Deliverable No. 2.6

Regular update of the user needs and requirements based on evaluation and validation

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ABSTRACT:

This deliverable collected and presented the available updates of the user needs and requirements for the proposed for implementation p-medicine's scenarios and use cases. This report defines the scenarios as detailed use cases, and provides the information on end user needs and end user requirements necessary to guide the activities of all project's work packages.

KEYWORD LIST: user needs, requirements, use cases, evaluation, validation, update

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[1] **R**=Report, **P**=Prototype, **D**=Demonstrator, **O**=Other

[2] **PU**=Public, **PP**=Restricted to other programme participants (including the Commission Services), **RE**=Restricted to a group specified by the consortium (including the Commission Services), **CO**=Confidential, only for members of the consortium (including the Commission Services)

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Contents

1 Executive Summary

Introduction

The main objective of this deliverable is to collect and present the available updates of the user needs and requirements for the proposed implementation of the p-medicine platform.

This report has been elaborated also to fulfil the necessity of a iterative process of requirements analysis, elicitation, documentation and validation described in the related deliverables. The main followed technique remains the scenarios elaboration and – if applicable – prototyping. This report defines the scenarios as detailed use cases, and provides the comprehensive information on end user needs and requirements necessary to guide the activities of related work packages.

Along with the main tasks of collecting and presenting the updates of the user needs and requirements based on evaluation and validation, this deliverable serves as an advanced, extended view on the proposals for implementing the p-medicine project scenarios. The additional goal is to serve as an updated guideline and/or "handbook" for all project partners.

Additionally, it is important to mention the structure of this document in order to guide the readers (partners) through the available and complex scenario descriptions. Every chapter could be treated as a 'mirror' of all already elaborated and (partially) implemented scenarios. For example, Chapter 9 "Update of the ObTiMA Scenarios" has short and narrative scenarios description with a related Use Case / Scenario in the Appendix 5 of the Deliverable 2.2 "Definition on scenarios and use cases and report on scenario based user needs and requirements", where the detailed scenario description is available. This setup is applicable in general to all chapters, and in special to:

- Update of the **VPH Scenarios**
- Update of the **Security Scenarios**
- Update of the **Clinical Scenarios**
- Update of the **Clinical Trial Scenarios**
- Update of the **Education and Patient Empowerment Scenarios**
- Update of the **Biobank, Portal and IT Scenarios**
- Update of the **ObTiMA Scenarios**
- Update of the **DoctorEye Scenarios**

2 Update of the Project Background

Introduction

It is the purpose of p-medicine to deliver an architecture that allows driving medicine to more individualized treatments based on exploiting the vast amount of heterogeneous data of single patients by software, services, tools and models that will support physicians in decision making in their daily care of patients. Today we are facing a paradigm shift in medicine going from hospital and clinical based care to a new standards approach, which is not yet completely defined. Comparing changes in other areas of daily life they can be described as consumer controlled compared to producer controlled in former times. Nowadays the producer needs to respond to the consumer (Fig. 2.1). Translating this to healthcare patient empowerment cannot be neglected anymore and will influence healthcare in all dimensions.

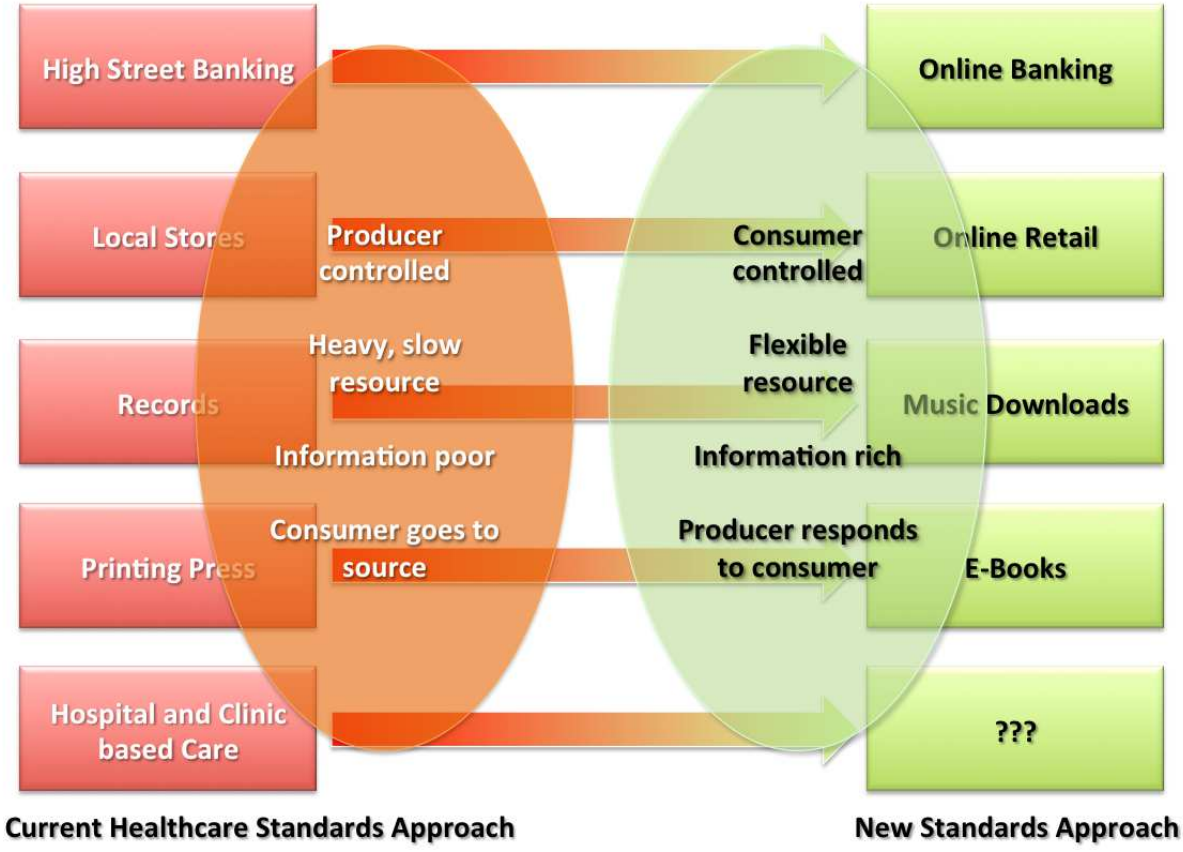

Figure 2.1: Paradigm shift in daily life including healthcare. (Adapted from Ken Lunn, CMLS Network Annual Symposium, London, 23rd June 2011)

In connection with the scientific/technical dimensions of the work *p-medicine* will develop a data warehouse and a workbench with a tools repository. Heterogeneous pseudonymized/anonymized data from different origins will be stored in a data warehouse for further use by the scientific community. Clinical data will be exploited coming from hospital information systems and clinical trials. The legal framework of the project, which is based on the results of ACGT (Advancing Clinico-genomic Trials[3]), will be further developed and will

[3] http://eu-acgt.org (January 2013)

guarantee data privacy and security. Most important for *p-medicine* are validated tools and services that provide interfaces to allow interoperability with biobanks, genetic databases, and medical imaging systems and data warehouses. These tools have to meet requirements to be used in large, international multicentre clinical GCP conform trials and need to be able to be integrated into existing systems used by ECRIN and other communities. This includes aspects like data security by adopting the legal and ethical framework based on international requirements and approved concepts for anonymization and pseudonymization including validation. Previous R&D work done in European funded projects like ACGT, ContraCancrum and ECRIN (European Clinical Research Infrastructures Network) fit perfectly into this approach and will be heavily drawn on. The following figure (Fig. 2.2) shows the main components and their interdependency of the *p-medicine* system architecture from a clinical perspective.

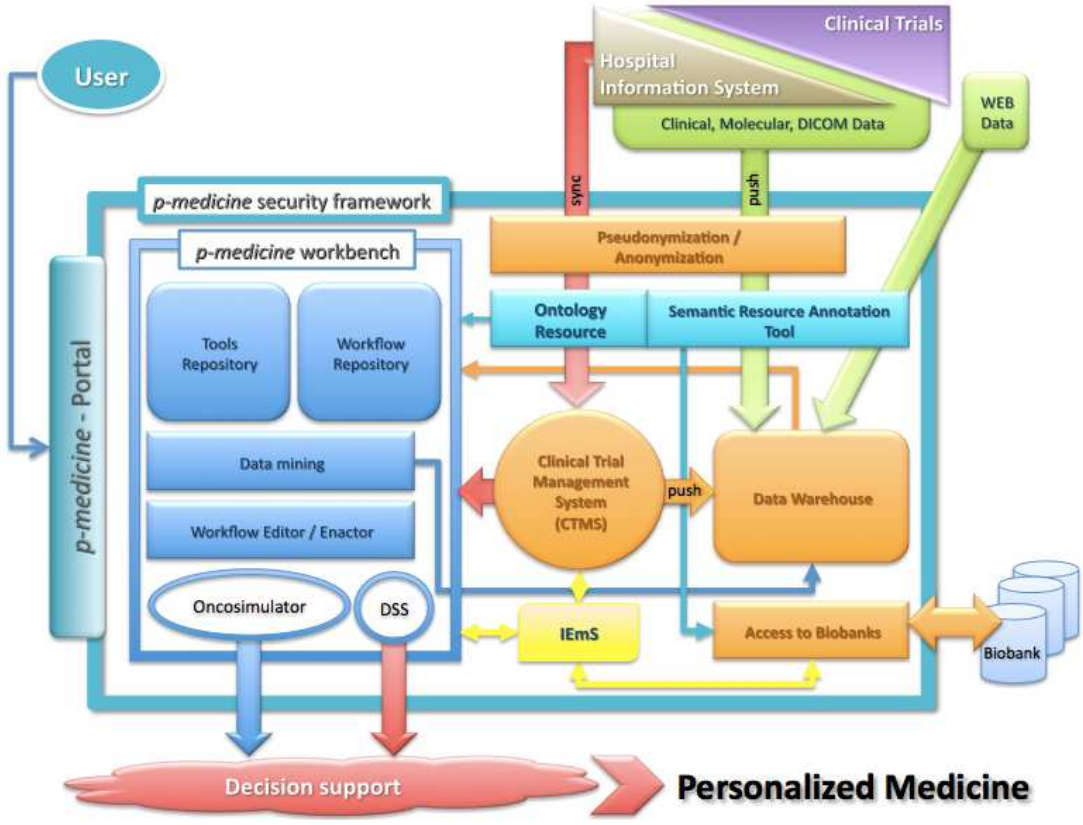

Figure 2.2: The architecture of p-medicine from a clinical perspective

3 Update of the VPH Scenarios

Introduction

The Virtual Physiological Human (VPH) is synonymous with a programme in computational biomedicine which aims to develop a framework of methods and technologies to investigate the human body as a whole.[4] The goal of the VPH is to achieve a more efficient and effective twenty-first century healthcare system and to create new economic opportunities for European healthcare industries.

3.1.1 VPH Toolbox Scenario

The Toolbox Scenario has no available updates and it remains focused on the VPH-Toolkit serving as a source of existing tools, services, models for use in p-medicine as well as a 'toolbox' for uploading newly developed tools, services and models. This scenario covers the bellow basic workflow (see Appendix 5 of the Deliverable 2.2 "Definition on scenarios and use cases and report on scenario based user needs and requirements"):

- Download of a tool, service or method
- Upload of a tool, service or method

[4] Coveney PV, Diaz V, Hunter P, Kohl P, and Viceconti M, The Virtual Physiological Human, Interface Focus, June 6, 2011 1:281-285

4 Update of the Security Scenarios

Introduction

Security scenarios are related and need to be available in most of the components of the p-medicine platform. There are some important security components that are in development in order to offer a reliable and secure system. First a mechanism that allows the users to authenticate themselves by providing personal credentials is expected. In this way the users can confirm their identity on the different sites/services of the platform. Another important part of security is access control. A user may only see and manipulate resources of the p-medicine to which he has access rights. Other security components include: encrypted storage of data, pseudonymisation of patients, safe transmission of data (confidentiality and integrity).

4.1.1 Single Sign-on Scenario

A p-medicine end-user will typically access multiple p-medicine sites/services. To avoid that this end-user would have to login on each site/service separately, he authenticates himself only once on a central p-medicine Identity Provider (or another federated identity provider). This provider will issue credentials that can be used for accessing protected p-medicine sites/services.

4.1.2 Single Sign-out Scenario

An end-user, who wishes to logout from the p-medicine platform, performs one sign-out operation signing him out from all sites/services he is actively involved with in his current browser session.

4.1.3 Access Rights Scenario

This scenario will be specified after further analysis of the access control model requirements and research into possible approaches.

The sites/services of the p-medicine platform are protected by access control, meaning that every user needs to have access rights to view or manipulate resources of these sites/services. How these access rights could be granted is described in the following scenario.

4.1.4 User Enrolment Scenario

An end-user wants to register himself on a p-medicine site/service: In order to accomplish this, two user accounts are created, one for the local site/service and one for the central identity provider (IdP). Both accounts are linked using a pseudonymisation service.

5 Update of the Clinical Scenarios

Introduction

As p-medicine is clinically driven, the clinical scenarios are central for the project ALL, Breast Cancer and Nephroblastoma serve as test cases for the p-medicine platform. The developed tools will be disease-specific but they are built in a way that they can easily be transferred to other cancer types and even to other domains. This approach has been achieved by the modular way tools are built and by keeping aspects of generalization in mind.

5.1 Nephroblastoma

Wilms tumour or nephroblastoma is the second most common intraabdominal cancer of childhood and the fifth most common paediatric malignancy overall. It represents approximately six percent of all paediatric cancers and accounts for more than 95% of all tumours of the kidney in the paediatric age group.[5] [6] [7]

From the perspective of the 'patients' as end-users, patients with nephroblastoma are children with no access to the p-medicine platform. This needs to be taken into account particularily for developmental strategies. The same is the case for acute lymphoplastic leukaemia. In both diseases the p-medicine platform has to accept new user registrations and data submission frames from the patients' parents. These needs are considered within the Patient Consent and Patient Empowerment scenarios as well.

Of particular interest in nephroblastoma is the Oncosimulator scenario, the development of which started during the lifetime of ACGT (Advancing Clinico-Genomic Trials), an Integrated Project, partly funded by the EC (FP6-2005-IST-026996)[8]. The research has been focusing on elaborating a state-of-art concept as an integrated software system simulating in vivo tumour response to therapeutic modalities within the clinical trial environment.

5.1.1 Pathway Scenario

In the pathway scenario, clinical, molecular and open source data are integrated to find those pathways that are mainly disrupted in nephroblastoma in general, in specific subtypes of nephroblastoma, and in single patients. In single patients, this finding can help to select specific drugs for the treatment of a given patient and can serve as a basis for a decision support tool. A detailed scenario description is given in the Appendix 5 of the Deliverable 2.2 "Definition on scenarios and use cases and report on scenario based user needs and requirements".

5.1.2 Imaging Scenario

The imaging scenario encompasses two different features: First, DICOM data of patients with nephroblastoma need to be stored in the data warehouse for further analysis and, second, these imaging data need to be post-processed for usages in the Oncosimulator.

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[5] Pastore G, Znaor A, Spreafico F, et al. Malignant renal tumours incidence and survival in European children (1978–1997): report from the Automated Childhood Cancer Information System project. Eur J Cancer. 2006;42:2103–2114.

[6] Breslow N, Olshan A, Beckwith JB, et al. Epidemiology of Wilms tumor. Med Pediatr Oncol. 1993;21:172–181.

[7] Davidoff A, WILMS TUMOR, Curr Opin Pediatr. 2009 June; 21(3): 357–364.

[8] http://eu-acgt.org (January 2013)

5.1.3 (Severe) Adverse Event ((S)AE) Prediction Scenario

The prediction of an SAE within a clinical trial would help to make treatment safer for patients. By extracting an individual patient's profile from his/her data – including pharmacogenomics data (if available) – and performing data mining in literature, SAE/SUSAR databanks and clinical trials, in which the specific drug is used, the individual risk of possible (S)AEs can be predicted. Despite the fact that this use case deals with patients with nephroblastoma, it can be generalized to any other disease, if the disease domain is taken into consideration during data mining.

5.1.4 Tumour Marker Scenario

There are no serum tumor markers known in nephroblastoma predicting outcome or specific subtypes. This use case will define a pattern of miRNAs, tumour specific autoantibodies and other serum proteins as specific markers for nephroblastoma.

5.1.5 Oncosimulator Scenario

The Oncosimulator is at the same time a concept of multilevel integrative cancer biology, a complex algorithmic construct, a biomedical engineering system and, eventually, a clinical tool which primarily aims at supporting the clinician in the process of optimizing cancer treatment in the patient's individualized context through conducting experiments in silico, i.e. on a computer. Additionally, it is a platform for simulating, investigating, better understanding and exploring the natural phenomenon of cancer, supporting the design and interpretation of clinicogenomic trials and, finally, training doctors, researchers and interested patients alike. The present scenario version of the Oncosimulator refers to nephroblastoma.

5.2 Breast Cancer

Breast cancer is the most common cancer in women worldwide, comprising 16% of all female cancers. It is estimated that 519 000 women died in 2004 due to breast cancer, and although breast cancer is thought to be a disease of the developed world, a majority (69%) of all breast cancer deaths occurs in developing countries[9].

p-medicine project will focus (in close collaboration with project partners) in special on targeted drugs, pathway and oncosimulator scenarios. The clinical aspects related to breast cancer pathophysiology, treatment and/or genetic pathways and some other major tumor related particularities are described in clinical trial related deliverables (Work package 9 - Clinical Trials):

- Breast Cancer treatment and/or related clinical trials:
  - Task 9.2: Clinical trials;
  - Subtask 9.2.2: Breast Cancer phase II trial (Bevacizumab trial -1);
  - Subtask 9.2.3: Breast Cancer phase II pharmacodynamic trial (Bevacizumab trial-2)
  - Subtask 9.2.4: Breast Cancer (Circulating tumour cells (CTCs) trial)
  - Subtask 9.2.5: Breast Cancer Stem cell models
- Breast Cancer VPH Modelling and the Integrated Oncosimulator:
  - Task 12.1: Development of the Breast Cancer p-medicine Oncosimulator models

[9] WHO Global Burden of Disease, 2004

- Task 12.2: Clinical adaptation, optimization and partial validation of the Oncosimulator models

5.2.1 Breast Cancer Scenarios

The Breast Cancer scenarios are being implemented in close collaboration with p-medicine project partners enrolled in the breast cancer trials within WP12 (VPH modelling and integrated Oncosimulator). The specific scenario suggested for the breast cancer VPH will be to model the response to preoperative therapy using the available trials. This will be done within WP12 in two phases:

- Response to anti-angiogenic treatment
- Response to combined modalities of biological drugs with standard cytotoxic and/or hormonal therapies

The first phases will be the primary aim and will be validated within the duration of the project using the existing Bevacizumab phase II trials (Bevacizumab 1 and 2 trials, please explore WP9 for further information). Both of these trials address the same drug and the data from the trials will be merged in a single meta-entity to be used tuning and validation of the Oncosimulator breast cancer model. Thus, the primary aim would be to have a solid and validated modelling of angiogenesis and response to anti-angiogenic drugs. Furthermore, due to the high number of trials in breast cancer, we will explore the possibility of validating further combined therapies models using large-scale data-mining of published CTs. This will be done in collaboration with partners responsible for WP 7 and WP 11.

5.2.2 Oncosimulator Scenario

The presented version of the oncosimulator scenario (Appendix 5 of the Deliverable 2.2 "Definition on scenarios and use cases and report on scenario based user needs and requirements") refers to breast cancer and it is in the process of implementation. No updates in terms of end-user needs or requirements are available or reported by the project partners for inclusion in this deliverable.

5.3 Acute Lymphoblastic Leukaemia

Leukaemia is the most common childhood malignancy. It accounts for 30% of all cancers diagnosed in children under 15 years of age in industrialized countries. Around 2000, the average incidence for this age group in the European Region was 46.7 cases per million per year, with a slightly lower level in eastern than in western European countries. European population-based cancer registries show an average increase in the incidence of childhood leukaemia of 0.7% per year between 1970 and 1999.[10]

This deliverable is not focused on providing detailed and informative description of ALL clinical aspects, pathophysiology, treatment and/or genetic pathways but the major particularities related to the mutations of genes regulating B-lymphoid development in ALL presented in the Deliverable 2.2 could serve as a background for further research activities.

5.3.1 Oncosimulator Scenario

The presented version of the oncosimulator scenario (Appendix 5 of the Deliverable 2.2 "Definition on scenarios and use cases and report on scenario based user needs and requirements") refers to ALL and it is in the process of implementation. No additional updates in terms of end-user needs or requirements are available or reported by the project partners for inclusion in this deliverable.

[10] WHO, INCIDENCE OF CHILDHOOD LEUKAEMIA, FACT SHEET 4.1, December 2009, CODE: RPG4_Rad_E1

6 Update of the Clinical Trial Scenarios

Introduction

The main objectives of the activities related to clinical scenarios are to validate the p-medicine environment by focusing on running clinical trials. The three selected diseases remain Wilms Tumour, Breast Cancer and Acute Lymphoblastic Leukaemia (ALL). Trials for these diseases were selected by p-medicine in a way that they can address different aspects of the project. Relevant use cases have been defined for all clinical trials and partially implemented. Sample data coming from these trials will be stored in the data warehouse in a secure and anonymized way according to the legal and ethical framework of p-medicine.

The Wilms tumour, Breast Cancer and ALLs trials will be used to employ the newly developed and validated tools of p-medicine. The trials also provide data for the Oncosimulator related scenarios.

In general terms, the clinical trials scenarios which have been previously proposed contain no major updates and remain similar to the description presented in Deliverable 2.2 (Definition on scenarios and use cases and report on Scenario based user needs and requirements).

6.1.1 Statistical analysis of cancer samples with associated gene expression data and clinical data

Uveal melanoma cancer samples: Affymetrix HG-U133 Plus 2 expression arrays are extracted. The following clinical and personal features could be available: tissue, age, gender, eye (right, left), tumor location, tumor diameter (mm), tumor thickness (mm), tumor cell type, retinal detachment, extrascleral extension, chromosome 3 status, months to endpoint, metastasis.

6.1.2 Data management in international clinical trials by ECRIN

Data management in international clinical trials is especially challenging. During protocol implementation, data entry and trials conduct, specific requirements exist regarding countries involved, user training and languages; further, differences in time zones must be considered. The CDMS (Clinical Data Management System) will be installed at an ECRIN data centre, guaranteeing that clinical trials can be performed according to GCP. User training and first level user support will be conducted by national ECRIN representatives using their native languages. The CDMS must not only support data entry including data checks during input, but also to support data querying, Adverse Events (AE) collection, simple data analysis and reporting (e.g. number of queries per site, increase in enrolled patients) to guarantee data quality and efficient data collection in clinical trials.

6.1.3 Use of data mining to improve study feasibility

The data mining functionality of the p-medicine platform can be used to improve protocol feasibility for planned clinical trials. Data warehouses containing data from hospital information systems, registers, biobanks, study databases are part of the p-medicine platform and are searched to identify possible patient populations, number of eligible patients, efficiency of defined inclusion / exclusion criteria, availability of special surgical or therapeutic procedures, cancer treatment options, etc. In this way potential study populations, effects of changes in inclusion / exclusion criteria on recruitment, availability

of medical treatments are determined and modelled. The results could be used for improving the planning of studies.

6.1.4 Improved patient recruitment in oncological clinical trials

The p-medicine platform delivers a unique combination of data warehouse with data mining tools, biobank access, import of data from HIS, laboratories and clinical trials databases and an integrated patient empowerment tool. This novel combination of components can be used to improve patient recruitment in oncological clinical trials.

The improvement of patient recruitment is of special importance. The process covers the aspects of advertising the trial, identifying and contacting patients, pre-screening of patients, information of patient and informed consent, monitoring patient flow throughout the enrolment process. p-medicine's tools can be used to identify possible candidates and conduct some pre-screening to increase patient quality and help investigator sites. Because successful recruitment is determined by the patient's understanding and acceptance of the trial, the Patient Empowerment Tool is used to enable information exchange with the patient.

6.1.5 Use of p-medicine platform with decision support to conduct oncological clinical trials by ECRIN

The p-medicine platform will offer a set of tools like data warehouse, biobank access, decision support and a CDMS to increase the efficiency of oncological clinical trials and enable translational research. Through the deployment by ECRIN, the p-medicine platform can be used in large international trials. Decision support can be evaluated as part of the intervention. Based on the prediction of the decision support tool, patients in clinical trials obtain different treatments. Training and support for the application of the decision support tool in the environment of an international clinical trial will be of special importance.

6.1.6 Increased subject retention rates in oncological clinical trials

p-medicine tools can be used to improve patient retention in oncological clinical trials. Especially in oncological trials, visit reminders, compliance reminders, assistance, self-monitoring and educational support can improve patient retention by, for example, offering the possibility to intercept potential drop-outs. The Patient Empowerment Tool is used to enable such information exchange with the patient during the clinical trial flow.

7 Update of the Education and Patient Empowerment Scenarios

7.1 Education and Training

The p-medicine project aims to create a set of tools that will challenge and inspire the medical community. The use of these tools in a clinical setting is what will bridge the gap between technological development and patient benefit.

In order for the p-medicine tools to be used successfully, it is vitally important that end-users are properly educated and trained. The end-users will range from clinicians to patients, from basic scientists to data managers. All of the educational tools will be developed putting the needs of these extremely heterogenous end-user groups first.

7.1.1 Help patients understand the patient empowerment tool

“Patient empowerment” is a relatively new concept and will be quite daunting for a number of patients (as well as doctors). Patients will have varied educational backgrounds, different levels of pre-existing knowledge, different psychological states as well as differing levels of interest in becoming “empowered”. These factors will combine to create a very challenging environment for the educational tools to function within.

7.1.2 Teach health care professionals when to use the p-medicine tools

Along with teaching health care professionals how to use the p-medicine tools, it is vital to teach which tool to use when and how to make each tool work to bring most benefit to the patient. Ensuring a high level of competence within the medical community will ensure that patient benefit is demonstrated on a continuous basis.

7.1.3 Impart understanding of the p-medicine environment

The increasing pace of technological advances has resulted in the majority of physicians being unaware of the possibilities of what modern IT can achieve. Educational tools will be developed to ensure that the medical health community are aware of today’s possibilities and feel comfortable with the language and interactivity. Vital importance will also be placed on users of the tools having confidence in the background technology and security elements of the p-medicine environment.

7.1.4 Scenario for Education and Training

Educating end-users in how to best use the tools created by p-medicine will be vital to their continued use and success. The eLearning tools will be designed with the end-users’ needs in mind. Different user-groups will be using different educational tools and therefore a different set of user requirements will be identified for each tool.

A different educational tool will be required for each of the tools created by p-medicine, these tools will need to be populated with fake, but realistic data to allow the end-users to practice and demonstrate competence. Each educational tool will be created in close cooperation with WP15 to submit them to the project’s validation process. The educational tools will be hosted on ecancer.eu as well as the p-medicine website and will be annotated to the corresponding tool within p-medicine environment.

Each tool will contain an end-user data capture introduction with a short pre-test to determine pre-existing knowledge followed by the educational content. Users will then have a practice environment with a final competence and validation requirement. An automatic reminder will be sent out after completion to help ensure retention of knowledge and competence leading to patient benefit.

7.2 Educational tools requirements

The educational tools produced within p-medicine will be web-based and hosted on a dedicated area of the ecancer.eu website. Ecancer.eu is a completely open access site and will give the educational tools the largest possible audience. The tools will be linked to from within the p-medicine environment so that users are able to find the required educational tools easily.

The educational tools will encapsulate a blended approach to learning and will include video content, narrated animations as well as a “mentoring service”. It is the aim for all of the tools to be SCORM compliant as well as EACCME accredited, however user needs will not be hampered in order to achieve these goals. It is our aim to host “lite” versions of elements of the completed p-medicine tools in order to allow users to test their competencies on dummy data within the larger educational environment.

7.3 Patient Empowerment

The patient empowerment tools must feel easy and comfortable for patients. To help ensure this, there are a few guiding principles for the creation of the tools

- There should be one tool composed of different sub-tools and not a series of different tools
- The tool should be cloud based
- Patients and professionals will both be users of the different elements of the tool, with access via the p-medicine portal according to their rights and roles
- The tool must communicate with patients using language they are comfortable with
- The tool must be totally secure giving patients the confidence to share their data
- Touch screen technology should be used where possible

Elements of the patient empowerment tool will be used in the Clinical Decision Support work package; therefore it is very important that the WPs work together closely to find an integrated solution.

This work deals with the development of the Interactive Empowerment Service (IEmS). The aim in providing IEmS is twofold:

- Help the patient to understand her/his medical documentation.
- Empower the patient to make informed choices.

In line with the aim to develop a personalized medicine, the empowerment tool will aim at enabling the patients understanding of the whole data set that the hospital has collected. This process implies that patients are able to understand medical statements, as well as legal and ethical considerations. Thus, the empowerment tool must not only represent data in a convenient format, but data must also be translated into a language that is understandable to the patient. Of course, this does not only entail the wording of the information, but there is the need to come up with ways to organize the data in a manner that makes it easier to decide for the patient what is of interest to him/her at the moment. This statement is consistent with a second goal of the empowerment tool: to give a patient a chance to make an informed choice. In order to build the IEmS the patient view is of utmost importance. Task 14.2 of the DoW will provide the necessary linguistic analysis to develop the Patient View.

Use cases for patient empowerment that will be supported and tested within *p-medicine* are the following:

1. Search for running clinical trials in Europe
2. Consent and re-consent
3. Usage of the own data and own biomaterial
4. Summarize the history of the disease in an understandable way and increase patient-doctor understanding

These use cases will increase the compliance of patients to their treatment and will improve the quantity and the quality of data for research purposes. Transparency in data handling, augmentation of the patient's knowledge about his/her disease and participation as an active partner in a shared decision process in the management of his/her disease increases trust in the Health Care System including data handling and demands for more research by patients allowing the use of his/her individual data to solve his/her personal medical problem.

7.3.1 Search for running clinical trials in Europe

The search for the best treatment for a given patient has to get access to running trials in Europe (Eudract database) by selecting those trials that fit the best to the patients disease characterized by the individual data of the disease of the single patient. Data mining tools should also be used to search other databases, literature and results of closed trials and patient cohorts treated outside of trials. Such a tool should suggest those treatments with the highest survival rates or the lowest toxicity, or other characteristics that can be chosen. The tool should be useable for patients but also for physicians. The result given to patients must be given in a patient understandable language whereas it can be in more detail displayed for clinicians, giving also the references for further information.

7.3.2 Consent and Re-consent Scenario

Data created from a clinical trial should be securely stored in the data warehouse as done for other clinical or molecular data. The analysis of the individual profile of the patient might serve as a discriminator in an econsent tool as part of the IEmS. Such an approach will lead to an individualized econsent adjusted to the patients needs. For the future such an approach would mean that patients primarily have to answer a questionnaire online (part of the tool) before they are guided to the individual consent form to sign. The signature should be possible to do electronically as well as paper based (possibility to print the individual consent form). To create such a form automatically data about the disease, the treatment etc. are needed as well. Such informed consent can be done for patients within or outside trials. Functionality for re-consent needs to be implemented. Access to the informed consent by different stakeholders has to be considered. The patient needs to get the possibility to reject informed consent at any time, or to restrict consent to only specific items, etc. Further functionalities of such an IT tool is described in more detail in the corresponding scenario.

7.3.3 Informed Consent (Patient's Perspective)

Informed consent from Patient's Perspective should be clearly visible and accessible for all p-medicine end users (patients and/or patient's relative). Patients need to be aware about the term "informed consent" in an easy understandable way. A close collaboration with the EU project CONTRACT[11] is given.

[11] http://www.contract-fp7.eu/ (January 2013)

7.3.4 Own Data Scenario

As needed for the consent tool, patients should have the possibility to see which of their data are stored electronically. He might also be able to validate his own data, as well as giving input to missing data. Even eCRFs for patients can be built. Such a tool might be built in ObTiMA.

7.3.5 Summarize the history of the disease in an understandable way and increase patient-doctor understanding

This use case summarizes the usage of data mining and knowledge discovery tools that are able to summarize the history of a patient's specific disease with all relevant information and in a language understandable by patients. Patients will complete a questionnaire that will allow a psycho-cognitive profile to be developed. This profile will then be displayed to the doctor as part of the suit of clinical decision support tools aiding the appropriate decision making for each individual patient.

8 Update of the Biobank Access, Portal and IT Scenarios

Introduction

A biobank, also known as a bio-repository, is a place that collects, stores, processes and distributes biological materials and the data associated with those materials. These may include human bio-specimens such as tissue or blood and related clinical information pertaining to the donor of that bio-specimen. All biobank related scenarios are in development and will be described in detail in the related deliverable from Work Package 8 "Access to Biobanks".

In p-medicine project the following biobank access scenarios are in development:

- Linking the own biomaterial data repository to the p-medicine biobank access framework for the collaboration with specific user groups
- Managing patient's biomaterial and related data within p-medicine infrastructure for clinical trials
- Offering human biomaterial to a closed and/or open clinical research community for research
- Requesting specific human biomaterial within a closed and/or an open clinical research community for research purposes

8.1.1 Access to Biobanks Scenario

Patients could be able to access the biobank data with the information "translated" into a patient-friendly format and language. This scenario has a medium priority and current activities are focused on developing the general biobank interface.

8.1.2 Linking the own biomaterial data repository to the p-medicine biobank access framework for the collaboration with specific user groups

The end-user could have the possibility to link his own biomaterial data repository to the p-medicine biobank access framework in order to share data and material with his research community as further described in the scenarios below.

8.1.3 Managing patient's biomaterial and related data in clinical trials with ObTiMA

This scenario describes how an end-user collects biomaterial in a clinical trial, conducted with ObTiMA within p-medicine environment. The user wants to manage biomaterial and related data with ObTiMA that will enable him to link the biomaterial data directly to the clinical data of the patients and facilitates the sharing of the data and material within the trial community.

8.1.4 Offering human biomaterial to a closed and/or open clinical research community for research

This use case is an extension of the next related scenario (Requesting specific human biomaterial within a closed and/or an open clinical research community for research purposes). The search engine includes an indicator whether and how much material is available for research and allows placing requests.

8.1.5 Requesting specific human biomaterial within a closed and/or an open clinical research community for research purposes

This scenario complements the above use case from the perspective of the researcher who wants to get biomaterial.

8.1.6 p-medicine portal scenario

The p-medicine portal will provide clinicians, patients and researchers a platform to collaborate, share data and expertise, and use tools and services to improve personalized treatments of patients.

The Deliverable 8.1.2 “Design and prototype implementation of the p-medicine portal” presented why we need a portal solution for the p-medicine project and described how the portal for p-medicine has been developed and how the users involved into the project can use the portal. The document analyses user requirements for the portal and defines the portal user groups and their roles in the portal. Furthermore, several technical solutions that seem appropriate to fulfil the complex user requirements for the p-medicine portal are evaluated and the decision for using the Liferay framework for the p-medicine project is explained. Also information is provided about the p-medicine services and tools that will be directly or indirectly integrated into the portal as well as the community based architecture of the portal. In addition, the deliverable contains a description of the integration of the p-medicine security framework into the portal. Finally, this document presents the current state of the portal with the tools and services that are already accessible through it and how they can be used.

8.1.7 Sync and Push services

Data stored in hospital information systems (HIS), clinical trial management systems and trial repositories provide a precious source for clinical research, especially in the field of personalized medicine. However, it is difficult to exploit such data for VPH modelling, data mining or decision support applications because the data sources are mostly heterogeneous, unstructured and the semantics is often not defined unambiguously. The aim of p-medicine remains to integrate the data from these sources syntactically and semantically in a data warehouse, in order that tools and services can exploit the data seamlessly.

8.1.8 Data translation for PUSH services

The data translation of external databases is executed when a database is pushed into the p-medicine data framework. This scenario forms part of the data PUSH scenario and is conducted by the Data Translation service. This service is invoked locally by the Data Warehouse which is in charge of storing HDOT-compliant versions of the pushed data. There are three situations that can trigger this scenario:

- A new database is received. The data has to be translated into an HDOT-compliant form before storing it in the Data Warehouse.

- An existing database is updated. In this case, the complete database has to be translated again to create an updated HDOT representation of the new data.
- The annotation of an existing database is updated. Annotations are the descriptions of the databases in terms of HDOT, and are used during the translation process. If the annotation is modified, the HDOT form of the database will differ and thus will have to be recalculated.

The result of the data translation process is that the external database is translated into an HDOT form and stored in the Data Warehouse, integrating it with the previously translated databases.

8.1.9 Ontology annotation of external databases

The annotation of external databases allows creating descriptions of these databases in terms of the HDOT ontology. The goal is to allow the automatic translation of data sources into an HDOT-compliant form and the subsequent integration in the p-medicine Data Warehouse. The scenario involves the actual use of the Ontology Annotator tool by end-users (generally, database administrators) who wish to have their databases integrated in the p-medicine infrastructure.

8.1.10 Ontology-Based Semantic Search Framework

p-medicine platform could benefit by implementing the described Ontology-Based Semantic Framework (OBSF) Scenario. This framework will be able to connect highly heterogeneous data and textual information and could be based on gene, tissue, disease and compound ontologies (important for drugs and clinical research frames). It could contain information from different organisms, platforms, data types and research areas which is then integrated into and correlated within a single searchable environment using search algorithms. It will further provide a unified interface for all p-medicine end-users to formulate, explore and identify new information (according to specific preferences and needs) across vast collections of experimental data.

Due to the high complexity of this scenario, it is currently under technical review and some ontology-related aspects are/will be implemented in the context of other scenarios.

9 Update of the ObTiMA Scenarios

Introduction

ObTiMA[12], an ontology-based clinical trial management system, has been developed in special as a proof-of-concept application to highlight the possibilities of ontology based creation and managing of clinical trials within the ACGT (Advancing Clinico-Genomic Trials on Cancer)[13] project.

ObTiMA is developed in a modular fashion with a core module for data management of clinical trials. Various other modules are under active development at the time of writing.

9.1.1 Pseudonymization Scenario

Pseudonymization in ObTiMA is under development and, in general, means that a local user treating a patient always works with the real personal data whereas other users will never see patient's personal data.

9.1.2 Data Entry of Prospective Clinical Trial Data

Clinical trials of investigational medicinal products must be carried out in accordance with ICH GCP and national legislation. Requirements for the data capture include quality control, quality assurance. The end user is expected to receive clear instructions and prompts, drop-down lists, etc., to help with speed and accuracy of data input.

9.1.3 Data Manager of Prospective Clinical Trials

This end-user is expected to have the facility to raise data clarification queries within the ObTiMA software, and allocate status to queries (e.g. close them when satisfied); the role plays an important part in demonstrable quality assurance.

9.1.4 eCRF Developer for Prospective Clinical Trials

The eCRF Developer scenario is currently under active development and continuously adjusted according to the end user needs, requirements and expectations. At this stage, the eCRF development frames already assure an efficient development and managing of the eCRFs.

9.1.5 Data Synchronization with HIS during running trial in ObTiMA

This scenario is under development and, at this stage, divided into a couple of smaller use cases able focusing on facilitating (different technological and legal requirements are under review) the data import from a hospital information system (HIS) to fill the patient's eCRFs.

9.1.6 SAE/SUSAR Scenario

Reporting and handling of SAEs and SUSARs in clinical trials has to be done according to GCP criteria. All additional requirements are according to the EudraVigilance network and this scenario is currently under development.

[12] http://www.obtima.org (January 2013)
[13] http://www.eu-acgt.org (January 2013)

9.1.7 Drug interaction Scenario

The tool should help to find dangerous interaction between two drugs that are prescribed to a patient. A physician should do this check always before subscribing drugs. If all the drugs a patient gets are stored in CRFs in ObTiMA then such a service can automatically check for interaction and send a warning to the treating physician, announcing that there is incompatibility between drugs. In addition this service names the drugs and gives information about what are the risks for the patient.

9.1.8 DICOM Scenario

This use-case describes how DICOM data can be send from a local hospital to the data warehouse after automatic pseudonymization of the data. In a second step it describes how DICOM data can be downloaded for reviewing or post-processing.

9.1.9 Consultation Scenario

In this scenario a local physicians can ask for consultation of a patient treated within a clinical trial.

9.1.10 Trial Development Scenario

The trial development scenario describes the availability of trial templates in order to guide the trial chairman or people responsible for writing a new trial through all required tasks according to legal, ethical and GCP regulations. There are also could be templates available for writing a standardized trial protocol.

9.1.11 Trial Outline Builder Scenarios

The Trial Outline Builder scenario is under development and encompasses two scenarios described as use cases:

- Statistical Toolbox - this use case describes how clinical data from a clinical trial can be statistically analysed;
- Gene Expression Parallel Coordinates - this use case describes how clinical data from a clinical trial can be statistically analysed together with molecular data.

9.1.12 Participating Centres Scenario

In clinical trials the selection of participating centres is of utmost importance. The trial chairman needs to know which centres are compliant with GCP criteria and which physicians can work as trial investigators from a centre. Such information can be stored in a database, which needs regular updates. A graphical view or representation of participating centres on a map would be beneficial.

A trial chairman could be able to select participating centres and trial investigators from specific centres. Researchers could also include research institutes in this tool.

9.1.13 Patient Access to his/her trial data and Diary Scenario

The patients enrolled in clinical trials could be allowed to access stored data and might be able to write the specific diary CRFs. This will allow patient's data checking and validation as well as the enhancing of data curation. The patient will not be allowed to change data in the database, but he could be allowed to comment on existing entries. Patients would be able to write in the diary CRF.

9.1.14 Repository Scenario

The repository scenario is under active development and the end-user interface is already successfully integrated into ObTiMA. An end-user can store CRFs into a (centralized)

repository and later, he/she or others could subsequently retrieve, (re)assemble and reuse those full or partial CRFs in other new trials or studies.

9.1.15 Semantic Interoperability Scenario

Data from both external as well as internal data sources could be integrated and used along with the data collected using the CRFs within ObTiMA.

9.1.16 Reporting Scenario

The reporting scenario is under development but the initial interfaces are already integrated, the reports of the collected data of a patient and/or trial could be exported according to the CDISC ODM data standard.

10 Update of the DoctorEye Scenarios

Introduction

DoctorEye is a flexible, clinically driven and easy-to-use annotation platform for quick and precise identification and delineation of tumors in medical images. The platform has been tested over additional MRI datasets to assess usability, extensibility and the proposed for implementation scenarios. A detailed report has been successfully described in the Deliverable No. 9.4 "Report on the segmentation of Wilms tumours using DoctorEye" and a summary of the archived results have been presented in the frames of the 5th International Advanced Research Workshop on In Silico Oncology and Cancer Investigation event[14] (October 22-23, 2012, Athens, Greece).

10.1.1 Segmenting Nephroblastoma MRI

The main goal of the conducted Wilms' tumor segmentation activities was to address the pre/post chemotherapy changes in MR images. The aim of this research was to identify and to report changes after chemotherapy in tumor volume estimated with DoctorEye platform, and to compare the histopathological class to these changes.

Close to annotated/segmented MR images, DoctorEye platform has been used as well to identify the pre/post chemotherapy tumor volume change. The generated histograms of the annotated/segmented MR images have been divided in pre/post chemotherapy charts.

Wilms' tumor presents as a large, solid tumor of renal origin. The tumor may be homogeneous, but typically appears heterogeneous with intermediate signal intensity on T1-weighted images and high signal intensity on T2-weighted images. In our cases we decided to annotate/segment only T2-weighted images due to increased signal intensity specifically in T2 images. Size and extent of tumor regions have been precisely identified and annotated/segmented (Table 10.1).

Table 10.1. The Results of Wilms' Tumour Segmentation (16 cases)

Cases	Necrosis / Regression	Histopathological type	Post chemotherapy histogram
C1	80%	70% Blastema 30% Epithelia 0% Stroma	Left shift
C2	80%	80% Blastema 20% Epithelia 0% Stroma	Left shift
C3	20%	50% Blastema 25% Epithelia 25% Stroma	Left shift
C4	5%	0% Blastema 100% Epithelia 0% Stroma	Median
C5	2%	4% Blastema 2% Epithelia 94% Stroma	Slight left shift
C6	50%	10% Blastema 60% Epithelia	Slight left shift

[14] http://www.5th-iarwisoci.iccs.ntua.gr (January 2013)

		30% Stroma	
C7	10%	20% Blastema 30% Epithelia 50% Stroma	Left shift
C8	10%	0% Blastema 50% Epithelia 50% Stroma	Almost median
C9	30%	40% Blastema 30% Epithelia 30% Stroma	Right shift
C10	5%	50% Blastema 45% Epithelia 5% Stroma	Right shift
C11	95%	90% Blastema 10% Epithelia 0% Stroma	Left shift
C12	30%	2% Blastema 8% Epithelia 90% Stroma	Almost median
C13	90%	50% Blastema 50% Epithelia 0% Stroma	Slight left shift
C14	70%	90% Blastema 0% Epithelia 10% Stroma	Right shift
C15	25%	10% Blastema 60% Epithelia 30% Stroma	Right shift
C16	30%	15% Blastema 25% Epithelia 60% Stroma	Left shift

10.1.2 Preliminary Findings and Conclusions of Further Work

DoctorEye's manual and semi-automatic segmentation techniques combined with integrated correction tools assist in the fast and refined delineation of Wilms' tumors and different users are able to add different components such as tumor growth and simulation algorithms for improving therapy planning. DoctorEye platform has been successfully tested and practically used over a large number of Wilms' tumor MRI datasets and it ensured stability, usability, extensibility and robustness with promising results.

Our preliminarily findings confirm the evidence of significant shrinkage or volume change of all tumors following primary chemotherapy. Changes in Wilms' tumor after chemotherapy have been addressed for the first time (to our knowledge) by using the advanced segmentation/annotation techniques and the histogram generation interfaces of DoctorEye platform. This research was the first report to specifically present pre/post chemotherapy changes of Wilms' tumor histograms close to the related volume changes.

We hypothesize that the histograms of Wilms tumor images (MR) might have prognostic and histopathological diagnostic information with implications for the clinical assessment of response to chemotherapy. These data can then be used to optimize the Oncosimulator for predicting response to preoperative chemotherapy in Wilms tumor. More research activities and clinical cases are required in order to confirm our preliminary hypothesis and we are expecting that in the nearest future we will strengthen our initial findings with additional evidence-based results.

10.1.3 Signal Intensity Scenario

In this section we describe shortly an extension proposal of the DoctorEye platform's functionality by including an Angiomap-based enhancement classification algorithm that

automatically categorizes the enhancement of each voxel in the three types that are widely accepted. The preliminary available results are for an analysis on infiltrative ductal carcinoma pre- and post-chemotherapy (Wilms' tumour MR images analyses are expected at latter stages).

All these findings support the conclusion of diffusion analysis that the tumour is responding to the chemotherapy scheme applied in this particular case. This would be an important further functionality in DoctorEye platform that could give the clinician an advanced viewpoint concerning the individual (personalised) therapy response.

11 Evaluation and Validation

Introduction

In line with D15.1, the Quality Control administrators started their activity by monitoring several of the p-medicine tools and their functionalities.

The p-medicine portal, a web based portal has been implemented to integrate, among the other activities, to the implemented tools as portlets or links. A Security Gateway has been implemented as well for authentication and authorization (see Figure 11.1 for complete overview of the planned structure).

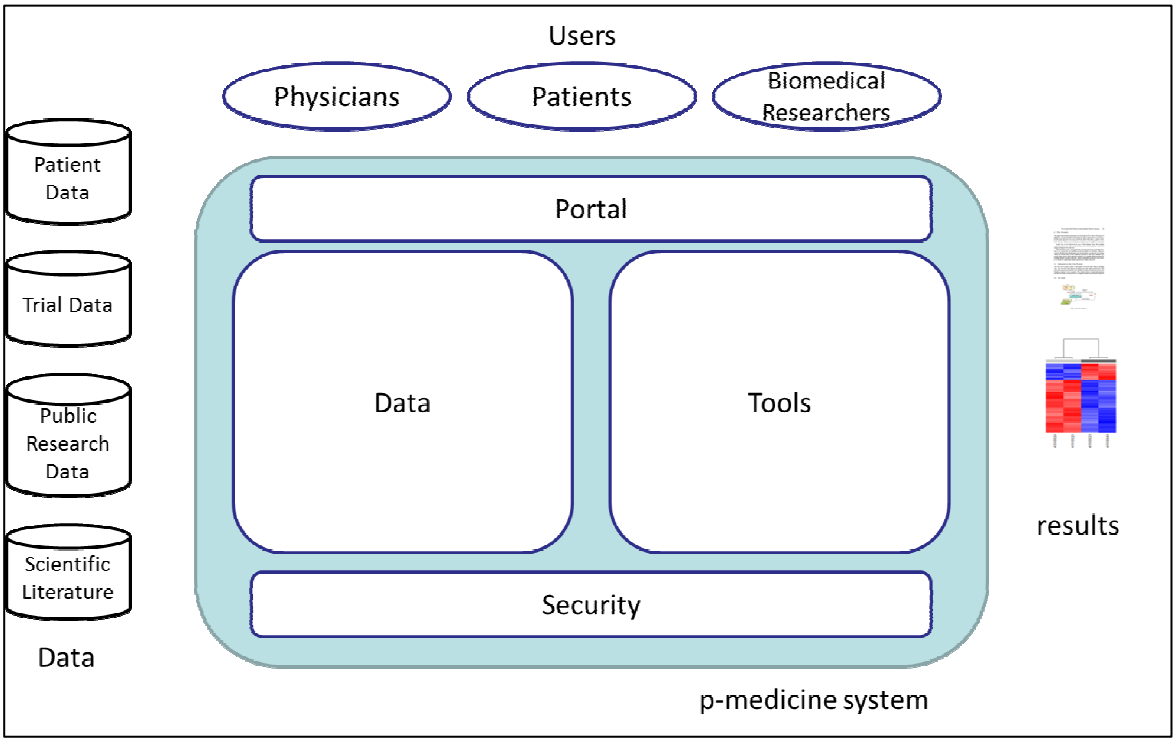

Figure 11.1: Overview of the planned structure

The tools that are listed via portal under the menu called p-medicine Tools are (Figure 11.2):

- Workbench
- Oncosimulator
- Data Mining
- ObTiMA
- Biobank Access
- Data Warehouse
- Cloud Services
- Ontology Annotator
- Ontology Aggregator

Of them, Data Mining, ObTiMA and the Ontology Annotator are accessible through the portal, the others are still under local development and they will be integrated later on as planned. During the 1st p-medicine review several demonstrators have been described and presented: Data Mining (Literature, R workflow and workflow development) and ObTiMA.

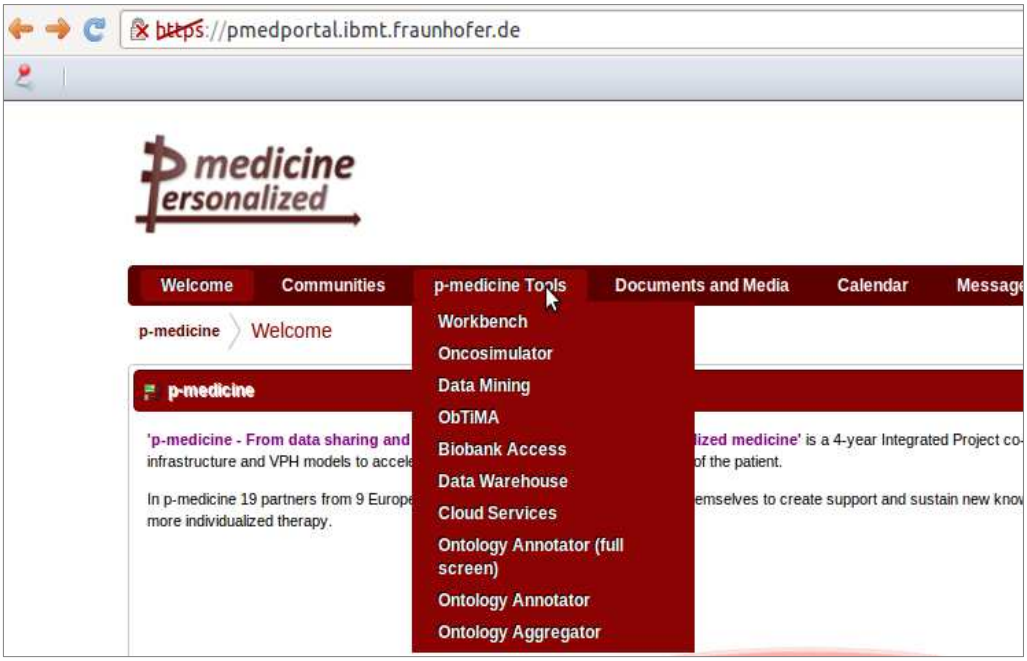

Figure 11.2: p-medicine portal screen shot

It is also our plan to have a repository where all tools will be registered (as to replace the first idea of an independent database, D15.1). This repository will hold various data about each tool, including also information about the quality management. An RDF triple store, similarly to the Data Warehouse, will be used in order to be able to provide more semantically rich annotations and relationships between the tools and services that will use it.

In the following paragraphs are summarized the evaluation activities for each one of the accessible tools through the portal.

11.1 Data Mining: R workflow

The Data Mining Tools contain at the moment 24 workflows, among them the R workflow (as described in the Context Scenario from D2.2 (Pages 126-135)) has been run for usability and evaluation purposes. Briefly, it involves bioinformaticians carrying out statistical analyses on data extracted from high-throughput biological experiments (Fig. 11.3). The user (a bioinformatician) evaluated the ability of the tool to reproduce the results as expected, the evaluation record can be found in Scenario Evaluation Form called R workflow.

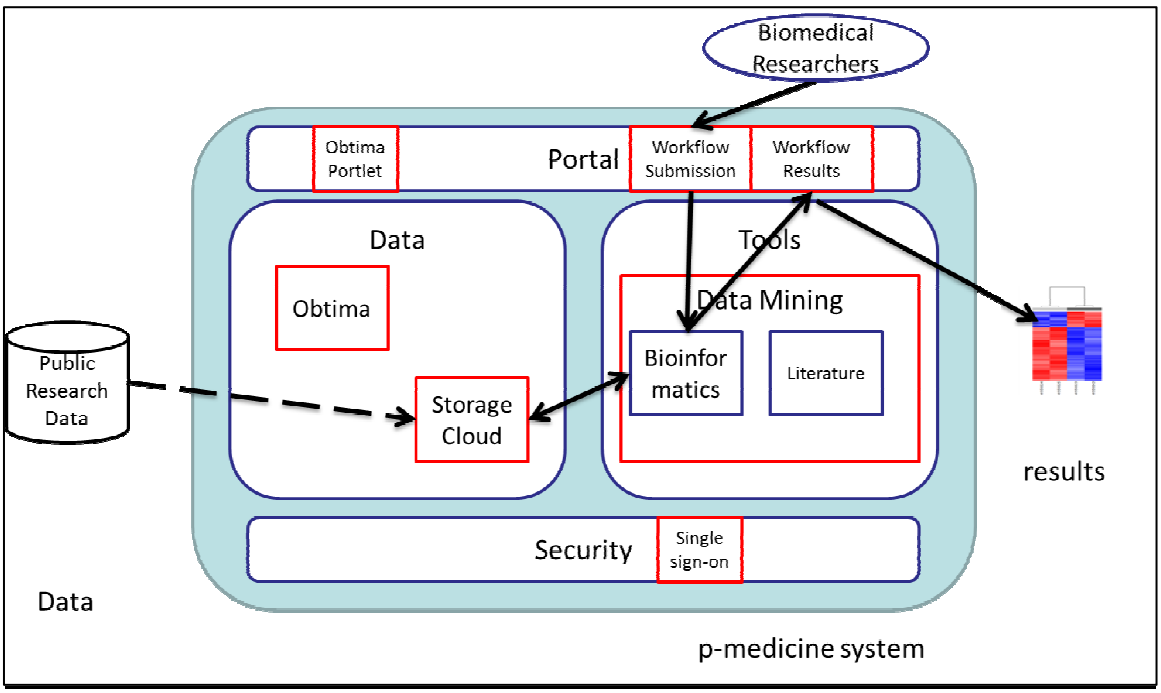

Figure 11.3: R workflow: statistical analyses on data extracted from high-throughput biological experiments

Workpackage 11 has focused on the integration of the workflow execution environment with the updated p-medicine security infrastructure. In particular, after the first version presented at the first review, the update of the security infrastructure required in-depth changes of the p-medicine portal, making the portal and services provided by the portal temporarily unavailable. The security integration is still ongoing, such that the R workflow needs to be re-evaluated as well as the others that still present some incongruence between the demo server version and the one portal integrated.

Scenario evaluation form: R workflow							
Name of evaluator(s)	Simona Rossi						
Evaluation start date	May 2012				end date	May 2012	
Task	Success Level				Date	Note	
Run the R workflow on the Data Mining Web application	1	2 X	3	4	May 2012		
Prerequisite tools and data	Description					Note	
R/Bioconductor	Bioconductor provides tools for the analysis and comprehension of high-throughput genomic data. Bioconductor uses the R statistical programming language, and is open source and open development.					http://www.bioconductor.org/ http://www.r-project.org/	

GSE22138	Expression Data from Uveal Melanoma primary tumors	http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE22138
Scenario steps	Description	Note
Read raw data	import data in R	
Import clinic-pathological variables	Import variables that will be further used to compare gene expression data	
Quality control	Plots to assess good quality and discover outliers	
normalization	Normalization is carried out to reduce technical variations	
Find differentially expressed genes	Find those genes that are statistically differentially expressed between classes of samples	
Plot heatmap	Plot for the visualization of the genes differentially expressed	
Survival analysis	The DE genes are also tested for overall survival	
Expected results	Description	Note
Heatmap plot	Plot for the visualization of the genes differentially expressed	
Kaplan-Meier plots	They show the probability of survival for patients belonging to a certain category	

Rate of success and uncompleted task priority assignment						
Level done	1	X2	3	4		No uncompleted tasks
Comment on rating Further development will be the independent upload of the data without having pre-uploaded data to be imported, but as prototype the workflow successfully met the expectations						

11.2 ObTiMA

ObTiMA has been run for usability by several user's categories: clinician, data manager, and researcher. Main functionalities have been evaluated and issues reported to the developers.

For a detailed overview about the first usability test with the ontology-based trial management application ObTiMA, please explore "D15.2 - First Evaluation Workshops Round."

The first two tests with a clinician and a study nurse were taken with the first prototype of ObTiMA. These tests were participated both by a usability engineer and the developers. The tests result in form of use scenarios in D15.2 and the occurred usage problems were improved in the next prototype.

The second tests with a data manager were performed without the participatory observation of the usability engineer. The recorded tests and the continued usability tests will also be described in form of use scenarios in the future D15.4. This is an important step to involve the end-user during the early development stages relating to implement ergonomic qualitative usable software.

11.3 Ontology Annotator

This tool is aimed at providing users with a GUI to annotate an existing database schema in terms of HDOT (the ontology to be developed in p-medicine for describing the data contained in the data warehouse). The results of this annotation process will allow to seamlessly access heterogeneous data in terms of the HDOT model, thus achieving semantic integration of such data. The tool assists users in establishing semantic correspondences between an external database schema and the HDOT model. The output data is submitted to the data warehouse.

The tool has been evaluated by running an example and a prototype tutorial in terms of functionalities description and hands on basic functions, videos as well as documentation describing the activities are available on the FhG-IAIS server for further development and evaluation, documentation is also available on the p-medicine wiki.

Scenario evaluation form: Ontology Annotator (example, hands on basic function)						
Name of evaluator(s)	Simona Rossi					
Evaluation start date	December 2012			end date	December 2012	
Task	Success Level				Date	Note
Run an example and record a tutorial on the Ontology Annotator	1	x2	3	4		
Prerequisite tools and data	Description					Note
Web access to the Ontology Annotator	http://servet.dia.fi.upm.es:8080/OntologyAnnotator-test/mainWindow.jsp or https://pmedportal.ibmt.fraunhofer.de/web/guest/ontology-tools (portal integrated)					
Scenario steps	Description					Note
Introduce the terminology	RDF terminology that allows the user a correct use of the tool					
Hands on basic functions	Describe the windows and the available actions					
Run an example	Mapping of classes from the existing dataset into the HDOT					
Expected results	Description					Note

Correct actions	The tool should act in agreement with the selected functions	

Rate of success and uncompleted task priority assignment						
Level done	1	X2	3	4		
Comment on rating						Encountered problems will be fixed and re-evaluated in time for the 2nd project review

1) The help button does not work, but its purpose is solely to enable/disable the appearing tooltips. This maybe does not have much sense as no one would actually really want to disable the tooltips, and that maybe the help button could link to a separate page with documentation, a FAQ, etc.	
2) The button in the HDOT window that allows displaying the HDOT classes for adding them or removing them could be replaced with a small cross image when this sub-window is shown. And it will be probably more intuitive.	
The exit button does not work yet. We will take care of it in the upcoming weeks.	
3) When an entry is saved, it would be good to ask the user for an entry name	
4) After several minutes of inactivity, if the user select a class, an error message appears, it is sufficient to refresh the test window to solve this problem.	
5) It would be probably better to have an icon and a message “esc or exit” instead of “cancel” since the user use it to exit and close the window.	

12 Conclusions

Introduction

The main objective of this deliverable was to collect, identify and to describe the available updates of the user needs and requirements for the proposed for implementation p-medicine project scenarios.

This report has been elaborated as well to fulfil the necessity of a spiral process of requirements analysis, elicitation, documentation and validation described in the related deliverables. The main followed technique remains the scenarios elaboration and (if applicable) prototyping. This report provided detailed information on end user needs and end user requirements necessary to guide the activities of all project work packages.

12.1 Project Partners Enrolment

Close to the task to present and to describe the regular update of the user needs and requirements based on evaluation and validation this report served as an example of continuous commitment of all project partners to the proposed for implementation project activities. All project partners have been informed about this deliverable and all contributed with available updates and in special with references to the published and in elaboration, related deliverables and reports.

A new scenario has been as well submitted and it is presented in the Appendix 1 (New Use Case / Scenario) of this document.

12.2 Further Deliverable Version

p-medicine project has a well-defined DoW document and this deliverable is an example of the continuous process of identifying and presenting regular update of the user needs and requirements based on evaluation and validation. Close to it we would like to emphasise that further and updated use case scenarios would be presented as well in the frames of the next version of this deliverable (D2.6 - Regular update of the user needs and requirements based on evaluation and validation: Updates in M36).

12.3 Linkage to other Activities, Deliverables and Work Packages

This document is in a strong linkage with other deliverables and Work Packages, of special interest are the reports from the Work Package 15 (Quality Assurance, Evaluation and Validation). This WP is crucial because it is assessing continuously the quality of all services and tasks of the p-medicine environment and iteratively gives feedback to all responsible persons. It initially created a set of guidelines and check-lists to support evaluators in setting-up their evaluation reports. These reports in turn will provide issues and suggest possible improvements and possible modifications of presented use cases, scenarios. The linkages to other deliverables and Work Packages are mentioned in the text of this document.

Furthermore, workshops are held regularly to perform dedicated evaluation sessions and scenarios update collection by engaging both end-users and developers.

As conclusion, this report has been elaborated in a close and a successful collaboration with all project partners and it will guide all our further project related activities.

Appendix 1 – New Use Case / Scenario

For all other Use Cases / Scenarios see the Appendix 5 of the Deliverable 2.2 "Definition on scenarios and use cases and report on scenario based user needs and requirements"

Item	Description
Identifier	SA_01
Version	1.0
Name	Annotation of existing data set
Description of the use case (enduser perspective)	The goal is to create new HDOT module in order to enable the annotation of the given data whenever the Annotator tool cannot provide suitable HDOT class. This happens in case HDOT does not contain class that is specific enough to map the required annotation value to.
Problem(s) to solve	The user is not able to annotate his/hers data set because the annotator tool cannot find an adequate specific and meaningful HDOT class to map user's annotation value to. Annotation process failed.
Challenges	Determine criteria for constraints: 1. on the results returned by the BioPortal search on ontology level(list with preferred ontologies) 2. to give the single appropriate class that will be integrated into HDOT By selecting terms in BioPortal: The same semantic resource could have different URIs for the same term. E.g. in SINOMED CT -> Nephroblastoma: http://purl.bioontology.org/ontology/SNOMEDCT/25081006 http://purl.bioontology.org/ontology/SNOMEDCT/302849000 In such cases we can check the root path and thus we will see the integration of which one will be smoother.
Risks	
Expected benefits	Better coverage and greater expressivity of HDOT. Thus enabling annotation process using only one resource. Continuous enrichment of HDOT with new reusable modules of guaranteed quality.
Characterization	○ fundamental ◉ general ○ specific
If specific, please give the Domain	○ Acute lymphoblastic leukaemia ○ Breast Cancer

	○ Nephroblastoma ○ other Cancer, please specify: ○ Non-Cancer Domain, please specify:
Enduser	○ system ○ person ○ basic scientist ○ clinician ○ computer scientist ○ regulatory body, lawyer, ethicist ○ patient ○ other, please specify:
Pre-condition(s)/pre-requisite(s)	The Annotator tool fails.(trigger) The Annotator tool passes the information provided by the user so far (e.g. the searched term, status of the user expert, clinician etc.).
Requisite(s)	Back up of the current HDOT version.
Post-condition(s)/post-requisite(s)	HDOT version is updated by including the created module. The Annotator tool can access the new HDOT class and map the annotation value to it.
Constraints	
External sources needed from outside p-medicine	○ data, please specify: ○ tools, please specify: ◉ services, please specify: BioPortal search functionality accessed via REST interface which is wrapped in the OntoCat project. BioPortal SPARQL endpoint to get the path from a term to the root in a given resource. ○ models, please specify: ○ other, please specify:
Data used	○ personal ○ only non-personal ○ target population, please specify:
Input data	○ internal database, please specify: ○ external database, please specify: ◉ online input: term in raw text
Output data	○ database, please specify: ○ variables for use, please specify: ◉ structured document, please specify: yyyy-mm-dd-hh:mm:ss_loggingSearchEngine.html yyyy-mm-dd-hh:mm:ss-concept-ontology stores the path of a concept to the root in the ontology. (one for each term) Still experimental and thus final form is not yet determined. ○ graphic, please specify:

Data volume		
Dataflow	Please specify: The term(s) that is(are) searched by the user is specified in raw text and is stored in an external txt file. The term(s) is(are) read in and put into a list. The list is given as an input for the BioPortal search service. One term per iteration is processed until the list is empty. BioPortal search service works with predefined list of ontologies, which are sorted by another module. The search with presorted list of resources guarantees that the list of the found concepts is also sorted according to the resource the concept originates from. The next step is to get the path to the root of the best(first) n-concepts and check the similarity of the parents with the leafs in HDOT in order to ensure smooth integration of the new concept.	
Data storage	Please specify:	
Successful End Condition	The user agrees with the recommendation given by the OAT. New module that contains a class for user's term is integrated in HDOT. The annotation, that initially was not possible, can be performed, i.e. annotator tool can now access OAT-updated HDOT version.	
Fail End Condition	The user does not agree with the recommendation of the OAT. 1. If fail for the first time: user is redirected to the previous step in order to select the alternative option (term vs. term plus a selection of sub-trees). 2. If both options were already tried and user still disagree. OAT might consider further semantic resources (problematic: user might be bugged for so long interaction with the system).	
Basic workflow	Actor Action	System response
	1. Look for single term, set of terms or trees of terms	1. Annotator fails
	2.	2. OAT is called (automatically or by the user)
	3.	3. OAT gets the term(s) that the user is interested in from the Annotator tool
	4.	4. OAT uses the BioPortal search function to find semantic resources for the given term(s).
	5.	5. the results delivered by BioPortal are already sorted by relevance of the resource they originate from

	6.	6. OAT displays the recommendation and asks the user to select just one term or several terms from its sub-tree. "Do you want to reuse thisTerm or thisTerm+subtrees?"
	7. Select an option	7. OAT provides a single recommendation of a term to be integrated into HDOT. "Do you want to integrate thisTerm into HDOT? Yes | No"
	8. Select "Yes"	8. "Thank you for creating a new HDOT module!"
	9. Select "No"	9. If the user do not want to integrate the module under HDOT than OAT needs more input. In this manner either new query or resorting of the delivered results can be carried out.
Expected usage frequency	medium	
Needed for DSS	○ yes ◉ no	
Needs HPC	○ yes ◉ no	
Needs Grid	○ yes ◉ no	
Priority for development	high	
Responsible for development	USAAR (IFOMIS)	
Mockup needed	◉ yes ○ no	
Responsible for Mockup		
Who is building the tool	USAAR (IFOMIS)	
Open Source tool	◉ yes ○ no, please specify why:	

Appendix 2 – Abbreviations and acronyms

AE	Adverse Event
ALL	Acute Lymphoblastic Leukaemia
CDA	Clinical Document Architecture
CDISC	Clinical Data Interchange Standards Consortium
CRO	Clinical Research Organisation
DICOM	Digital Imaging and Communications in Medicine
DSS	Decision Support Service
ECRIN	European Clinical Infrastructure Network
EDC	Electronic Data Capture
EMA	European Medicines Agency
EMR	Electronic Medical Records
ENCCA	European Network for Cancer in Children and Adolescents
EHR	Electronic Health Record
EMA	European Medicines Agency
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GRID	Distributed parallel computing
GUI	Graphical User Interface
HIS	Hospital Information System
LIMS	Laboratory Information Management System
PHR	Personal Health Record
SaaS	Software as a service
SAE	Severe Adverse Event
SOA	Service Oriented Architecture
SUSAR	Suspected Unexpected Severe Adverse Reaction
TOB	Trial Outline Builder in ObTiMA