Service models were integrated, which is a necessity for the acceptance of the reconstruction service in clinical practice.
All the application tasks within GEMSS demonstrate the development of Grid architectures from distributed data models towards workload sharing. This prospering field of Grid research is based on highly sophisticated Quality of Service models, providing accurate runtime prediction. Exactly defined performance models build the basis for a reliable end user scenario.
Beyond the scope of the GEMSS project, but as a further step towards more stability and reliability of the services, integrated tools for real time monitoring of the processes and work-load should be developed. Until now only basic failure redundancy strategies are implemented, further developments of the middleware would cover this topic. Valuable end user experience should be reported after further large scale clinical field studies.

3.5 Workpackage 5: Exploitation, Information Dissemination and Clustering

This workpackage is executing tasks related to exploitation and information dissemination. In particular it will plan and co-ordinate information dissemination activities among the partners, as well as produce a post-project exploitation roadmap. A second task will support project clustering activities along two axes: generic GRID technologies and technologies for applications in the health care domain.

3.5.1 Exploitation Planning

The Full Technology Implementation Plan (D5.3b) has been finalised.

3.5.2 Dissemination Activities

For a full list of dissemination activities (publications, talks and conferences) see the final report (D63a).

3.6 Workpackage 6: Project Management

This workpackage co-ordinates day-to-day running of the project and maintains all correspondence with the European Commission. The main goal of WP6 is to ensure the project's success by monitoring and reporting progress against goals and time scales, by establishing processes to ensure quality in project work and by anticipating and managing risk and change to the project.

3.6.1 Management Overview

The Annual Technical Review in October 2004 (ATR2004) resulted in an execellent reviewer´s report. Further regular project meetings were held in Vienna (6.-7.12.2004) and St. Augustin (final meeting, 24.-25.2.2005). All project deliverables have been submitted on time. In general, the project proceeded on budget and on time.