A Demonstration of 4D Digital Avatar Infrastructure for Access of Complete Patient Information

Project acronym: MyHealthAvatar

Deliverable No. 9.1
Definition of the demos

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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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ABSTRACT:
This document defines and presents in details MHA high end clinical demos selected for further implementation and evaluation. All demos are close related to the prioritised and final set of Use Cases / Scenarios reported in WP7

KEYWORD LIST:
Demo, high end clinical demo, implementation, evaluation, use case, scenario

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

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Contents

1 Executive Summary

This document defines and presents in details MHA high end clinical demos selected for further implementation and evaluation. All demos are close related to the prioritised and final set of Use Cases / Scenarios reported in WP7 and attached for further references to the this document in **Appendix 2**.

Chapter 2 presents the demos and mock-up design presentation model broadly discussed and accepted for implementation by all project members.

All demos are close related to the Digital Avatar display, and we are taking into account the current status of the legal and ethical environment accomplishments described (some activities are ongoing) in WP3, WP7 and WP11. It allowed us to:

- address the main MHA platform roles and rights management requiremetns
- address in advance the possible interoperability issues
- refine and refresh the scenarios for data access and collection
- identify the use of the data collection utilities (i.e EHR information extraction, mobile apps)
- define the linkage to external data/model repositories, external hospital systems (e.g. EHRs). and to social network

On the main achievement of this document is the detailed presentation of the high end clinical scenarios in Chapter 3.

Each demo is close related and associated not only to a specific tool or application but as well to a set of specific Use Cases / Scenarios (see table below). All are defined within complex but very concrete and focused clinical contexts. The demos, at this stage, have already the potential to demonstrate the clear benefits for enrolled end-users.

	UAC	3DS	DB	VC	DCU	TOOL	HIS	CHF	OST	DIAB	NEPH	EME
CHF(FORTH)												
OST(FORTH)												
DIAB-EME (BED)												
NEPH (ICCS / USAAR)												

The template table used for the presentation of the relationships between high end scenarios and the final set of specific Use Cases / Scenarios.

This document presents as well concrete flow diagrams for every high end demo. The required timeframes for each step of development and implementation are presented in a Gantt chart template presented below.

Milestones	**Year 1**												**Year 2**												**Year 3**											
	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
Task 1																																				
M1																																				
Task 2																																				

M2																																
Task 3																																
M3																																
Task 4																																
M4																																

Gantt chart template

Additionally, each demo has the detailed description of mock-ups and evaluation actions. It will serve as a solid background for the next MHA project's tasks and activities.

2 Demos and Mock-up Design

2.1 Introduction

Demo is usually defined as a way to demonstrate a prototype or an incomplete version of a product, with the primary purpose of showcasing the idea, performance, method or features of the product… we are following the general definitions of 'demo' term and our main goal is to define and to present the concept of MHA by demonstrating its clear benefits.

2.2 MHA Scenarios / Use Cases

The final set of MHA Scenarios / Use Cases servers as a main background for this document. The activities from WP7 allowed us not only to define but as well to apply the ranking and to prioritize further development of all MHA Scenarios / Use Cases. This ranking (low, medium, high) is presented in **Table 1**.

MHA Scenarios / Use Cases ranking has been defined and agreed with all project partners in the frames of the last consortium meetings and regular Skype project meetings.

ID	Scenario / Use Case Name	Ranking
UAC	MHA User Accounts	High
3DS	3D Avatar Visualization	High
DB	MHA Data Browse	High
VC	MHA Virtual Community	High
DCU	Self Data Collection	High
TOOL	MHA Toolbox and MHA Simulation Models	High
HIS	Link MHA to HIS and CTMS	High
CHF	Personalized CHF Related Risk Profiles and "Real-Time Monitoring"	High
OST	Osteoarthritis	High
DIAB	Diabetes	High
NEPH	Nephroblastoma (Wilms Tumour) Simulation Model and Clinical Trial	High
EME	Emergency contact	High
TBI	Brain Trauma	Medium
APLA	Anti-Platelet & Anticoagulation Therapy in the Pre-Operative Patients	Medium

Table 1. Ranking of MHA Scenarios / Use Cases

2.3 Demos Presentation Model

As it has been presented in the frames of the D 2.2 and D 7.1 our approach was to integrate the Scenarios descriptions with the related Use Cases. We designed and presented a complex template with sections very useful for demo elaboration and presentation activities.

By following and by implementing the 'Scenario / Use Case' strategy, we, now, are able to describe the MHA Demos with less efforts. It demonstrates once more that the accepted Scenario / Use Case approach was a good decision and it allowed us to focus on additional important aspects by elaborating high end clinical demos (e.g. mock-up presentation, evaluation, etc.).

The elaborated and accepted by all partners demo's presentation template is presented below.

High End Clinical Demo (HECD)

Table Use case (column) vs HECD(row)

	UAC	3DS	DB	VC	DCU	TOOL	HIS	CHF	OST	DIAB	NEPH	EME
CHF(FORTH)												
OST(FORTH)												
DIAB-EME (BED)	x	x	x	x	x	x	x			x		x
NEPH (ICCS / USAAR)												

The above table shows the link between the use cases presented in D7.1 and HECD. All the use cases in D7.1 will be demonstrated through the 4 HECDs.

Template for information collection of the HECDs.

1. **Introduction**
   Please introduce the background of your high-end clinical mock-up and its potential impact.

2. **Mock up descriptions**
   Please describe your mock up in terms of
   a) *objectives*
   b) *targeted end-users*
   c) *Functionalities (i.e. what does your mock do)*
   d) *Data involved(e.g. synthetic data or real data. For real data, who/how to collect them; for synthetic data,*
   e) *Added value of MHA (e.g. explain why the MHA platform is needed)*

3. **Design & components**
   Please use diagrams and text to describe the components of your mock-up and their relationships with the architectural components in the MHA platform (Note, the architectural components can be found in D3.2 under the Functional View section between page 23-50).

4. **Implementation**
   Please provide implementation details in terms of
   a) *a number of implementation stages*

b) milestones associated to each implementation stage

c) a Gantt chart of the implementation

Milestones	Year 1												Year 2												Year 3											
	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
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M2																																				
Task 3																																				
M3.1																																				
M3.2																																				
Task 4																																				
M4.1																																				
M4.2																																				

5. Evaluation

Please provide the evaluation scheme in terms of

a) evaluation targets (i.e. what the evaluation aim at)

b) the participants (i.e. who will do the evaluation)

c) the activities (e.g. survey, focus groups, or interviews)

d) data analysis (i.e. what evaluation data will be collected & how to process the data)

3 High End Clinical Demos (HECD)

3.1 Diabetes and Emergency Demo (DIAB-EME)

High end clinical demo (HECD): DIAB-EME

	UAC	3DS	DB	VC	DCU	TOOL	HIS	CHF	OST	DIAB	NEPH	EME
CHF(FORTH)												
OST(FORTH)												
DIAB-EME (BED)	x	x	x	x	x	x	x			x		x
NEPH (ICCS / USAAR)												

Table 2 Use cases (column) vs DIAB-EME

Demonstration for the pre-diabetes and emergency contact

1. Introduction

Diabetes is the world's fastest growing disease. The personal, social and economic costs of the diabetes epidemic are substantial. It is a major cause of cardiovascular disease; the most common reason for commencing renal dialysis; the most common cause of blindness in people under the age of 60 years; the most common cause of non-traumatic lower-limb amputation; and one of the most common chronic diseases in children – to name but a few. Type 2 diabetes in particular is a serious and growing health problem affecting all sectors of the population, and accounts for approximately 85 % of diagnosed cases.

Prediabetes, also commonly referred to as borderline diabetes, is a metabolic condition and growing global problem that is closely tied to obesity [3]. Prediabetes referred to the person's blood glucose, or blood sugar, levels that are higher than normal but not high enough to be diagnosed as diabetes. [4] People are more likely to develop type 2 diabetes if they have prediabetes , heart disease, and stroke. It is estimated to affect more than 32 million EU citizens (nearly 10% of the total EU population), an additional 32 million citizens have not yet been diagnosed, or with pre-diabetes[5].

Cases of prediabetes that are identified early on can be reversed, and therefore preventing them from progressing into full-blown type 2 diabetes. Each year in the UK, 5% to 10% of people diagnosed with prediabetes go on to develop type 2 diabetes [6]. The two principle actions that can be taken to prevent developing of type 2 diabetes from prediabetes are:

- Making changes to your diet and
- Appropriate physical exercise to your lifestyle

While some risk factors such as age, race/ethnicity, gender, family history are not modifiable, patients do have control over their weight, unhealthy cholesterol levels, high blood pressure, smoking, sedentary lifestyle, unhealthy diet and high blood glucose level. These include a long-term

[3] http://www.diabetes.co.uk/pre-diabetes.html (November 2014)
[4] http://vsearch.nlm.nih.gov/vivisimo/cgi-bin/query-meta?v%3Aproject=medlineplus&query=pre+diabetes&x=12&y=10 (November 2014)
[5] International Diabetes Federation. IDF Diabetes Atlas, 4th ed. 2009, http://www.diabetesatlas.org/downloads (November 2014)

commitment of dietary change, exercise, regular self-medication, self-monitoring of blood glucose, regular attendance at clinic and for screening programmes.

However, these healthy behaviours are often NOT achieved in practice by prediabetic patients, despite their value being understood by both patients and medical professional. Studies show only 30% adults who have modifiable risk factors for diabetes have sufficient level of self-awareness. Nearly 80% of prediabetic patients think they are in “excellent” or “good” health, even though they don’t regularly implement good health habits. According to many healthcare professionals, the greatest barrier to treating the pre-diabetic patients is their non-compliance with lifestyle recommendations.

Self-management is described as the lifestyle and medication-taking patterns that people with diabetes engage in, in order to control diabetes and reduce the risk of complications. Evidence suggests that assisting prediabetic patients in self-management can result in significant gains in health status and reduced risk in progression to diabetes. Diabetes self-care is not a unitary concept but rather consists of several unrelated behaviours (e.g. remembering to take medication, reducing saturated fat intake, increasing physical activity, checking one’s feet and so on).

This demonstration (PDIAB-EME) will be designed for the long-term self-management of healthy citizens, especially for those at the risk of developing diabetes in near future, supporting increased role of patients in prediabetes care. The demonstration will utilise the MHA platform to support and empower patients.

MHA provides a unique platform that empowers normal citizens in terms of supporting their life management and healthy lifestyles. It offers a one-stop service for citizens in terms of data collection, and self-management services, such as monitor, record, and education. The system will support the storage of behaviours and daily activities of citizen. It will function as a supportive environment to empower normal citizens in looking after their own health, raising their self-awareness of any potential risk of developing diseases while encouraging their healthy lifestyles in terms of doing routine daily exercises, stopping smoking and controlling their diet. Therefore, naturally many existing functionalities in MHA can be directly used for the needs of pre-diabetic care. In addition, we will incorporate tailored services, such as diabetes risk assessment models for pre-diabetic care, which will be used by the users to understand their personal risk of developing diabetes, and the impact of their behaviour and lifestyles towards the risk.

Also, a known condition in diabetic patients is ‘passing out’ due to hypoglycaemia. In such cases (or due to another reason), if the patient is unconscious, the attending doctor would not be able to access the electronic health records which are necessary for proper diagnosis and treatment. This case will also demonstrate the value of the MHA platform in emergency cases where the patient could be unconscious, it is imperative that certain critical medical data and the next-of-kin of the patient are known to the attending doctor e.g., if the patient is in a foreign country. Key information such as known allergies to drugs, medications currently being taken, pregnancy status in females, past medical history, insulin resistance in pre-diabetes and the food or beverage recently consumed by the patient can help the doctor to more precisely plan the treatment. Though data access in the patient’s vital interests is permitted without consent, the patient is empowered by the

MyHeathAvatar platform to create his unique ID and link it to the next-of-kin and relevant medical data which can be fetched by the attending doctor. By this, MyHealthAvatar will fully respect the patient's self-determination.

2. Mock up descriptions

2.1 Objectives

The outcome of this demo is set to empower citizens by providing a supportive environment for the self-management of lifestyles for general health and wellbeing. Our particular focus will be cast on risk analysis for diabetes, enabling more effective pre-diabetic care in terms of risk reduction through improving compliance with healthy lifestyle recommendation. The demonstration will allow the users to play a key role in monitoring and managing their own health.

More specifically, we are aiming at the following objectives:

- Enriching the functionalities of the MHA platform in terms of enhancing user experiences in behaviour monitoring and facilitating their lifestyle management
- Incorporating verified risk assessment models for diabetes into the MHA platform
- Incorporating personal behaviour intervention modules that allow for planning and remaindering services for daily physical exercises, diet control and medication where necessary.
- A mobile app that allows for easy access to the platform via mobile devices.
- An emergency identification service, My Emergency Identifier, which will allow the attending doctor to identify the patient, using an appropriate way (e.g. his finger prints), in emergency cases where patient is not in a state to provide ID. The summarised information made available to the doctor in such cases will help improve management regimen and avoid any complications.

2.2 Targeted end-users

This demonstration will target healthy citizens to facilitate their self-management of lifestyles for general health and well-being, with a particular focus on the risk assessment for diabetes and lifestyle management for reducing the risk.

Also, synthetic patients will be used to demonstrate the scenario of emergency contact.

2.3 Functionalities

We define the prediabetes services provided by the MHA platform as the engagement of individuals, in activities and practices that sustain and promote health and well-being by:

- Assisting individual to carry out self-monitoring of their own health-status including daily activities
- Providing risk analysis for individual to monitor their personal risk of developing diabetes and analysis the impact of their behaviour to their risk
- (Optional) Providing target educational material to the individuals based on their conditions and lifestyle

More specifically, we will implement the functionalities as follows:

2..1 Enriching the functionalities of the MHA platform in terms of enhancing user experiences in behaviour monitoring and facilitating their lifestyle management. These will include:

- Monitoring: sensors and mobiles will be used to enable users to easily upload their own health data into the platform. This will include a wide range of data including their activities, movement, step accounts, diet and other health-related behaviours and events. We will allow the users to do this at any time, requiring them to take very simple actions such as press a single button.
- Personal Diary: Storage and management of the health status of the individual and their behaviours. This will rely on techniques of self-monitoring, which will monitor a wide range of daily activities and behaviours of the citizen/patient, including their locations, movements, diet, quality of life, environment, mood, blood pressure, glucose, alcohol, smoking, and other symptoms, etc. Visual analytics will be used to display individual/aggregated data items to allow easy interpretation of the data from the patients. With the search bar of the system, the users can easily send queries about their activities, movements, diet, etc.

2..2 Incorporating verified risk assessment models for diabetes into the MHA platform

- Risk assessment and warning: The system will allow for the progress review of the individual by comparing the personal diary with the behaviour prescription as men. The avatar system will send reminder messages at various priorities in one of the following occasions: medication reminder, due hospital visit (for screening etc.), sign of change of conditions, early sign of one of developing diabetes with constant scored as high risk.

2..3 Incorporating personal behaviour intervention modules that allow for planning and remaindering for daily physical exercise, diet and medication where necessary.

- Intervention: allowing for multi-modal intervention of lifestyle in a shared decision manner between the doctor and citizens/patients. In the case of pre-diabetes, MHA will be able to demonstrate to the citizens/patients the relations between the outcomes of the self-management/treatment using prediction models. . “Behaviour prescription” will be issued based on clinical guidelines and trusted sources (such as NICE), which is expected to include a set of targets in terms of daily activities, calorie intake and energy consumption, etc.
- (Optional) Education intervention: the life style intervention will be provided with relevant educational materials. The healthy life style for diabetes patients has been intensively researched. There are general recommendations available in terms of diet and life style[7], and other target recommendations for people at certain conditions, such as age and medication8. MHA will deliver these materials to the citizens in needs. For example, when the diary shows that individual did not reach the planned

[7] http://www.hopkinsmedicine.org/gim/core_resources/Patient%20Handouts/ (November 2014)

[8] Exercise and Type 2 Diabetes, joint position statement of ‘American College of Sports Medicines’ and American Diabetes Association

amount of exercise, the contents of the recommended weekly exercises will be delivered to the individual as a reminder.

2..4 A mobile app that allow for easy access to the platform via mobile devices.

- Mobile app: a mobile app will be built that will allow users to access the MHA platform, especially their personal health data in the MHA data repository from mobile devices such as smart phone. We can view the mobile app as a simple version of the web-based MHA platform, with a particular focus on easy data upload and easy data access through the mobile phones.

2..5 A service, called My Emergency Identifier, will be provided by MyHeathAvatar to grant limited access (snapshot view) to data of the patient in case the patient is passed out (unconscious). The attending doctor will use his own ID and the patient's finger print to generate a unique identifier. The MyHeathAvatar service will recognise this identifier and provide summarised information such as:

- past medical history, known allergies and sensitivity to drugs,
- insulin resistance in prediabetics,
- information of pregnancy in case of females e.g., if they are in first trimester and certain drugs are contraindicated,
- impaired glucose tolerance tests during gestational diabetes in females,
- medications being currently taken by the patient to prevent giving contraindicated medication,
- HBA1C results and fasting and random glucose levels,
- life style such as food and beverage intake history for the last 1-2 day which could help in identification of cases such as intoxication,
- Exercise history for the last 1-2 days (number of steps etc.) which can be useful in establishing decreased glucose levels, ketoacidosis etc.,
- Also, the contact information of next-of-kin whose consent might be legally required in case of relevant medical/surgical intervention.

2.4 Data involved

The demonstration will aim at two types of end-users. This will include:

- Healthy citizens who will the MHA platform for lifestyle management and risk assessment. A considerable number of participants will be recruited to test the platform and they will contribute a significant amount of data to the platform. The risk assessment model of diabetes will be applied to access their risk in developing diabetes, and behaviour intervention schemes will be adopted to help the users improve their compliance to healthy lifestyles.
- Synthetic (dummy) patients who are classified as pre-diabetic along with family history of diabetes. The timeline with show the progression of symptoms and the course of action MyHeathAvatar takes to alert the patient about being in the risk group who can develop type 2 diabetes. The timeline will show exercise routines, weight and glucose levels in the

form of a monthly graph along with behaviour intervention initiatives suggested to the patient for compliance to healthy lifestyle.

2.5 Added values of the MHA platform

MHA provides a unique platform that empowers normal citizens in terms of supporting their life management and healthy lifestyles. Whereas in the past, the so-called 'grey area' patients with prediabetes were not looked after by the health care system. As a citizen oriented platform, the MHA platform provides services to the general public that help them identify and mange their risk of developing diabetes. It is a perfect complement to the health care system. It offers a one-stop service for citizens in terms of data collection, and self-management services, such as monitor, record, and education. The system will support the storage the behaviours and daily activities of citizen. It will function as a supportive environment to empower normal citizens in looking after their own health, raising their self-awareness of any potential risk of developing diseases while encouraging their healthy lifestyles in terms of doing routine daily exercise, stopping smoking and controlling their diet. Therefore, naturally many existing functionalities in MHA can be directly used for the needs of pre-diabetic care. In addition, we will incorporate tailored services, such as diabetes risk assessment models for pre-diabetic care, which will be used by the users to understand their personal risk of developing diabetes, and the impact of their behaviour and lifestyles towards the risk.

In cases where the (unconscious) patient is unable to provide his identification information and the next-of-kin is not known, the attending doctor can request MyHeathAvatar to provide a limited access to the MyHeathAvatar records and fetch a summary of the data using patient's ID. Hence, MHA will provide the summarized medical information relevant to the treatment and also the next-of-kin information to get consent for any medical/surgical intervention that might be required.

3. Design & components

3.1 Overall design

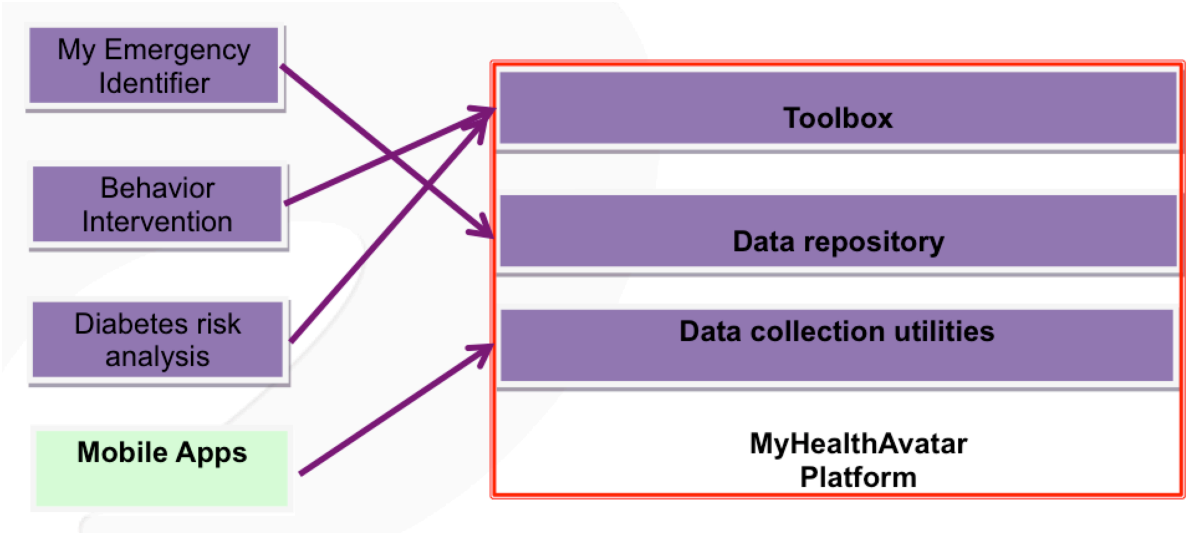

Figure 1. Implementation of PDIAB-EME(left) and the MHA Platform

Figure 1 is a diagram that shows the implementation of PDIAB-EME and its relationship with the MHA platform.

Notably, the implementation of the PDIAB-EME will be closely coupled with the implementation of the MHA platform. Many functionalities that will be utilised by the targeted end-users of PDIAB-EME will be implemented directly as inherent components of the platform, such as self-monitoring, emergency identifier and behaviour intervention.

Also, a verified risk assessment model for development diabetes (e.g. the model from the Framingham study) will be integrated into the system for raising users' self-awareness of their risk in diabetes.

In addition, the mobile app will be implemented as an extended user interface to allow the users for easy access to the functionalities of the platform, including the data repository and the toolboxes.

To allow access to the stored data in cases where the patient is unable to provide ID, e.g., unconscious patient, MHA will provide the service of identification of the patient, called My Emergency Contact. Such request will be raised by the attending doctor and the service in MHA will recognise it as a legitimate request by identifying the patient and doctor's ID. Upon successful identification, MHA will grant access to summarized data from the patient's stored records to the doctor. The exception reports and session log of such requests will be stored in MHA to maintain audit trail.

3.2 Technology components

Correspondingly, research and technologies will be developed to facilitate the self-management, self-monitoring of patients, to support patient empowerment and engagement, offering a supportive environment from the users patients by means of offering advice, agreement, assistance assessment and arrangement; and by means of allowing health promotion Specifically, these will include:

- Techniques for self-monitoring, which will facilitate the monitoring of the health status and a wide range of daily activities and behaviours of the patients, including their location movements, diet, quality of life, environment, mood, blood pressure, glucose, alcohol, smoking, and other symptoms, etc.
- Visual analytics techniques that allow for easy data browsing and self behaviour review from the users, including:
    - Dashboard, which presents a summarisation of personal health status in graphs.
    - Patient Diary, which will support the viewing of the health status of the patients and their behaviours on daily basis.
    - Timeline, which will display health events along the timeline at different scales.
- Risk assessment: Risk assessment: Assess risk of the users in developing diabetes according to their information and behaviour data. Where necessary, alerts will be issued to ask the users to check their health with doctors.

- Behaviour intervention: This will support behaviour intervention of lifestyle including (but not limited to) physical exercise, diet, weight watching in a self-monitoring manner. The "behaviour prescription" will be advised to plan lifestyle targets, such as daily minutes of active minutes, step counts, calories intake. We will allow for progress review of the users by comparing their data with the behaviour prescription. Reminder services will be provided to the users aiming at increase their compliance to the behaviour prescriptions. This can also be (optionally) extended to many of the following occasions: medication reminder, due hospital visit (for screening etc.), sign of change of conditions, early sign of one of the diabetic complications.
- ID of the patient (such as finger print), will be stored in MHA and used to access data in case the patient is not able to provide login and password. A known condition in diabetic patients is 'passing out' due to hypoglycaemia. In such cases (or due to another reason), if the patient is unconscious, the attending doctor would not be able to access the electronic health records which are necessary for proper diagnosis and treatment. To circumvent any such problems, ID information, is stored in the MHA and the attending doctor can request for data using the ID of the patient.

3.3 Architectural support

This case is related to the following MHA architecture components

- MHA portal
- User management and consent
- Data repository
- Semantics repository
- Tool/Model repository
- Data collection utilities
- (Optional) link to hospital system

4. Implementation

4.1 Tasks and milestones

The tasks and milestones of this demonstration will include:

Task 1: Integration of a verified diabetes risk assessment model

M1: The MHA platform with diabetes risk assessment model included

Task 2: Implementation of the behaviour intervention model

M2: The MHA platform with behaviour intervention module included

Task 3: Development of MHA app

M3.1: MHA app v1

M3.2: MHA app v2

Task 4: Synthetic patient generation & emergency case demonstration

M4.1: The synthetic patient generated

M4.2: A virtual emergency case demonstrated

4.2 Gantt chart

The implementation Gantt chart is shown in the following diagram:

Milestones	Year 1												Year 2												Year 3											
	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
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Task 4																																				
M4.1																																				
M4.2																																				

5. Evaluation

5.1 Participants recruitment

We will carry out evaluation activities by exposing the system to its end-users through their experience gained through their experiments with the mock-ups. The validation of the developed demonstration will be done through a set of volunteers. The evaluations on the technical components will be done via the technical development team, and via the participants of the project.

The participants will be recruited in many different ways. We will seek to maximise patient variation and responses generated by including people from different ages, genders, geographical locations, disease duration and ethnic groups. These will include

- Normal citizens from the MHA consortium
- Students from the participated universities
- Normal citizens from linked projects, such as MyLifeHub, Carrer,
- Other volunteers
- Medical professionals from the MHA consortium
- Medical professionals from linked projects, such as MyLifeHub, Carrer,

5.2 Evaluation activities

The evaluation activities will include:

- Survey: this involves a set of written questionnaires to a sample population of users. The surveys will be carried out to the general public, to Group D, Group A for a few rounds;

- Focus group: this will bring together a cross-section of stakeholders in a discussion group format for a few rounds. Each participant can act to stimulate ideas in the other people present;
- Interview: this will be used to gain information about user needs in a semi-structured manner;
- Workshop: this is a way to help the multiple stakeholders understand the system design process and hence to deeply involve the end-users in the system development. The presentations and face-to-face discussions in the workshops allow good communications between the end-users and the system designer, leading to the forming of partnership for co-design.

5.3 Evaluation outcome analysis

We will analyse the information gathered in Section 5.2 on real patients.

- User feedback analysis: This will analyse the strength and weakness of the system by looking into the feedback from the participants.
- User behaviour analysis: This will analyse the user behaviours captured through the MHA platform, which will provide valuable first-hand information of user requirements.
- Conclusions: This will put together the outcome from the above analysis to draw conclusions on the evaluation outcomes.

For the synthetic patient, a synthetic scenario will be forged in which the patient falls into unconscious. Diagrams will be used to show the workflow of the treatment under the emergency situation. The demonstration will show the process with respect to how the patient ID is used to retrieve the key patient information summary.

3.2 Personalized CHF Related Risk Profiles and "Real-Time Monitoring" Demo (CHF)

High end clinical demo (HECD): CHF

	UAC	3DS	DB	VC	DCU	TOOL	HIS	CHF	OST	DIAB	NEPH	EME
CHF(FORTH)	x		x	x	x	x	x	x				
OST(FORTH)												
DIAB-EME (BED)												
NEPH (ICCS / USAAR)												

Table 3 Use cases (column) vs CHF

Demonstration for the Personalized CHF Related Risk Profiles and "Real-Time Monitoring" (CHF)

1. Introduction

A major challenge related to caring for patients with chronic conditions is the early detection of exacerbations of the disease that may be of great significance. In this use case and demonstration scenario we focus on methodologies that would facilitate the prevention, monitoring, and treatment of heart disease on a daily basis. Heart failure is caused by any condition, which reduces the efficiency of the myocardium, or heart muscle, through damage or overloading. As such, it can be caused by a diverse array of conditions, including myocardial infarction (in which the heart muscle is starved of oxygen and dies), hypertension (which increases the force of contraction needed to pump blood) and amyloidosis (in which protein is deposited in the heart muscle, causing it to stiffen). The major precursor of all cardiovascular diseases is attributed in congenital or acquired factors that lead to atherosclerosis disorders and in some cases to complications from diabetes, kidney disease and hypercholasterolaemia. There are many cases where more than one medications are prescribed due to disease progression or due to the wide appearance of both cardiac and non-cardiac co-morbidities (respiratory comorbidities, renal dysfunction, cognitive dysfunction, depression and in some cases arthritis). To this respect, there is an urgent need for providing information in both the treating physicians, but also the patient him/ herself regarding negative drug interactions.

Congestive heart failure (CHF) is a state in which the heart cannot provide sufficient cardiac output to satisfy the metabolic needs of the body. It is commonly termed congestive heart failure (CHF) since symptoms of increase venous pressure are often prominent. Its pathogeneis factors include: Age, Gender, Increased blood pressure, Smoking, Alcohol, Family and medical history, Genetic predisposition, Diabetes, Diet habits and Atherosclerosis. It's a pathophysiologic state in which the heart, via an abnormality of cardiac function (detectable or not), fails to pump blood at a rate commensurate with the requirements of the metabolizing tissues or is able to do so only with an elevated diastolic filling pressure.

- Common causes:
  - Coronary heart disease
  - Hypertension
  - Valvular heart disease

- General symptoms:
  - Shortness of breath
  - Leg swelling
  - Exercise intolerance
- Diagnosis:
  - Physical examination : *blood tests, blood pressure, body mass index, etc.*
  - Echocardiography
- Management:
  - Improving symptoms
  - Preventing disease progression,
  - Modulation of lifestyle (*Diet, smoking, alcohol, moderate physical activity*), Pharmacological intervention

2. Mock up descriptions

Generally, cardiovascular disorders as chronic diseases require a continuous everyday record for patient's status. The proposed scenario is built on the following two main pillars:

1) CHF Risk Assessment

In order to tailor the proposed system to the patient's profile and assist physicians in selecting people who are predisposed by coronary disease, hypertension, or valvular heart disease; we build a CHF related risk profile based on a risk appraisal function that is based on the diagnostic criteria [i.e. the Framingham Heart Study (486 heart failure cases during 38 years of follow-up)]. The predictors used are based on Age, Coronary heart disease and Valve disease status provided by the patient Electronic Health Record (EHR), as well as on HR, on blood pressure and on Body Mass Index (BMI) provided by the pulse oximeter, the blood pressure monitor and the weight scale, respectively. The calculated risk probability may be used to alter the default threshold values (higher risk probability adds more constraint on the physiological patterns). Furthermore, we present what else data regarding patients' health status could be embed into the platform towards the creation of a profile with necessary information for both patient and treating physicians. To this respect an approach of presenting data regarding demographic, physiology, diagnostic test results and disease management (i.e. prescribed drugs) is provided.

2) Real-time patient monitoring

In addition to the above the dedicated clinical personnel should be contacted immediately and possibly intervene in time before an acute state is reached, by changing medication, or any other interventions, in order to ensure patient safety. There is a need to support real-time remote monitoring of patients diagnosed with congestive heart failure and MHA, enhanced with semantic technologies, may host personalized, accurate and up-to-date clinical information. To this end we built a real-time patient/ doctor alarming will be built according to rule-based alarms enabling intelligent alerting of the dedicated physician in case of an emergency. The alarming process will be based on vital signs monitoring and specifically Heart Rate (HR), Pulse Oximetry, and Blood Pressure

acquisition, adapted according each specific patient's medical history and age, and even risk predictor's outcome.

2.1 Objectives

The outcome of this use case in to create a demonstration service able to empower citizens, patients and doctors by providing a supportive environment for the self-management of patients/citizens with cardiovascular disease risks.

We aim at the following objectives:

- Incorporating verified risk assessment models for cardiovascular diseases into the MHA platform
- Enhance and expand the functionalities of MHA platform in real time health monitoring and management
- Create a CHF Real Time mobile monitoring app to allow for easy access to the platform alarming will be built according to rule-based alarms enabling intelligent alerting of the dedicated physician in case of an emergency

2.2 Targeted end-users

This demonstration activity of MHA project targets healthy citizens/patients to facilitate their self-management CHF risk assessment for lifestyle management in order to reduce the foreseen risks and, close to it, targets the doctors that would be able to assess patient's health status. Synthetic (chimeric) patients will be used to demonstrate the CHF real time patient monitoring scenario.

2.3 Functionalities

1. CHF *"Real-time patient monitoring"* and the *"CHF Risk Assessment"* service

We define the "*CHF Real-time patient monitoring"* and the "*CHF Risk Assessment"* service provided by MHA platform in order to:

- Assist individualized out self-monitoring of their own health-status
- Provide risk analysis for personal risk monitoring for developing a cardiovascular related episode in the future
- (Optional) Provide comorbidities and drug interaction information in both the treating physicians, but also the patient him/ herself regarding negative drug interactions

More specifically, we will implement the functionalities give the following scenario flow:

a. Gathering all the necessary patient data
b. Creating MHA profile for this patient
c. Real-time patient data updates to detect possible deviations from normal values
d. Alarm Doctor for possible intervention
e. Alternative flows will be followed if patient data are not provided in full.

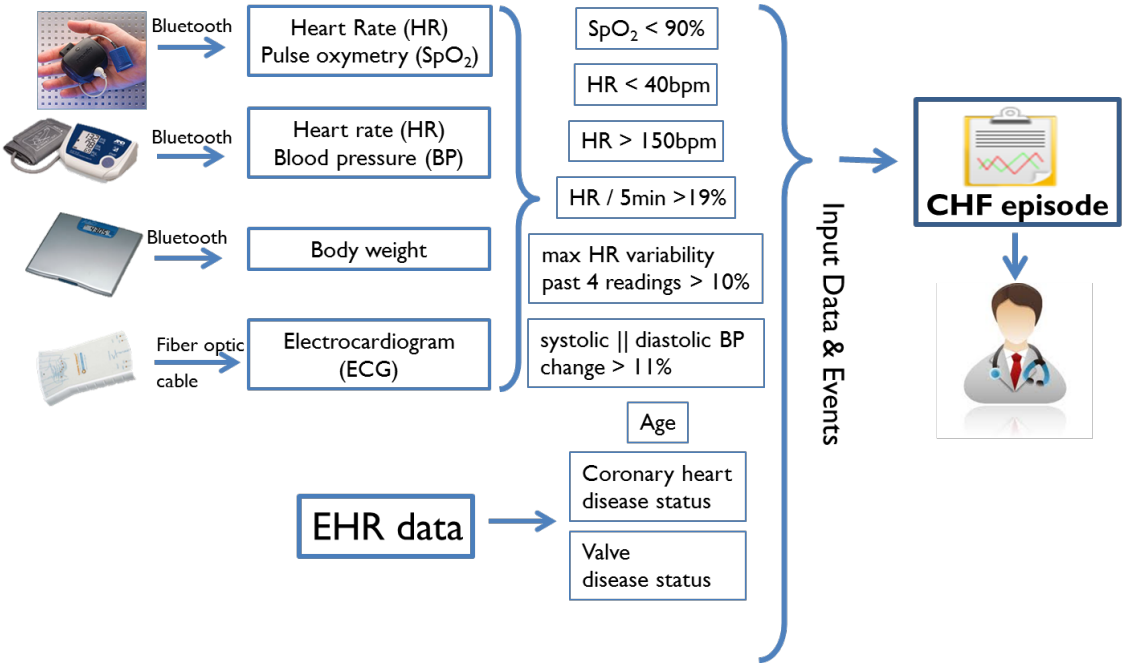


Figure 2. MHA CHF personalized real time monitoring and risk assessment

2. Expand MHA platform functionalities by creating an external monitoring specific tool for Personalized CHF risk assessment enhancing user experiences.

We use a number of medical devices such as Heart Rate, SpO2, ECG, Blood Pressure, medical sensors together with a mobile application and MHA's schematics layer in order to enable users' ability to easily upload their own health data into the platform and monitor their health status. The system is able also to use MHA link with external clinical information systems to acquire specific EHR patient related data.

- Upload patient's physiological and imaging data and past diagnosis in patient's electronic health record or during creation of patient's Avatar in MHA platform.
- Alternative the use case can be triggered after the condition is diagnosed by patient physical examination and confirmed with echocardiography.
- Remote monitoring of patient health status after diagnosis.
- Risk assessment and update data in MHA.
- Ontology-driven application intelligence capable of reasoning on the patient data.

3. Incorporating verified risk assessment models for CHF through MHA platform

We will build a CHF related risk profile based on a risk appraisal function that is based on specific diagnostic criteria [i.e. the Framingham Heart Study (486 heart failure cases during 38 years of follow-up)]. The predictors used are based on Age, Coronary heart disease and Valve disease status provided by the patient Electronic Health Record (EHR), as well as on HR, on blood pressure and on Body Mass Index (BMI) provided by the pulse oximeter, the blood pressure monitor and the weight scale, respectively. The calculated risk probability may be used to alter the default threshold values (higher risk probability adds more constraint on the physiological patterns). Furthermore, we present what else data regarding patients' health status could be embed into the platform towards the creation of a profile with necessary information for both patient and treating physicians. To this respect an approach of presenting data regarding demographic, physiology, diagnostic test results and disease management (i.e. prescribed drugs) is provided.

Figure 3. Framingham Heart Study

4. Comorbidities and Drug Interaction

There are many cases where more than one medications are prescribed due to disease progression or due to the wide appearance of both cardiac and non-cardiac co-morbidities (respiratory comorbidities, renal dysfunction, cognitive dysfunction, depression and in some cases arthritis). To this respect, there is an urgent need for providing information in both the treating physicians, but also the patient him/ herself regarding negative drug interactions.

5. A mobile app for easy access to the platform via smart phones, mobile devices and portable tablet computers.

The CHF risk management mobile app allows users to access MHA platform, especially their personal health data in the MHA data repository from mobile devices such as smart phone. The application is able to acquire data from medical sensors used by the user to gather biomedical data that can be used to assess if a CHF episode is eminent and to provide appropriate notification to the user. The application sends appropriate notification events to MHA platform with all CHF episodes detected.

2.4 Basic steps of interaction / scenario workflow

1. Generation of patient's avatar

- Register life style factors (i.e. diet habit, alcohol, smoking)
- Register of physiology, pathology, genetic information (i.e. pharmacogenomics) regarding patient's health
    - Age
    - Height
    - Weight
    - Body Mass Index(BMI)/Body Surface Area (BSA)
    - Blood pressure
    - Pulse (possible need for creating time graphs)
- Register life style factors (i.e. diet habit, alcohol, smoking physical activity)

2. Embed in Avatar platform of patient's examination results
    - Update of patient's basic examination outputs regarding cardiovascular system (blood test results, blood pressure, EEG results, imaging and physical exam)
3. Diagnosis of the heart failure and classification of patient according to one (or if possible more) categories (i.e. Framingham and or NYHA)
    - Matching of possible co-morbidities or setting alarms for possible complications due to disease progression (i.e. kidney function)
4. Record of patient's drug prescription (dose regiments) provided by the treating physician
5. Record of patient's compliance regarding provided treatment
    - Update avatar during last drug prescription for other diseases and alarm for possible interactions between medications (i.e. antibiotic medicines that could interact with cardiovascular treatments)
6. Real-time patient vital signs and data updates (if available) and processing to detect possible deviations from normal values

2.5 Data involved

The demonstration will aim at two types of end-users. This will include:

- Healthy citizens who will use MHA platform for CHF risk assessment management.
- Synthetic (dummy) patients with heart condition problems. MHA timeline with show the progression of symptoms and the course of action MHA takes to alert the patient about being in risk.

The Patient/citizen data that could be preferably involved are summarized below:

- Demographic
    - Gender
    - Age
    - Height
    - Weight
    - BMI/BSA
- Genetic
    - CHF related genome data
    - Pharmacogenomic data
- Physiology- Pathology

  - Blood pressure
  - Cardiac flow (BP and pulse)
  - Kidney function
  - Blood test results
  - Coagulation factors
  - Atherosclerosis level
- Clinical Data
  - Associated diseases
  - Physical examinations
  - Imaging
  - Electrocardiography
  - Echocardiogram
- Protocols/References regarding disease diagnosis/treatment
  - Available regimens for prescription and potential alternatives
  - Medline references
- Patients hand out from regulatory organizations for disease management

2.6 Added values of the MHA platform

MHA provides a unique platform that empowers normal citizens in terms of supporting their life management and healthy lifestyles. As a citizen oriented platform, the MHA platform provides services to the general public that help them identify and manage CHF related risks. It offers an easy to use service for citizens in terms of data collection, and real time self-management services, such as monitor, record, and alarm. The system will function as a supportive environment to empower citizens and patients in looking after their own health through self-awareness of potential risks of developing diseases. Therefore, many existing functionalities in MHA will be used for the needs of personalized CHF risk profile assessment and real-time monitoring.

3. Design & components

3.1 Overall design

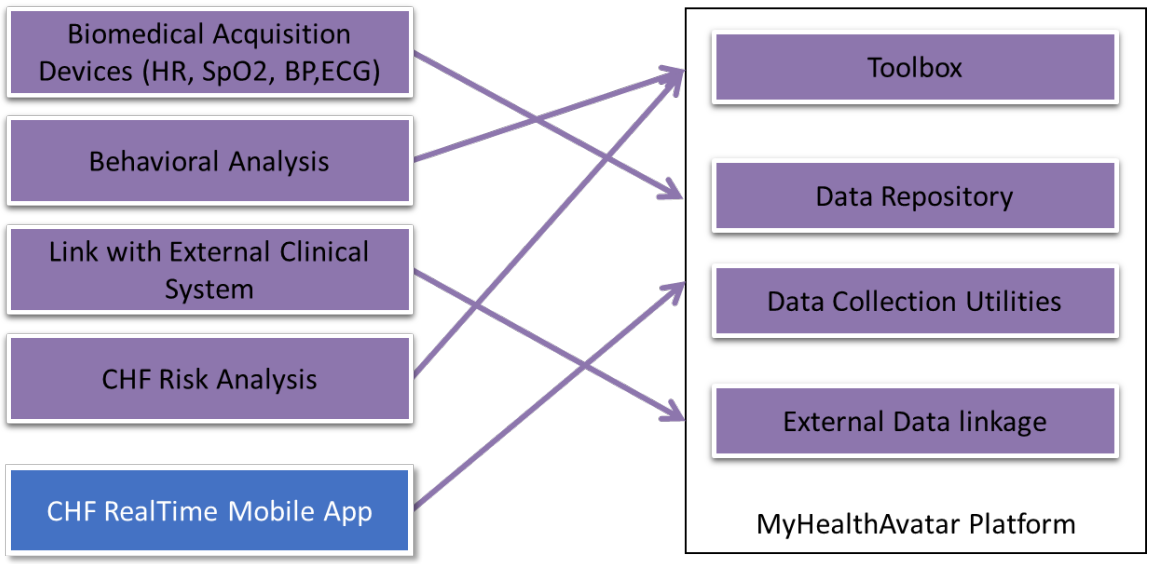


Figure 4. The diagram that shows the implementation of CHF Related Risk Profiles and "Real-Time Monitoring" and its relationship with the MHA platform

3.2 Technology components

Correspondingly, research and technologies will be developed to facilitate the self-management, self-monitoring of patients, to support patient empowerment and engagement, offering a supportive environment from the user's patients by means of offering advice, agreement, assistance assessment and arrangement; and by means of allowing health promotion. More specifically, these will include:

- Real time CHF self-monitoring and alarm, which will facilitate the biomedical monitoring of the health indicators and biometrics collected by a number of medical devices and a wide range of daily activities and behaviours of the patients, including their location movements, diet, quality of life, environment, mood, blood pressure, heart rate, SpO2, ECG, alcohol, smoking, and other, etc.
- Visual analytics techniques that allow for easy data browsing and self-behaviour review from the users, including:
    - Dashboard, which presents a summarisation of personal health status in graphs.
    - Timeline, which will display health events and issued alarms along the timeline at different scales.
- Risk assessment of the users based on CHF related risk profiles and a risk appraisal function that is based on the diagnostic criteria [i.e. the Framingham Heart Study (486 heart failure cases during 38 years of follow-up)]. Where necessary, alerts will be issued to ask the users to check their health with doctors.
- Comorbidities and Drug Interaction: there is a need for providing information in both the treating physicians, especially in case of a chronic condition, but also the patient him/ herself regarding negative drug interactions.

3.3 Architectural support

This case is related to the following MHA architecture components:

- MHA portal
- User management and consent
- Data repository
- External link to Electronic Health Records, Clinical Information Hospital system repository
- Semantics layer/repository, data extraction and data query translation
- Tool/Model repository
- Data collection utilities

4. Implementation

4.1 Tasks and milestones

The tasks and milestones of this demonstration will include:

Task 1: Implementation and integration of a verified CHF risk assessment model with MHA platform

M1: MHA platform with CHF risk assessment model included

Task 2: Link with external hospital systems

M2: MHA platform with link to external hospital system module included

Task 3: Development of MHA CHF services/mobile apps

M3.1: MHA mobile app v1 (prototype)

a) CHF real time monitoring and alarm

b) CHF Risk Assessment mobile app

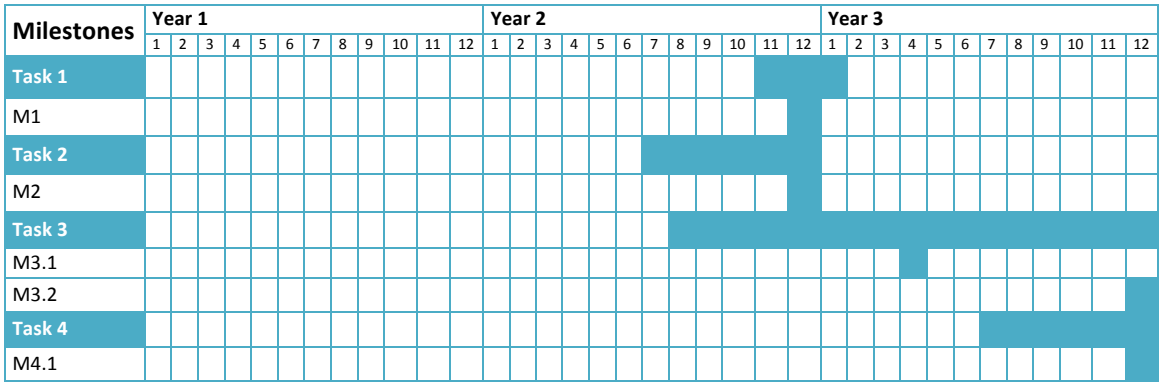
M3.2: MHA CHF mobile app (final/verification)

Task 4: Synthetic patient generation & demonstration

M4: The synthetic patient generated / CHF

4.2 Gantt chart

The implementation Gantt chart is shown in the following diagram:



5. Evaluation

5.1 Participants recruitment

The validation of the developed demonstration use case will be done through a set of volunteers. The evaluations on the technical components will be done via the technical development team and the technical manager, and via the participants of the project. The participants will be recruited in many different ways. We will seek to maximise patient variation and responses generated by including people from different ages, genders, geographical locations, disease duration and ethnic groups. These will include:

- Normal citizens from the MHA consortium
- Students from the participated universities
- Other volunteers

- Medical professionals from the MHA consortium
- Medical professionals from the university hospital of Heraklion
- Other volunteers

5.2 Evaluation activities

The evaluation activities will include:

- Survey: this involves a set of written questionnaires to a sample population of users.
- Focus group: this will bring together a cross-section of stakeholders in a discussion group format for a few rounds. Each participant can act to stimulate ideas in the other people present;
- Interview: this will be used to gain information about user needs in a semi-structured manner;
- Workshop: this is a way to help the multiple stakeholders understand the system design process and hence to deeply involve the end-users in the system development. The presentations and face-to-face discussions in the workshops allow good communications between the end-users and the system designer, leading to the forming of partnership for co-design.

5.3 Evaluation outcome analysis

We will analyse the information gathered in Section 5.2 on patients.

- User feedback analysis: This will analyse the strength and weakness of the system by looking into the feedback from the participants.
- User real time monitoring analysis: This will analyse the captured data through the MHA platform, which will provide valuable first-hand information of user requirements.
- Conclusions: This will put together the outcome from the above analysis to draw conclusions on the evaluation outcomes.

3.3 Osteoarthritis Demo (OST)

High end clinical demo (HECD): OST

	UAC	3DS	DB	VC	DCU	TOOL	HIS	CHF	OST	DIAB	NEPH	EME
CHF(FORTH)												
OST(FORTH)	x	x	x	x	x	x	x		x			
DIAB-EME (BED)												
NEPH (ICCS / USAAR)												

Table 4 Use cases (column) vs OST

Demonstration for the Osteoarthritis

1. Introduction

Osteoarthritis (OA) is a disabling degenerative joint condition leading to joint pain, stiffness and loss of function predominantly in the knees, hips, hands, and spine. The major histological finding in osteoarthritis is degeneration and loss of the articular cartilage that acts as a protective cushion between bones within a joint. An estimated 75% of adults over the age of 65 years have osteoarthritis resulting to impaired quality of life, and considerable healthcare costs. Moreover, about 100% of adults over the age of 80 years old have osteoarthritis.

Factors that may increase the risk of osteoarthritis include:

- *Older age*. The risk of osteoarthritis increases with age.
- *Sex*. Women are more likely to develop osteoarthritis, though it isn't clear why.
- *Obesity*. Carrying extra body weight contributes to osteoarthritis in several ways. It puts added stress on weight-bearing joints, such as your hips and knees. In addition, fat tissue produces proteins that may cause harmful inflammation in and around your joints.
- *Joint injuries*. Injuries, such as those that occur when playing sports or from an accident, may increase the risk of osteoarthritis.
- *Certain occupations*. If your job includes tasks that place repetitive stress on a particular joint, that joint may eventually develop osteoarthritis.
- *Genetics*. Some people inherit a tendency to develop osteoarthritis.
- *Bone deformities*. Some people are born with malformed joints or defective cartilage, which can increase the risk of osteoarthritis.
- *Other diseases*. Having diabetes or other rheumatic diseases such as gout and rheumatoid arthritis can increase your risk of osteoarthritis.

Osteoarthritis often gradually worsens, and no cure exists. Although, there is no cure, patients/citizens can manage this chronic condition with the medical professionals' help. The principal action that can be taken in order to slow down the progression of the condition and help το improve pain and joint function is to adopt a healthier lifestyle, i.e. follow a balanced diet combined with a good balance of rest and activity each day. Exercise, in conjunction with medication/supplements, can reduce the pain of arthritis and improve patients' overall condition. However, these healthy behaviours are not achieved in practice by patients, despite their value understood by both patients and medical professional. Moreover, medical professionals cannot usually ascertain if the patients follow the guidelines for a healthier lifestyle defined by them, parameters that would be helpful for better follow-up. This demonstration will be designed for empower both doctors and citizens (patients and healthy with high risk of developing osteoarthritis) for the long-term management of osteoarthritis condition utilizing the MHA platform.

MHA offers a one-stop service for citizens for data collection and self-management such as monitor, record and education. Precisely, the system will support the storage of behaviours and daily activities of citizen. It will function as a supportive environment to empower normal citizens in looking after their own health, raising their self-awareness of any potential risk of developing diseases while encouraging their healthy lifestyles in terms of doing routine daily exercises, stopping smoking and controlling their diet. Therefore, naturally many existing functionalities in MHA can be

directly used for the needs of osteoarthritis use case. In addition, we will incorporate genetic predisposition evaluation services for examining if an increased risk of developing osteoarthritis exists, which will be used by the citizens in order to understand their personal risk of developing osteoarthritis, and the impact of their behaviour and lifestyles towards the risk.

2. Mock up descriptions

2.1 Objectives

The objective of this demo is two-fold; to empower both patients/citizens and medical professionals by providing a supportive environment for the long-term management of osteoarthritis condition. Medical professionals (such as GPs) will be able to review together with patients a plethora of clinical and personal health information regarding the health status of patients/citizens through MHA platform. The related data (medical history, clinical examination, imaging data, evaluation metrics for measuring knee pain range of motion of the knee joint) will be properly visualized and presented using interactive multi-scale visualization techniques. This blend of medical imaging metrics and personal activity information, will give a better insight of the condition regarding OA diagnosis or progress and will allow the clinician to assess the situation in a more personalised fashion. In case where a GP is reviewing this information, it may also act as a baseline for better assessing if a referral to an expert is needed. In the suggested scenario, advanced personalized healthcare will also be enhanced by genomic predisposition evaluation for developing osteoarthritis. Although this might not be applicable at present, it is important to include it in the scenario in order to emphasise the vision on how MHA can really influence decision support in the future.

Patients/Citizens will be able to access a platform that will monitor their daily dietary and ambulatory activity and warn them, if they do not meet the recommendations that have been given to them (e.g. target activity, supplements etc.). Moreover, semi quantitative metrics, regarding knee pain and range of motion of the knee joint, will be collected periodically. The monitoring will rely on techniques of self-life logging for enhancing the patient engagement. Also, the platform will function as a supportive environment to the patients by means of offering advice and assistance. It is expected that a good knowledge of the condition will lead to enhanced patient behaviour. Thus, the demonstration will focus on how the users can play a key role in monitoring and managing their own health and become co-producers of their OA health management together with their GP.

2.2 Targeted end-users

This demonstration will target medical professionals, patients and healthy citizens with high risk of developing osteoarthritis in order to provide a complete, long-term management of the condition through lifestyle monitoring. Focus will also be on the genomic predisposition evaluation for developing osteoarthritis and lifestyle management for reducing the risk.

2.3 Functionalities

The functionalities that will be implemented in terms of the osteoarthritis use-case are:

1 A visualization toolbox providing proper interactive, multi-scale visualization techniques of the data related to osteoarthritis disease (e.g., medical history, clinical examination, imaging data, evaluation metrics). These techniques will offer a useful input to medical professionals in order

to carry out personalized medicine and for better follow-up. Visual analytics will also be used to display aggregated lifestyle data aiming to easy interpretation by both citizens (patients and healthy) and medical professionals.

2 For the needs of the osteoarthritis use case, we are going to use already the following existing functionalities in MHA platform.

2.1 Data collection: The users will be able to easily upload their own health data (e.g. activities, movements, step counts, diet etc.) into the platform using their mobiles. Part of this data are also related and will be used by the osteoarthritis use case (e.g. activities, movements, diet). Evaluation metrics, strongly related with the osteoarthritis condition, will also be collected periodically. These metrics include a number with regard to a certain pain-scale and a number with regard to the range of motion of knee joint (in degrees).

2.2 Personal Diary: This diary presents and manage the patients/citizens' health status and behaviours, including diet, movement, environment, mood, smoking, symptoms etc. Visual analytics will be used in order to display individual or aggregated data for easy interpretation from the patients/citizens. The personal diary will be used by the self-care module described below.

3 The MHA platform will incorporate personal self-care module that allow planning and reminding for daily physical exercises, diet and medication where necessary.

3.1 After clinical examination and diagnosis, the patient is guided properly by the medical professional. These guidelines include a set of targets in terms of daily activities, dietary etc., which are also valid for the healthy citizens with a high risk of developing osteoarthritis. Osteoarthritis service will review the progress of the patient/citizen by comparing the data originated from the patient diary module with the guidelines given to patient/citizen by the medical professional. If the patient/citizen did not manage to reach these special, periodic targets, a reminder service we warn the patient.

3.2 Education: The general recommendation for the osteoarthritis condition will be delivered to the patients/citizens in needs, as it is expected that a good knowledge of the condition will lead to enhanced patient behaviours.

4 MHA will incorporate genomic predisposition evaluation for estimating the risk of developing osteoarthritis for a patient/citizen. When a high risk of developing osteoarthritis is revealed for a healthy patient, he will be informed and guided for modifying and adopting a healthier lifestyle.

2.4 Data involved

The demonstration will aim at two types of end-users:

- Multi-level chimeric Patient information with osteoarthritis will be used in order to demonstrate the scenario in a case (e.g. progression of OA symptoms), and the course of actions that it will be taken for the health management. All this data in the platform will be used to highlight the necessary interplay of personal health information (e.g. activity, nutrition) to the medical imaging metrics. Self-care schemes will be adopted to help users improve their compliance to a healthy lifestyle.
- Healthy citizens with high risk of developing osteoarthritis in order to show the sequence of actions that will be taken in order to alert the citizen about being in the risk group and the course of actions for health management. Behaviour intervention schemes will be suggested to the citizen for compliance to healthy lifestyle.

2.5 Added values of the MHA platform

MHA provides a novel platform that empowers both citizens (patients and healthy) and medical professionals for the long-term management of OA. It will function as a supportive environment to empower citizens in looking after their own health, raising their self-awareness of any potential risk of developing OA while encouraging their healthy lifestyles in terms of doing routine daily exercise and controlling their diet according to the clinical recommendation (e.g. in cases of high risk of developing OA the clinician might suggest mild exercise and Calcium, vitamin D supplements). It offers a one-stop service for citizens in terms of data collection and self-management services such as record, monitor and education. Citizens will be able to upload periodically their own health data, e.g. evaluation metrics, using mobile apps. The avatar system will also monitor patients' daily dietary and ambulatory activity and warn patients if they are not compliant with the guidelines issued by the medical professionals. The avatar system will also promote citizens' education on the knowledge of OA. It is expected that a good knowledge of the disease parameters will lead to consistent citizen behavior.

In addition, medical professionals will be provided by a useful input regarding the health status of patients/citizens as the related data will be properly visualized and presented using interactive multi-scale visualization techniques. This will be a novel, enhanced clinical decision support tool that will blend medical imaging information with personal health information such as activity and nutrition trends which allow a more holistic assessment of the citizen's status regarding OA. In essence, this will give a better insight of the condition and its progress for carrying out personalized medicine and for better follow-up. Advanced personalized healthcare will also be enhanced by genomic predisposition evaluation for developing osteoarthritis.

3. Design & components

3.1 Overall design

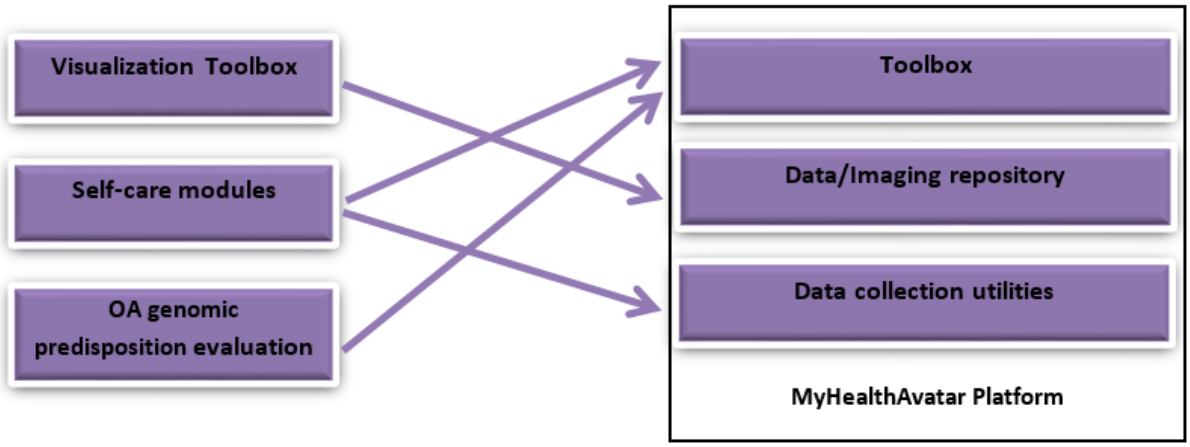


Figure 5. Implementation of Osteoarthritis case (left) and the MHA Platform

Figure 5 is a diagram that shows the implementation of the Osteoarthritis case and its relationship with the MHA platform. Figure 6 shows the interactions between MHA platform, external resources

and the users regarding the use case that was described (patient and GP reviewing the blended information for a more personalised assessment of OA risk or progression).

It should be stressed that the implementation of the scenario will be closely coupled with the implementation of the MHA platform. Many functionalities that will be utilised by the targeted end-users of the Osteoarthritis case will be implemented directly as inherent components of the platform.

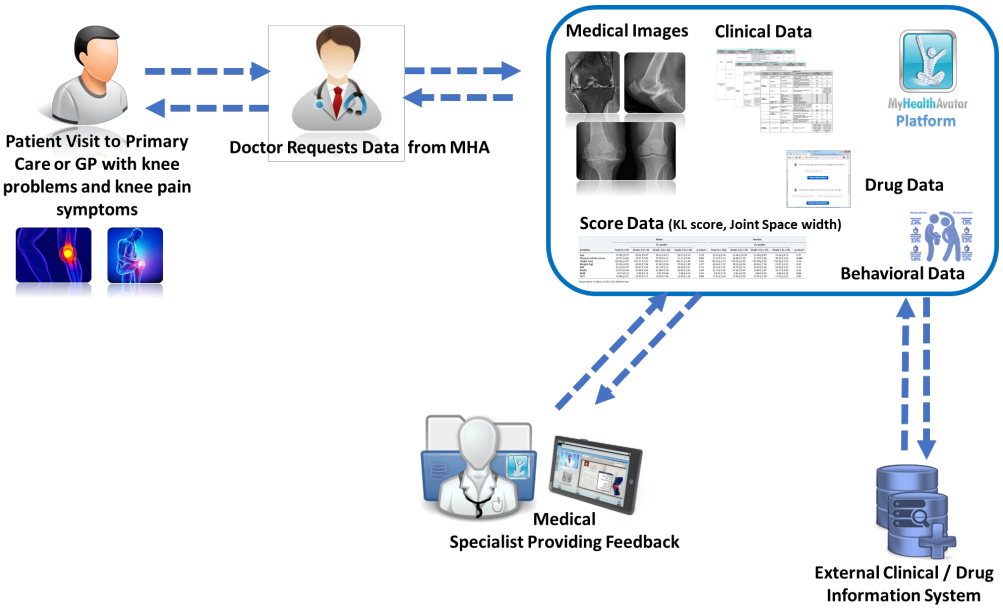


Figure 6. Osteoarthritis case (left) the link with MHA Platform

3.2 Technology components

In line with the scenario described, a number of R&D activities will be performed in order to facilitate the implementation of the functionalities described in detail in 2.3. For example, visual analytics for the representation and easy browsing of the osteoarthritis-related data to medical professionals, self-care module, genomic predisposition evaluation models for revealing high risk of developing osteoarthritis, reminder services aiming to increase users' compliance with the guidelines proposed by medical professionals.

3.3 This case is related to the following MHA architecture components:

- MHA portal
- User management and consent
- Data/ Imaging repository
- Semantics search/repository
- Tool repository
- Data collection utilities

4. Implementation

4.1 Tasks and milestones

The tasks and milestones of this demonstration will include:

Task 1: Implementation of the blended visualization toolbox

M1: Multi-scale visualization toolbox

Task 2: Implementation of the self-care module and genomic predisposition evaluation model integration

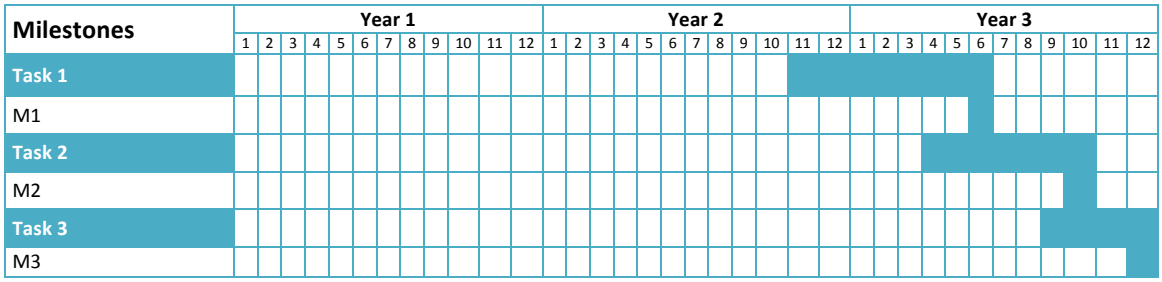
M2: The MHA platform with self-care module including osteoarthritis genomic predisposition

Task 3: Evaluation of the platform/scenario

M3: Platform evaluation / validation for demonstration

4.2 Gantt chart

The implementation Gantt chart is shown in the following diagram:



5. Evaluation

5.1 Participants recruitment

The evaluation of the developed platform will be done through a set of volunteers (FORTH is already actively trying to engage volunteers for this scenario). The evaluations on the technical components will be done via the technical development team, and via the participants of the project.

The participants will be recruited in many different ways. We will seek to maximise patient variation and responses generated by including people from different ages, genders, geographical locations, condition duration and ethnic groups. These will include:

- Normal citizens from the MHA consortium
- Individuals from the participated universities
- Normal citizens from linked projects, such as MyLifeHub, Carrer,
- Medical professionals from the MHA consortium
- Other volunteers

5.2 Evaluation activities

The evaluation activities will include:

- Survey: this involves a set of written questionnaires to a sample population of users.
- Focus group: this will bring together a cross-section of stakeholders in a discussion group format for a few rounds. Each participant can act to stimulate ideas in the other people present.
- Interview: this will be used to gain information about user needs in a semi-structured manner.
- Workshop: this is a way to help the multiple stakeholders understand the system design process and hence to deeply involve the end-users in the system development. The presentations and face-to-face discussions in the workshops allow good communications between the end-users and the system designer, leading to the forming of partnership for co-design.

5.3 Evaluation outcome analysis

We will analyse the information gathered in Section 5.2:

- User feedback analysis: This will analyse the strength and weakness of the system by looking into the feedback for the participants.
- User behaviour analysis: This will analyse the user behaviours captured through the MHA platform, which will provide valuable first-hand information of user requirements.
- Conclusions: This will put together the outcome from the above analysis to draw conclusions on the evaluation outcomes.

3.4 Nephroblastoma (Wilms Tumour) Simulation Model and Clinical Trial (UC-NEPH): In-silico Profiling of Patients and Predictions

High end clinical demo (HECD): UC-NEPH

	UAC	3DS	DB	VC	DCU	TOOL	HIS	CHF	OST	DIAB	NEPH	EME
CHF(FORTH)												
OST(FORTH)												
DIAB-EME (BED)												
NEPH (ICCS / USAAR)	x	x	x	x		x	x				x	

Table 5 Use cases (column) vs UC-NEPH

Demonstration for the UC-NEPH

1. Introduction

1.1 Nephroblastoma - Wilms Tumour

Wilms tumour is the most common malignant renal tumour in children. Dramatic improvements in survival have occurred over the last 40 years. Today treatments are based on several multicenter trials and studies conducted by the SIOP in Europe and COG in North America. The main objectives of these trials and studies are to treat patients according to well-defined risk groups in order to achieve the highest possible cure rates, to decrease the frequency and intensity of acute and late toxicities and to minimize the cost of therapy. In that way the SIOP trials and studies largely focus on the issue of preoperative therapy. The concept of neoadjuvant chemotherapy plays an important role in the treatment for most paediatric solid tumours today. The complete surgical removal of a shrunken tumour is facilitated, mutilation caused by surgical procedures is minimized or avoided and micrometastases, not visible at diagnosis, are treated as early as possible. Besides that, response to treatment can be measured individually by tumour volume reduction and / or percentage of therapy induced necrosis in the histological specimen.

The International Society of Paediatric Oncology (SIOP) enrolled children with Wilms tumour into 6 studies up to now (SIOP 1, SIOP 2, SIOP 5, SIOP 6, SIOP 9, SIOP 93-01). Graf et al give a review of these studies[9]. Since 1994 more than 2000 patients with a kidney tumour are enrolled in the SIOP / GPOH studies and trials. The 7th trial and study (SIOP 2001) started in 2002 (Figure 7). The randomized question of this trial was stopped in December 2009 after reaching the proposed number of patients. Results did show that anthracyclines are not needed to treat patients with stage II or III intermediate risk and localized nephroblastoma.

[9] Graf N, Tournade MF, de Kraker J: The Role of Preoperative Chemotherapy in the Management of Wilms Tumour - The SIOP Studies. Urologic Clinics of North America, 27:443-454, 2000

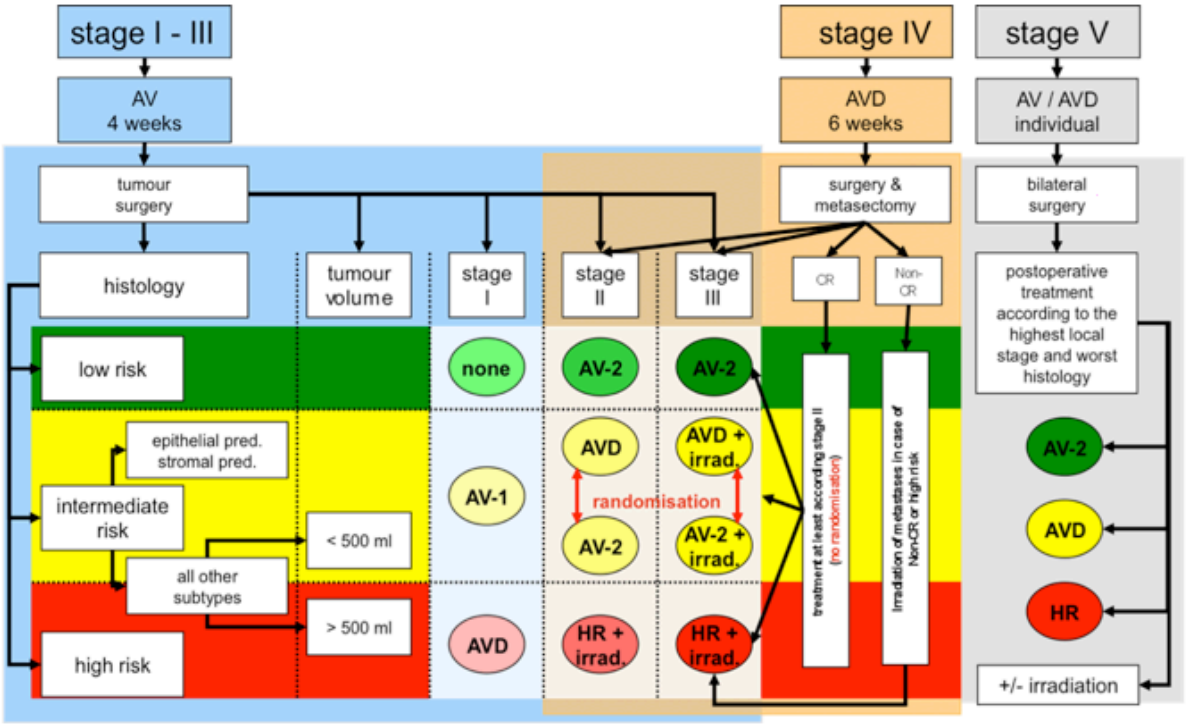


Figure 7. Outline of the nephroblastoma trial and study SIOP 2001/GPOH. CR: Chemotherapy. A: Actinomycin. V: Vincristine. D: Doxorubicin. 1,2: Different treatment schemas. HR: High Risk.

The main mission of the International Paediatric Oncology Society (SIOP) Renal Tumour Study Group (RTSG) is to increase survival and to reduce treatment toxicity in all children diagnosed with any renal tumour, aiming to offer them the same standardized high quality in diagnostics and treatment, independent of the tumour type, the socio-economic status or the geographic region.

Renal tumours include nephroblastoma or Wilms tumours (WT) in around 90% of the cases. The other tumours consist of rare subgroups including Clear Cell Sarcoma of the Kidney (CCSK), Renal Cell Carcinoma (RCC), Malignant Rhabdoid Tumours of the Kidney (MRTK), Congenital Mesoblastic Nephroma (CMN), and few others, even rarer tumours. This high-end scenario is dealing solely with nephroblastoma.

Given the relative rarity of paediatric renal tumours and in particular rare subgroups, it is necessary to recruit as many patients as possible. Over the last decades nearly 10.000 children are prospectively enrolled in SIOP Wilms Tumour studies and trials. Since SIOP 93-01 SIOP RTSG registered nearly 7.000 patients from 261 centres out of 28 countries with a renal tumour. All of them have been treated according to harmonised European trials. This has resulted in more standardised diagnostic procedures, improved risk stratification, and adjusted treatment recommendations for nephroblastoma.

The hallmark of the SIOP RTSG approach is the preoperative chemotherapy with Vincristine and Actinomycin-D without preceding mandatory histological assessment. This has the clear evidence-based benefit of down staging tumours, thereby sparing survivors the late effects of doxorubicin or

radiotherapy by around 20%[10]. Nevertheless, this approach carries the risk of misdiagnosis (< 5%), as currently the so-called non-Wilms tumours cannot be identified by standard radiology or biomarker assessment.

Although the overall and event-free survival of most renal tumours is excellent, further improvements are needed to find better risk stratifications and corresponding treatments, as some patients still have a poor clinical outcome despite intensive treatments. An example is the blastemal type nephroblastoma representing a subtype of post chemotherapy resistant blastema, which has already shown to benefit from intensive treatment in SIOP 2001. [11] [12] Nevertheless the definition of blastemal type WT is subjective and not taking the absolute blastemal volume into account. Therefore a better subtyping of WT and other renal tumours is mandatory. Such developments can only be achieved with the design of biological driven approaches.

The efforts made by the biology committee of the SIOP-RTSG allow now to set up a protocol for the whole spectrum of childhood renal tumours in Europe. In addition, the recent SIOP 2001 study has shown the importance of complete data collection, which will be guaranteed by real time online data collection in collaboration with the experienced data management of the international SIOP office in Amsterdam.

1.2 Nephroblastoma clinical trial management system (ObTiMA)

The current high-end scenario aims to provide a harmonised platform, which will test therapeutic preoperative approaches for nephroblastoma.

Data regarding radiology, histology, biological markers on blood and urine tests and genetic counselling will be recorded. In addition, the study aims to provide biomaterial for molecular and genetic research to find new biomarkers and targets for new compounds in the future. This will be done by storing and analysing biomaterial by a wide range of molecular and proteomic technologies from patients enrolled in the new nephroblastoma protocol and having given consent for this research. Together with radiological innovations this strategy will demonstrate early response to preoperative chemotherapy in ‘in silico’.

Data used in this high-end scenario will be managed with ObTiMA that is an ontology-based clinical trial management system. The design phase of a trial is facilitated by the Trial Builder of ObTiMA in which all aspects of a clinical trial can be specified: A trial chairman can define the outline and metadata of a trial in a master protocol to describe, e.g., trial goals or administrative data. The ontology-based creation of CRFs is one of ObTiMA major functionalities. A graphical user interface

[10] Mitchell, C., et al., Immediate nephrectomy versus preoperative chemotherapy in the management of non-metastatic Wilms' tumour: results of a randomised trial (UKW3) by the UK Children's Cancer Study Group. Eur J Cancer, 2006. 42(15): p. 2554-62.

[11] Vujanic, G.M., et al., Central pathology review in multicenter trials and studies: lessons from the nephroblastoma trials. Cancer, 2009. 115(9): p. 1977-83.

[12] Marry M. van den Heuvel-Eibrink, Harm van Tinteren, Christophe Bergeron, et al. Outcome of localised blastemal type Wilms tumour patients treated according to intensified treatment in the SIOP WT 2001 protocol, a report of the SIOP renal tumour study group (SIOP-RTSG). EJC submitted [Under revision]

allows defining content, navigation, and layout of CRFs to capture all patient data during a trial, e.g., medical findings or diagnostic data. Since many trials collect similar or equal data, it is possible to store components of or complete CRFs in a repository as templates. When setting-up a clinical trial, appropriate CRFs' template can either be directly reused or can be quickly created by composing them from existing CRF components. This in turn fosters the CRF standardization since CRFs can then readily be compared on the level of single items (through ontological concepts) and also on component level or in their entirety.

ObTiMA itself is composed of different modules and fulfils all GCP criteria, including an Audit Trail. Data safety and security are guaranteed as pseudonymization of private data is implemented according to roles and rights assigned to users of ObTiMA.

ObTiMA provides the following features

1. eCRFs
2. Access to biobanking
3. Access to a DICOM server
4. SAE and SUSAR reporting

The ObTiMA data are stored in a central database that is located in a militarized zone at the Saarland University Hospital to ensure data safety and data protection (Figure 8).

Via the Internet remote data entry is possible. To get access to ObTiMA and the eCRFs each participating centre needs to register for getting member of the SIOP-RTSG and the SIOP nephroblastoma study. After registration and signing a contract for participation in the UMBRELLA or any other study or trial credentials to use ObTiMA will be provided.

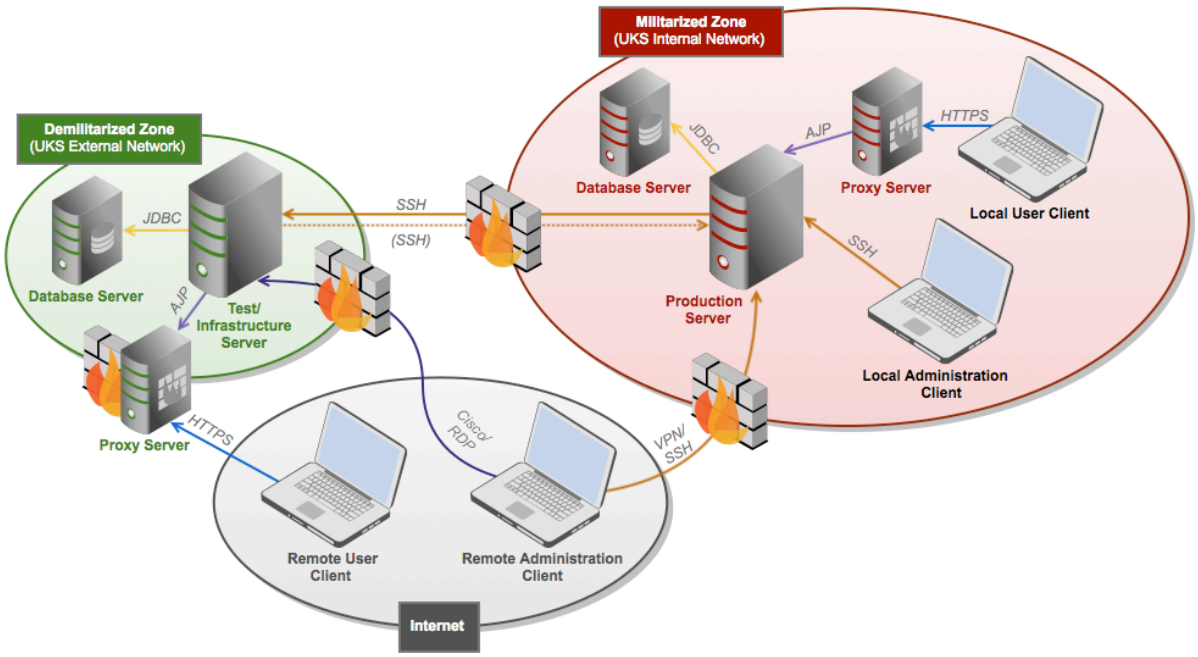


Figure 8. Infrastructure for ObTiMA

All data within ObTiMA will be encrypted and in addition personal data are pseudonymized. Only treating physicians can see real names and have only access to their patients.

1.3 Nephroblastoma Oncosimulator

The Oncosimulator for nephroblastoma is synoptically depicted in Figure 9.

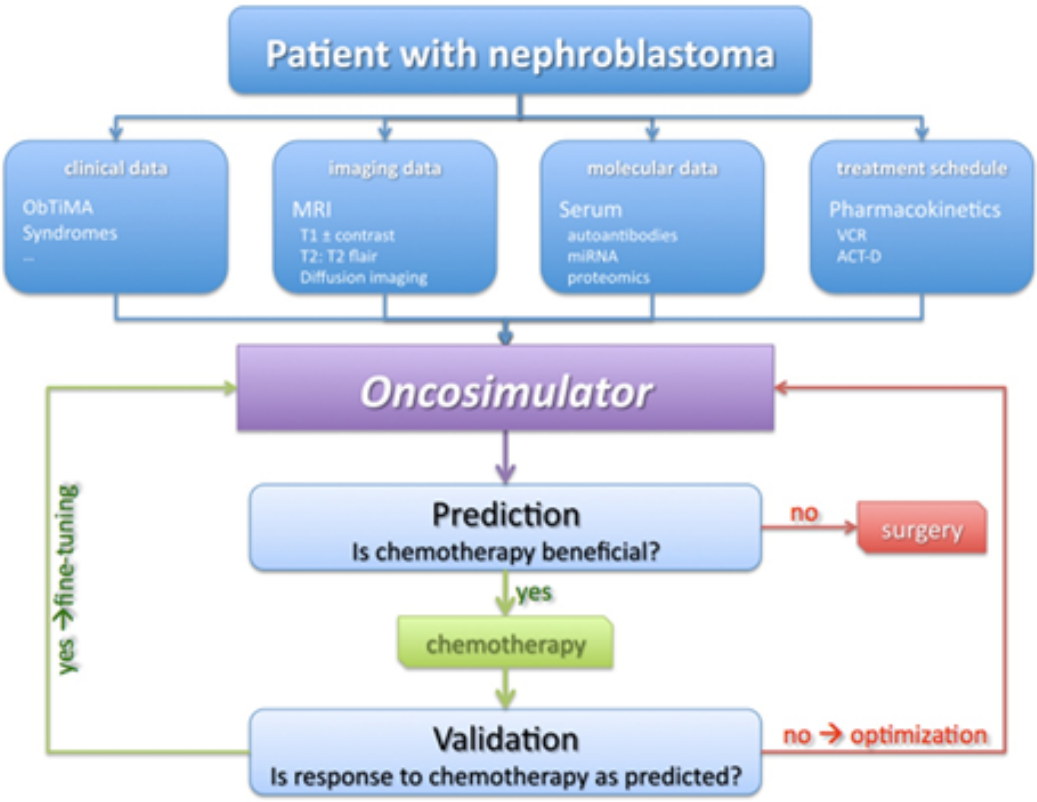


Figure 9. The workflow of the Oncosimulator for nephroblastoma

In this section a brief description of the basics of the Oncosimulator multiscale models is provided[13] . The models start from the macroscopic high biocomplexity level (imaging data) and proceed towards lower biocomplexity levels. The macroscopic anatomic region of interest is either manually or semi-automatically annotated by the clinicians on MRI imaging sets acquired at time of diagnosis. A virtual cubic mesh is used for the discretization of the area of interest (tumour) of which the elementary cube is termed geometrical cell. A hypermatrix i.e. a mathematical matrix of (matrices of (matrices…of (matrices or vectors or scalars))) corresponding to the anatomic region of interest is subsequently defined. The latter describes explicitly or implicitly the local biological, physical and

[13] G Stamatakos, Memeber , IEEE , D Dionysiou, A Lunzer, R Belleman, E Kolokotroni, E Georgiadi, M Erdt, J Pukacki, S Rueping, S Giatili, A d`Onofrio, S Sfakianakis, K Marias, Member , IEEE , C Desmedt, M Tsiknakis, Member , IEEE , and N Graf, Member , IEEE "The Technologically Integrated Oncosimulator: Combining Multiscale Cancer Modeling with Information Technology in the In Silico Oncology Context" DOI:10.1109/JBHI.2013.2284276 IEEE J Biomedical and Health Informatics vol.18, No. 3, pp.840-854 2014

chemical dynamics of the region. The following (sets of) parameters are used to identify a cluster of biological cells belonging to a given equivalence class within a geometrical cell of the mesh at a given time point:

I. The spatial coordinates of the discrete points of the discretization mesh with spatial indices i, j, k respectively. It is noted that each discrete spatial point lies at the center of a geometrical cell of the discretization mesh.

II. The temporal coordinate of the discrete time point with temporal index l.

III. The mitotic potential category (i.e. stem or progenitor or terminally differentiated) of the biological cells with mitotic potential category index m.

IV. The cell phase (within or out of the cell cycle) of the biological cells with cell phase index n. The following phases are considered: {G1, S, G2, M, G0, A, N, D}, where G1 denotes the G1 cell cycle phase; S denotes the DNA synthesis phase; G2 denotes the G2 cell cycle phase; M denotes mitosis; G0 denotes the quiescent (dormant) G0 phase; A denotes the apoptotic phase; N denotes the necrotic phase and D denotes the remnants of dead cells.

For the biological cells belonging to a given mitotic potential category AND residing in a given cell phase AND being accommodated within the geometrical cell whose center lies at a given spatial point AND being considered at a given time point; in other words for the biological cells clustered in the same equivalence class denoted by the index combination ijklmn, the following state parameters are provided:

i. local oxygen and nutrient provision level
ii. number of biological cells
iii. average time spent by the biological cells in the given phase,
iv. inumber of biological cells hit by treatment,
v. number of biological cells not hit by treatment.

The initial constitution of the tumour has to be estimated based on the available medical data through the application of pertinent algorithms. This state corresponds to the instant just before the start of the treatment course to be simulated. The entire simulation can be viewed as the periodic and sequential application of a number of algorithms (operators) on the hypermatrix of the anatomic region of interest which takes place in the following order: a) time updating i.e. increasing time by a time unit (e.g. 1h), b) estimation of the local oxygen and nutrient provision level. c) estimation of the effect of treatment referring mainly to cell hit by the treatment, cell killing and cell survival. Available molecular and/or histological information is integrated primarily at this point. d) application of cell cycling, possibly perturbed by treatment. Transition between mitotic potential cell categories such as transition of the offspring of a terminally divided progenitor cell into the terminally differentiated cell category is also tackled by this algorithm set. e) handling of differential tumour expansion/ shrinkage or more generally spatial geometry and tumour mechanical dynamics. f) updating the local oxygen and nutrient provision level at each time step. It is worth noting that stochastic perturbations about the mean values of several model parameters are considered

(hybridization with the Monte Carlo technique). A generic tumour cell cytokinetic model is depicted in Figure 10.

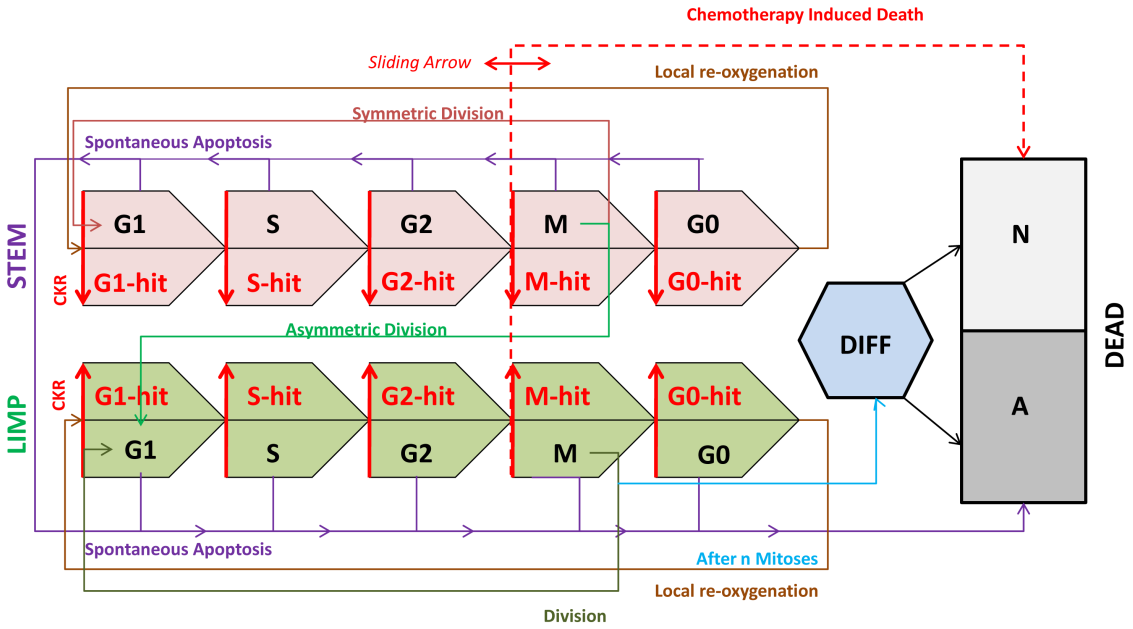


Figure 10. Generic cytokinetic model used. LIMP: LImited Mitotic Potential cells. DIFF: terminally differentiated cells. G1: Gap 1 phase. S: DNA synthesis phase. G2: Gap 2 phase. M: Mitosis. G0: dormant phase. N: necrosis. A: apoptosis. Hit: cells lethally hit by chemotherapy. CKR: Cell Kill Rate. The arrow indicating chemotherapy-induced death is a sliding arrow, with position dependent on drug pharmacodynamics.

2. Mock up descriptions

2.1 Objectives

The outcome of this high-end scenario is to provide a tool that demonstrates response of nephroblastoma to a given preoperative chemotherapy. This can be used in a fourfold way:

1. To demonstrate to patients / or parents of patients how a given tumour will respond to preoperative chemotherapy. This will help in explaining diagnosis and treatment of nephroblastoma to patients and/or parents of patients. Such a demo will not use the actual data of the given patient.
2. To give physicians treating a patient with a nephroblastoma the ability to check how this specific nephroblastoma will respond to preoperative treatment with vincristine and actinomycin-D.
3. To provide clinical researchers and modelers a powerful tool to define an in silico patient profile and further exploit it in other modelling approaches and VPH projects. Moreover, it could serve as a statistical tool to categorize patients (by associating their clinical and *in silico* profiles) and define ranges of model parameter values to guide the process of model adaptation for new patient cases.
4. To demonstrate to citizen what 'in silico' models/tools can do today. This can serve as a learning environment for 'in silico' models and will help to disseminate the importance of 'in silico' models in medicine to the public, to medical stakeholders, industry and funding agencies. It is pointed out that the purpose of the in silico experimentation functionality is currently limited to the education of the public so that they can be prepared for the future translation of thoroughly clinically validated models to clinical practice.

2.2 Targeted end-users

The high-end scenario will target patients and parents of patients, paediatric oncologists, researchers and the public as given by the 4 different objectives.

2.3 Functionalities

The application of nephroblastoma Oncosimulator into clinical practice will incorporate the following functionalities:

2.3.1 In-Silico Profiling of Patients

Nephroblastoma diagnosis is based on a variety of multiscale data. These data constitute the multiscale clinical profile of the tumour. After the necessary pre-processing of the available data of nephroblastoma patients, the data are fed into the nephroblastoma simulation model. By integrating insights from the personalized multiscale clinical profile of the patient, numerical parameter studies and any information that can be gleaned from the experimental and theoretical biology literature, semi-automatic adaptation of the model parameters is conducted. The determined model parameter values serve as a patient record for in silico tumor characteristics and form the 'in-silico profile' of the patient (Figure 11). Training the model with a patient's data gives a more accurate description of the specific kinetics of disease progression.

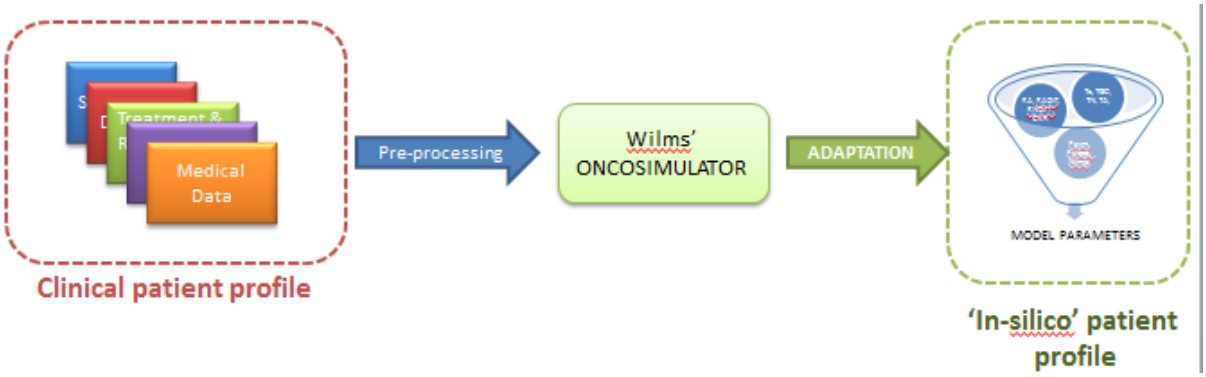


Figure 11. Schematic representation of stage 1 of the nephroblastoma use case (UC-NEPH, stage 1): 'In-siico profilng' of patients with Wilms' tumor .

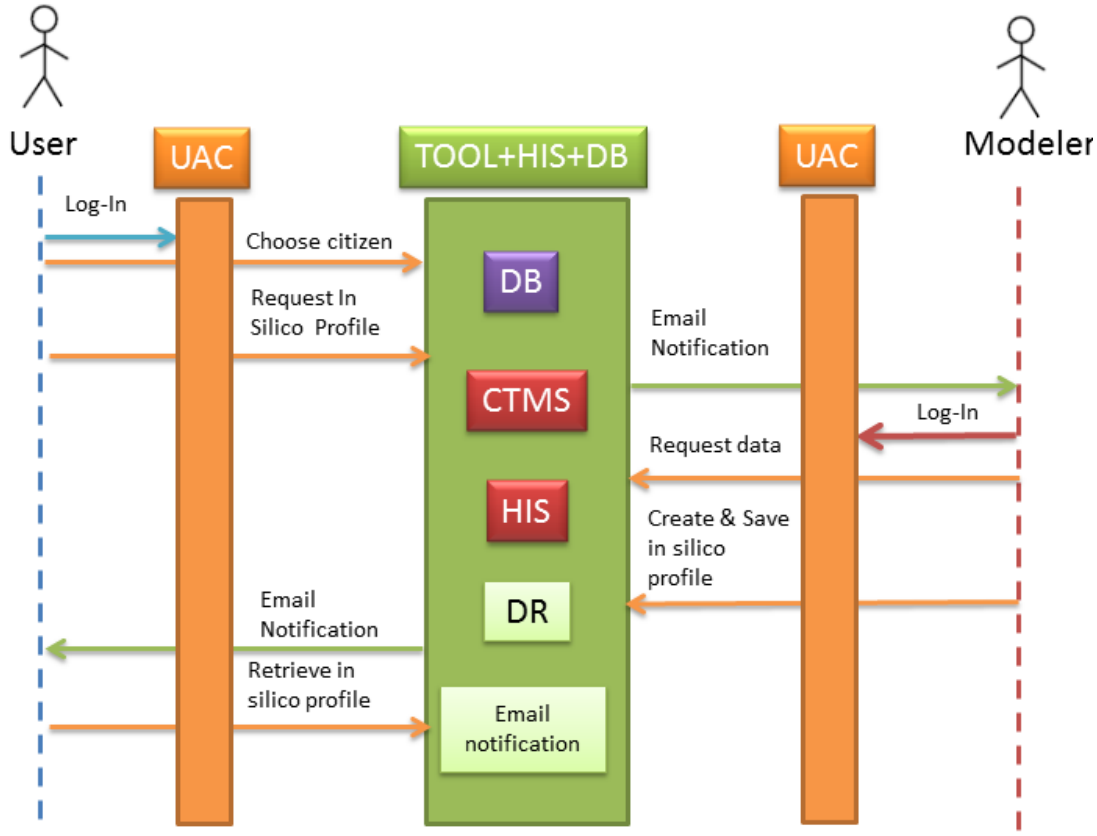


Figure 12. Sequence diagram of 'in silico profiling' (NEPH-UC- stage 1) . MR: Model Repository. DR: Data Repository for storing 'in silico profiles' and predictions. DB: MHA data repository. HIS: Hospital Information System. CTMS: Clinical Trial Management System.

The basic steps of the 'in silico profiling' demonstrator are:

1. The citizen or the doctor logs into platform.
2. If a doctor is the one that requests the generation of the 'in-silico profile', then a list with all the available citizens who have shared their data with this specific doctor is presented. The doctor chooses a citizen (Figure 13 and Figure 14). If a citizen is the one that have requested the generation of the "in silico profile", then this step is omitted.
3. The citizen or the doctor requests the generation of an 'in silico profile' (Figure 17). A notification email is sent to bio-informatician (modeler).
4. The bio-informatician (modeler) logs into the platform.
5. The bio-informaticion (modeler) uses the MHA platform in order to access and retrieve the necessary data from MHA data repository, hospital information systems(HIS), clinical trial management systems (CTMS) etc. If the citizen participates in a clinical trial, his/her clinical data are anonymized/pseudonymized.
6. The bio-information generates the 'in silico profile' of the citizen (offline) and uploads it to platform (Figure 15). He may also alter an existing 'in-silico profile' (Figure 16).
7. A notification email is sent to the citizen or the doctor that the requested ' in silico profile' is ready.
8. The citizen can monitor the status of 'in silico profiling' by entering a status page (Figure 17).
9. The citizen or the doctor retrieves the 'in silico profile' (Figure 17).

The following figures are GUI mock-ups of the aforementioned steps.

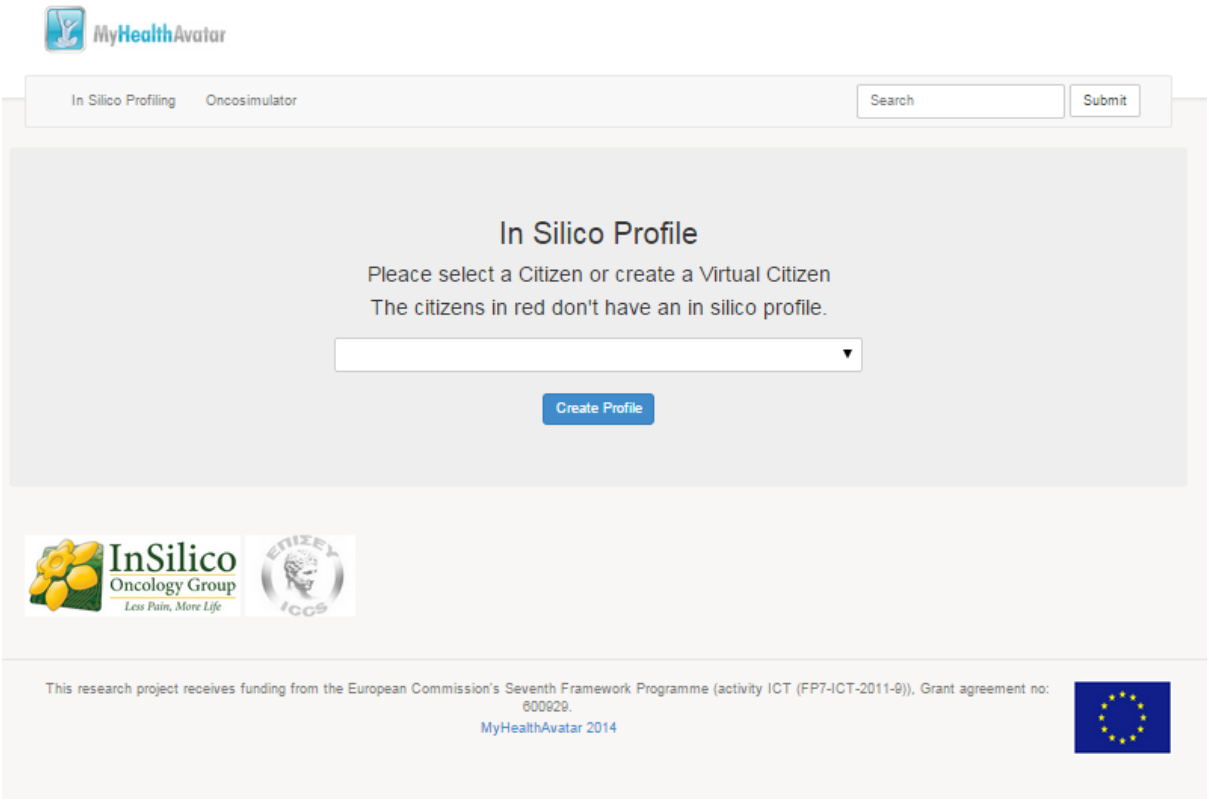


Figure 13. 'In silico profiling' start page.

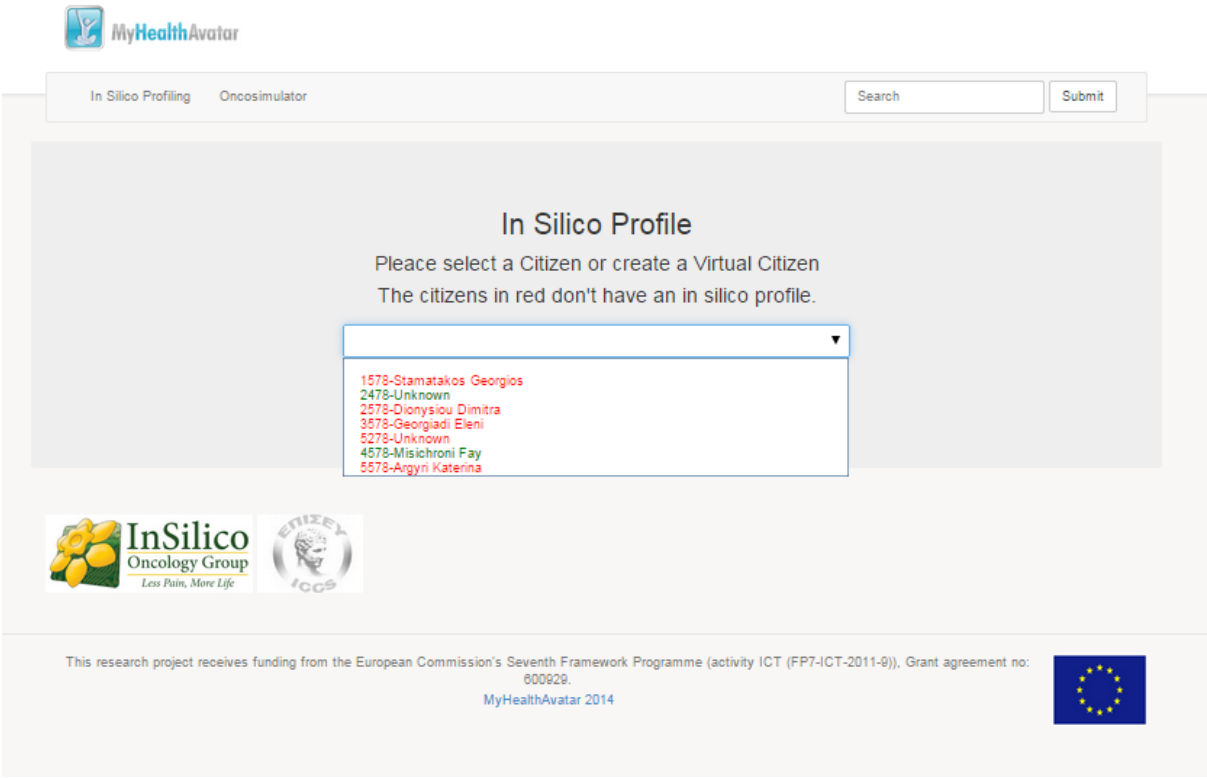


Figure 14. Choose citizen. If red the citizen doesn't have an 'in silico profile' yet.

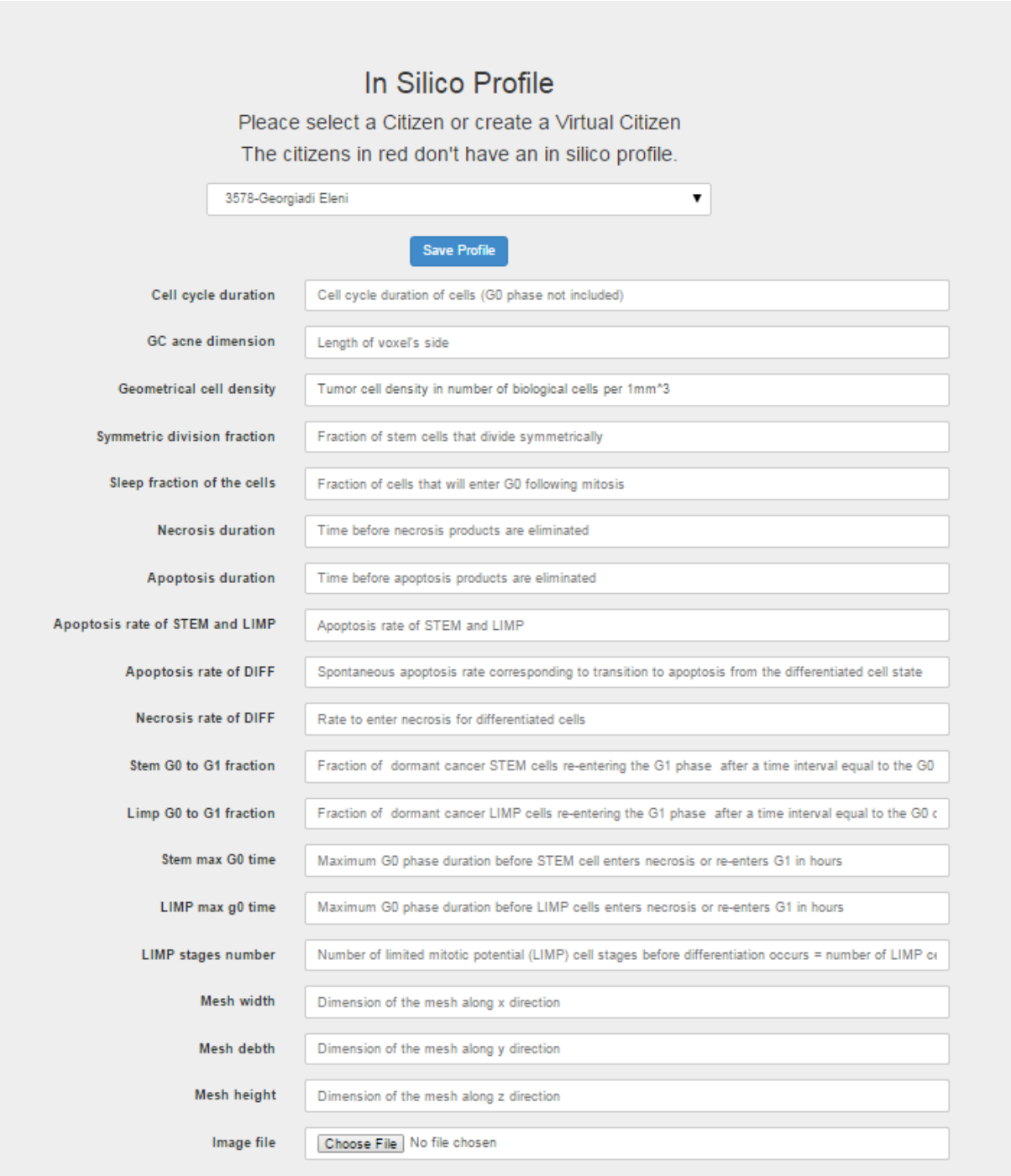


Figure 15. Create new 'in-silico profile' for citizen.

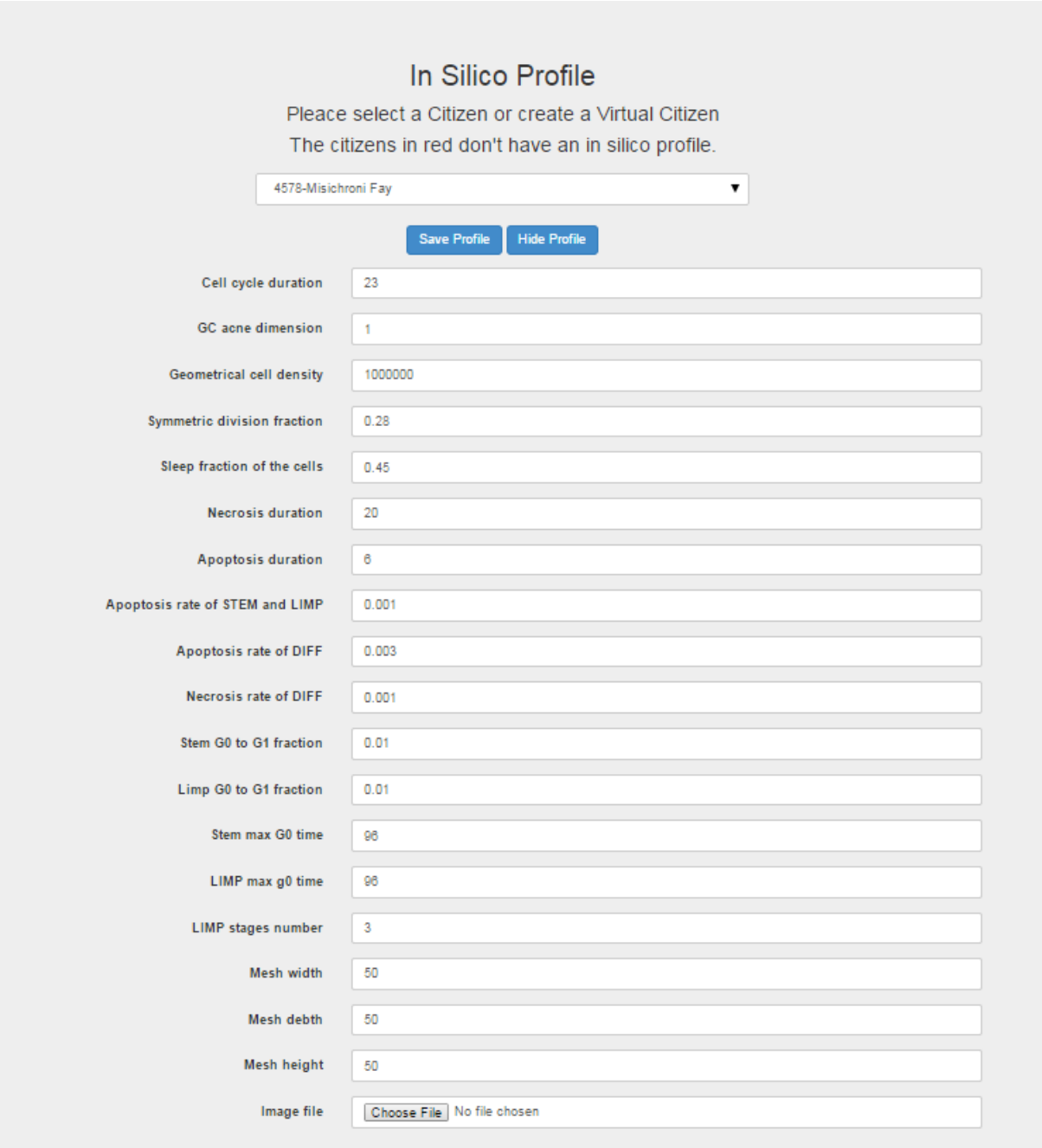


Figure 16. Alter 'in-silico profile' of a citizen.

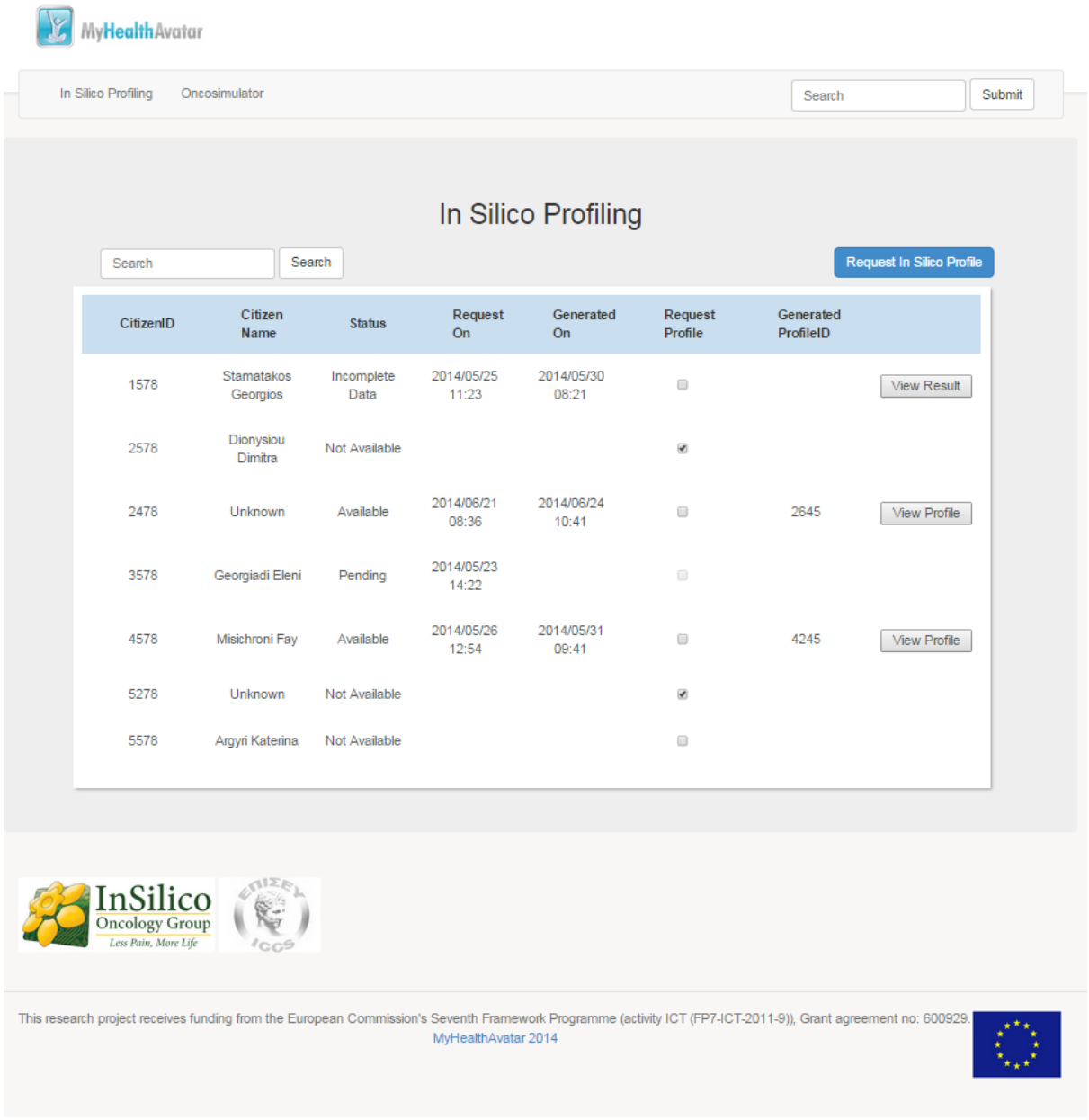


Figure 17. Monitoring of 'in silico profiling' requests.

2.3.2 In-silico predictions

This high end-scenario will demonstrate the response of preoperative chemotherapy in nephroblastoma. The demonstration will be graphically based. The user can select between 2 drugs treatment (actinomycin-D and vincristin in localized unilateral tumours over 4 weeks) and 3 drug treatment (addition of doxorubicin in metastatic tumors over 6 weeks). The tumour volume change will be dynamically shown over time (4 to 6 weeks, depending on the metastatic state). The user can interrupt the display at any timepoint between diagnosis and end of preoperative treatment. Additionally UC-NEPH scenario will give the tumour volume at diagnosis and at any time during the preoperative treatment. The difference of the tumour volume between diagnosis and end of preoperative treatment will be displayed. Depending on the availability of DWI-MRI, cell density will be shown by mapping ADC values on the tumour. This can be given as a parameter to the scenario.

The paediatric oncologist runs a number of experiments in silico (= on the computer) simulating the most likely response of the tumour to the most relevant candidate chemotherapeutic schemas. The outcomes of the simulations (predictions) help the oncologist decide the appropriate treatment plan (Figure 18).

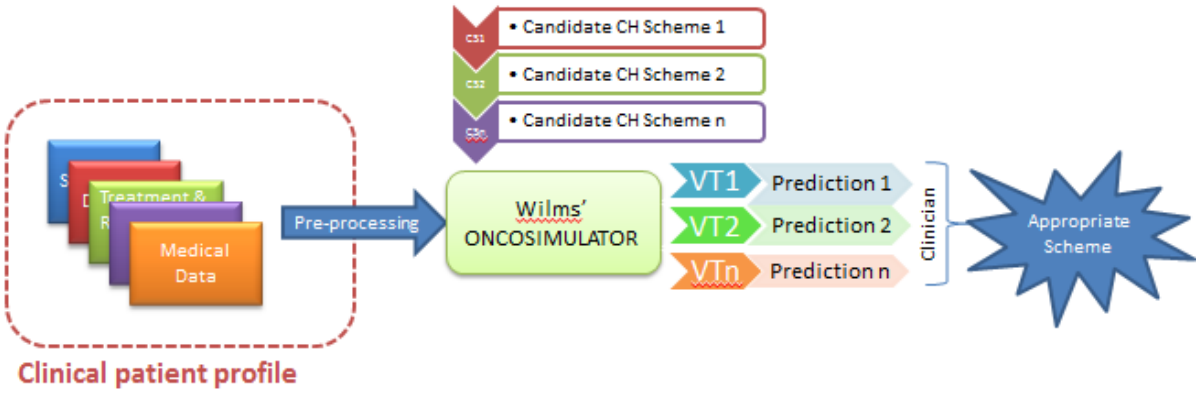


Figure 18. Schematic representation of stage 2 of the nephroblastoma use case (UC-NEPH, stage 2): Prediction simulations of patients with Wilms' tumor.

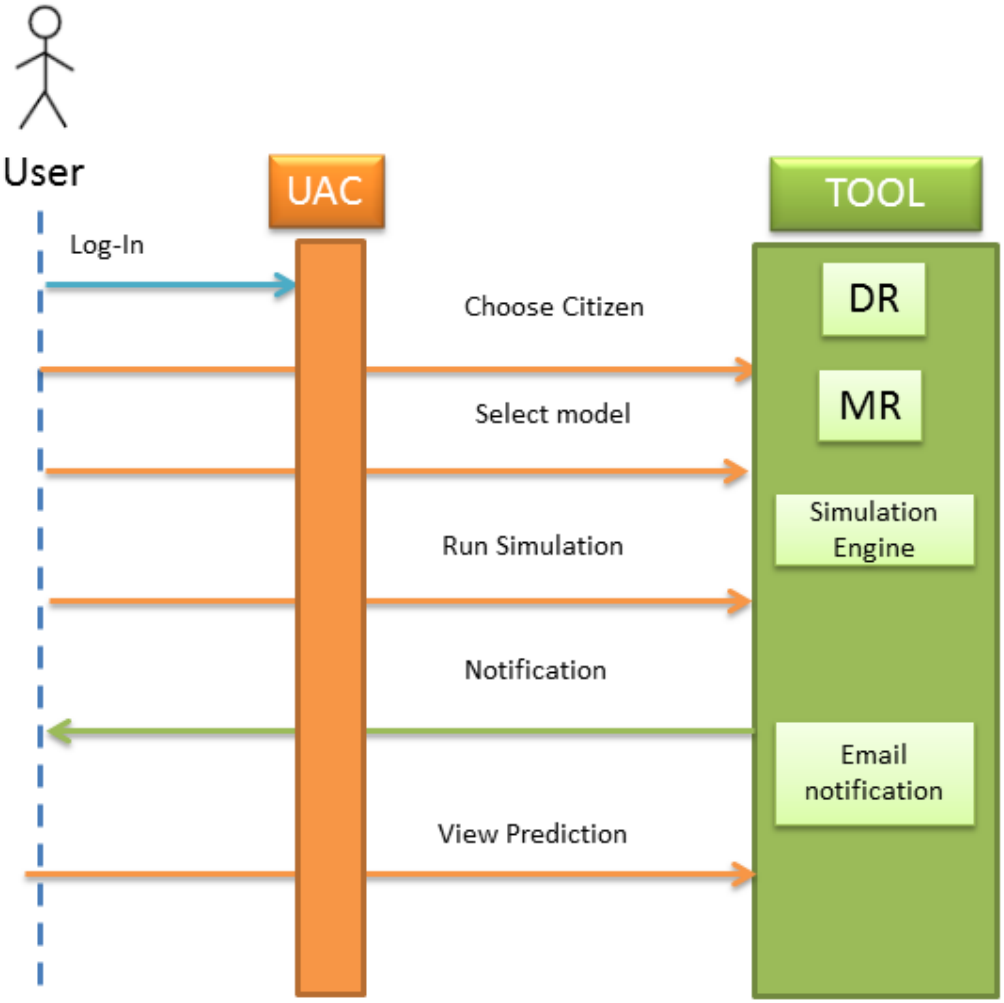


Figure 19. Sequence diagram of prediction simulations (NEPH-UC- stage 2) . MR: Model Repository. DR: Data Repository for storing 'in silico profiles' and predictions.

The basic steps of the demonstrator of the prediction simulations are:

1. The doctor logs in into platform.
2. A list with all the available citizens who have shared their data with this specific doctor is presented. The doctor chooses a citizen (Figure 20 and Figure 21).
3. The doctor can create an "in silico profile", if the citizen doesn't have one. If the citizen already has an 'in-silico' profile then it can review it and/or alter it.
4. The doctor chooses the treatment scheme that will be simulated (Figure 22). Three options are available:
    a. Free Growth,
    b. Actinomycin-Vinctristine,

c. Actinomycin-Vinctristine-Doxurubicin.

5. The doctor chooses the clinical question that the simulation will address (Figure 24). Three options are available:
   a. When to start Chemotherapy?
   b. How many days after chemotherapy to proceed to survey?
   c. Which chemotherapeutic sceme (administration points) is preferable?

   This step is omitted if in case 3 “Free Growth” is selected (Figure 23).
6. The doctor sets the simulation parameters. Depending on the treatment scheme and the clinical question that the simulation must address, different parameters are requested (Figure 25, Figure 26, Figure 27, Figure 28).
7. The doctor triggers the simulation.
8. A notification email is sent to the doctor when the simulation has been completed.
9. The doctor can monitor the status of the simulations by entering the status page (Figure 29).
10. The doctor review and retrieves the predictions (Figure 30 and Figure 29).

The following figures are GUI mock-ups of the aforementioned steps.

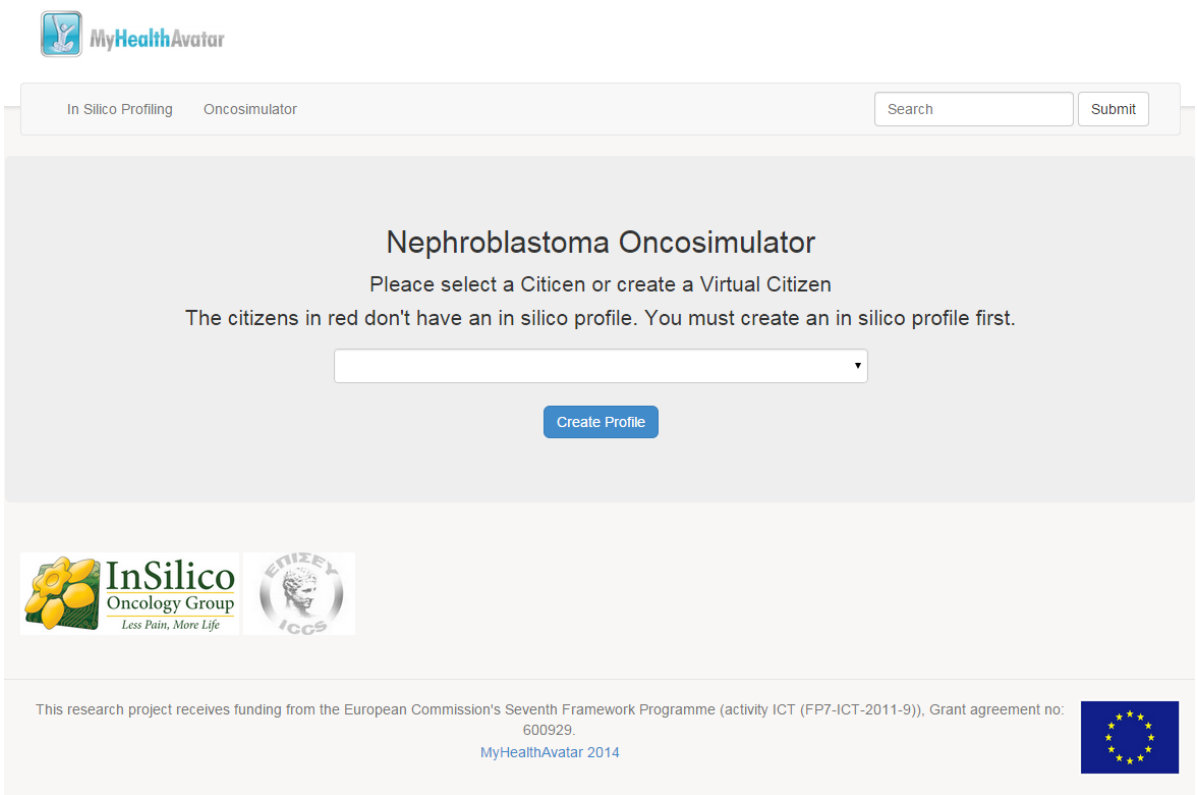


Figure 20. Nephroblastoma oncosimulator start page.

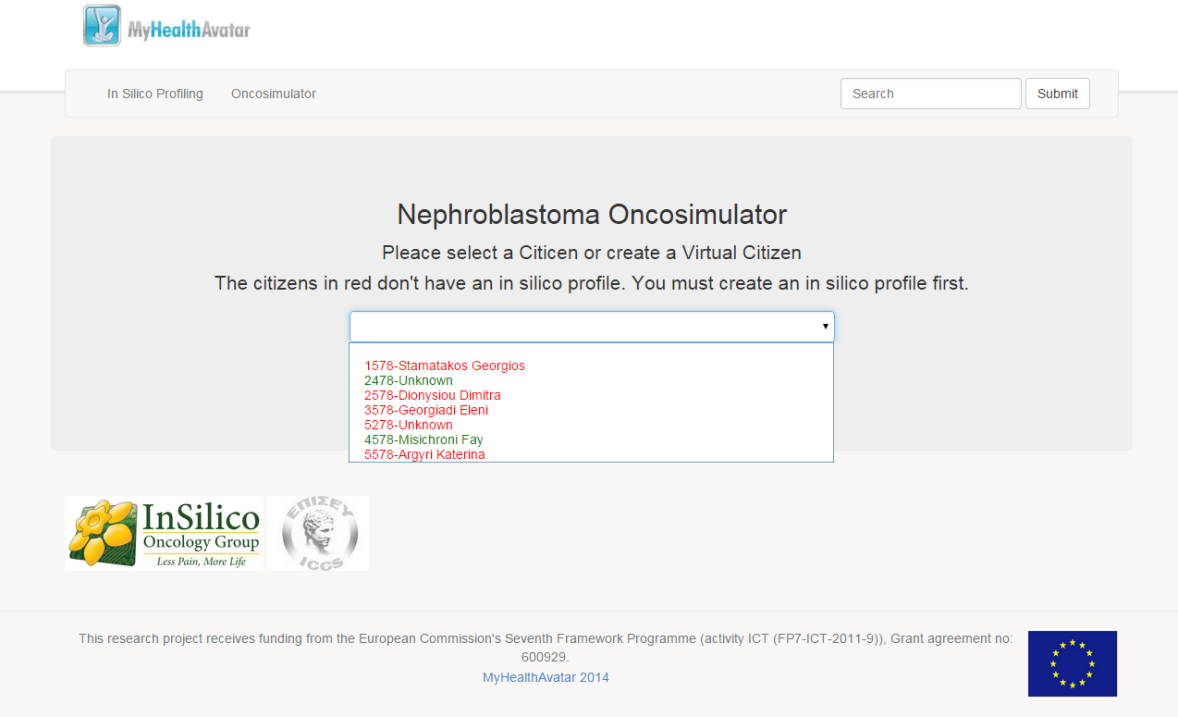


Figure 21. Choose citizen. If red the citizen doesn't have an in silico profile yet.

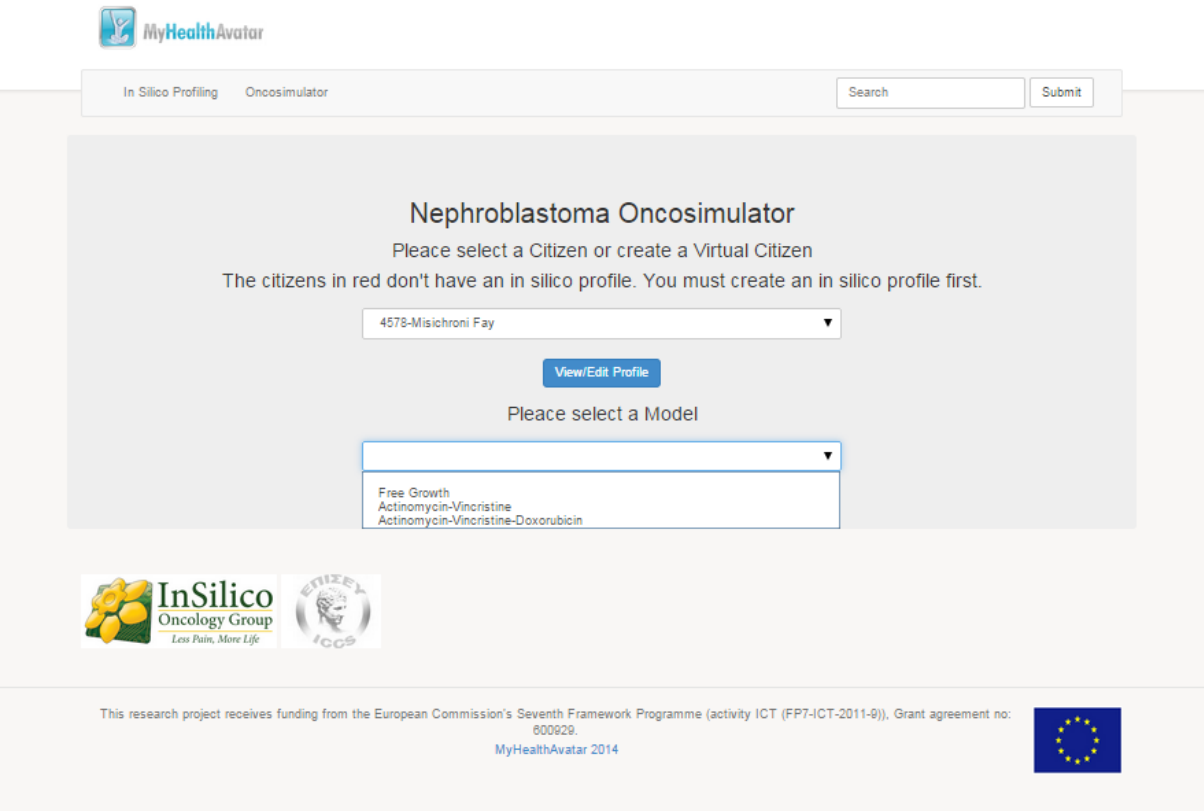


Figure 22. Choose model. Three models are available: Free Growth, Actinomycin-Vinctristine, Actinomycin-Vinctristine-Doxurubicin.

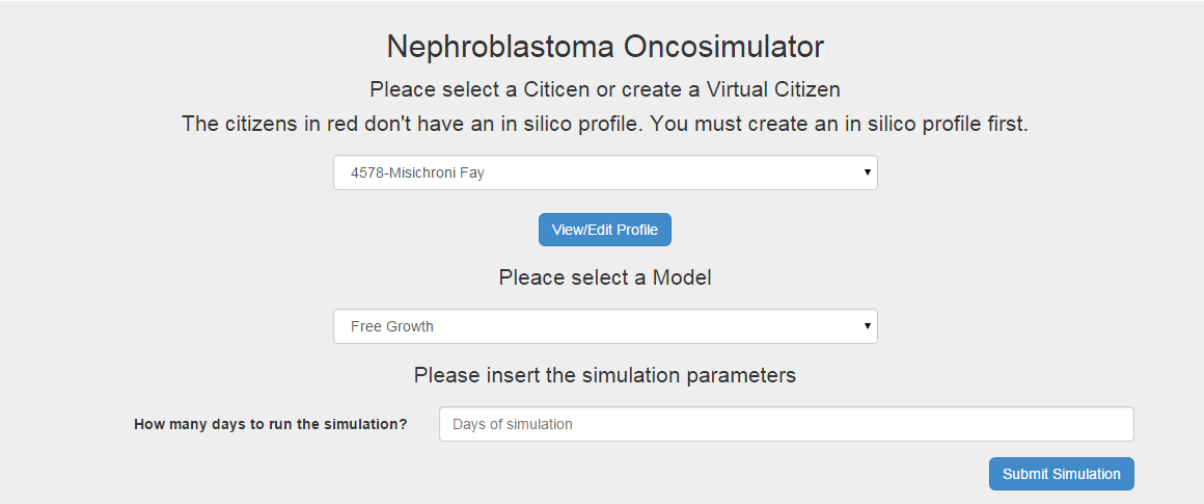


Figure 23. Parameter in case of free growth model.

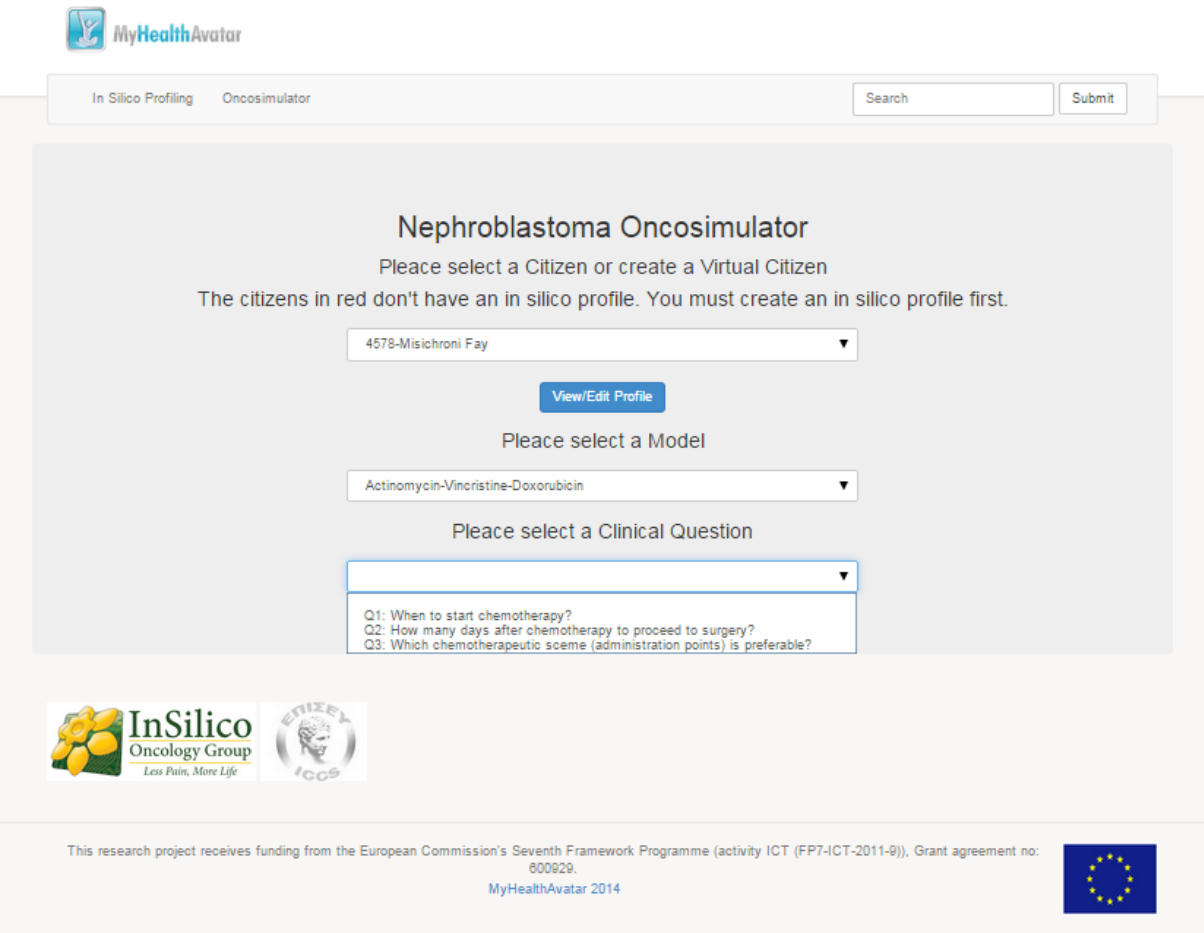


Figure 24. Choose the clinical question that the simulation will address. Three options are available: When to start Chemotherapy? How many days after chemotherapy to proceed to survey? Which chemotherapeutic sceme (administration points) is preferable?

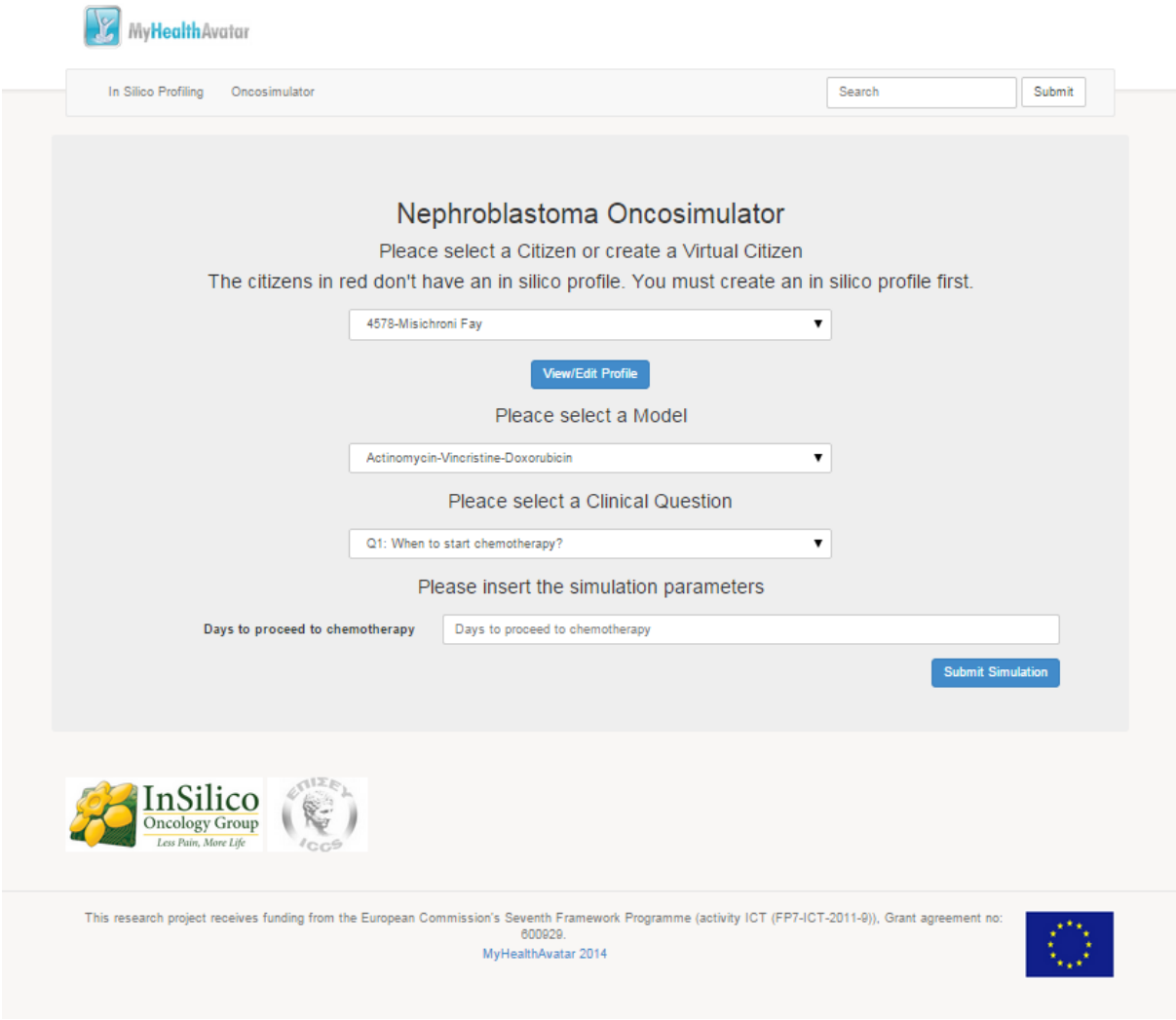


Figure 25. Parameter that is needed for Q1: When to start Chemotherapy ?

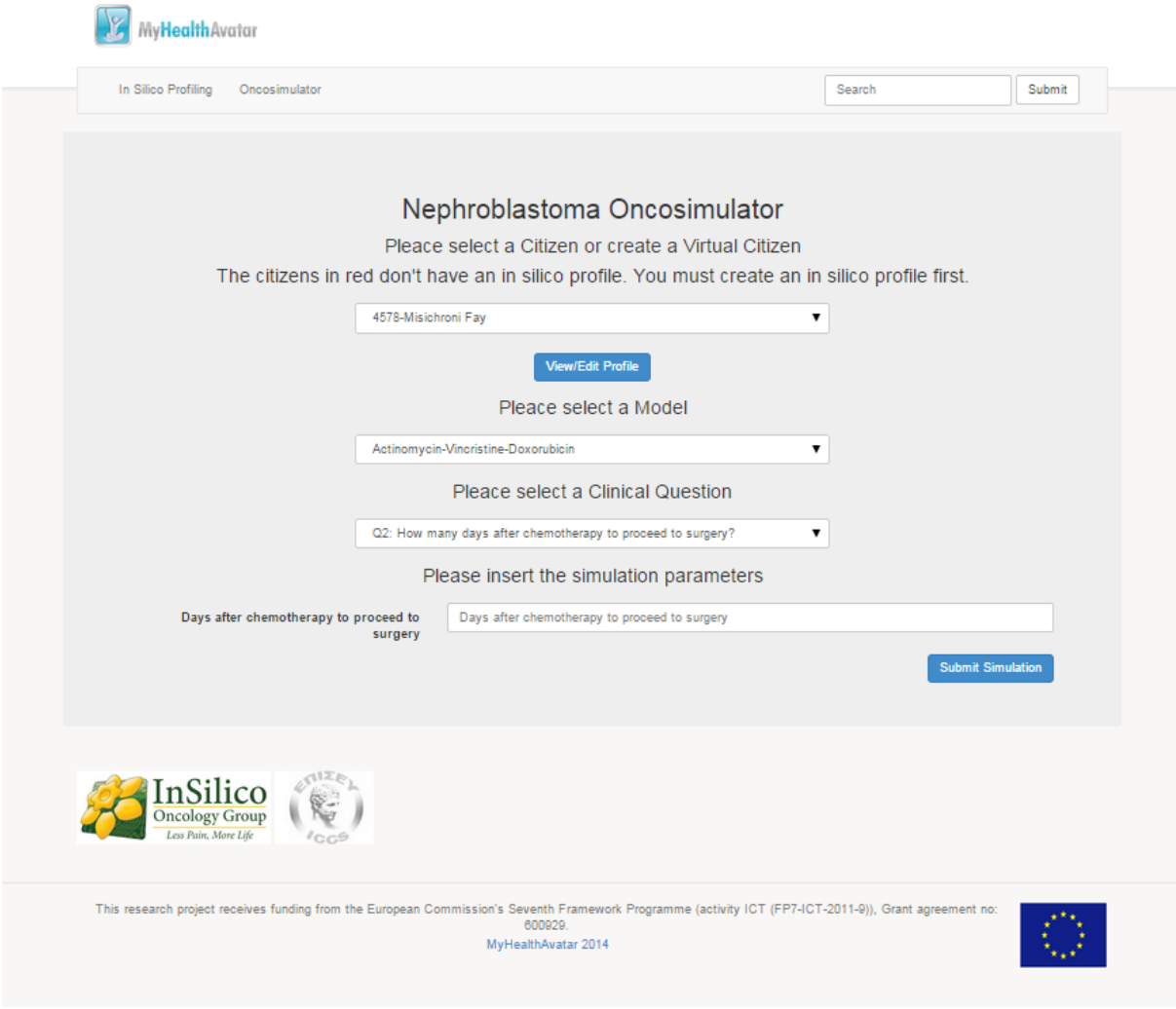


Figure 26. Parameter that is needed for Q2: How many days after chemotherapy to proceed to surgery?

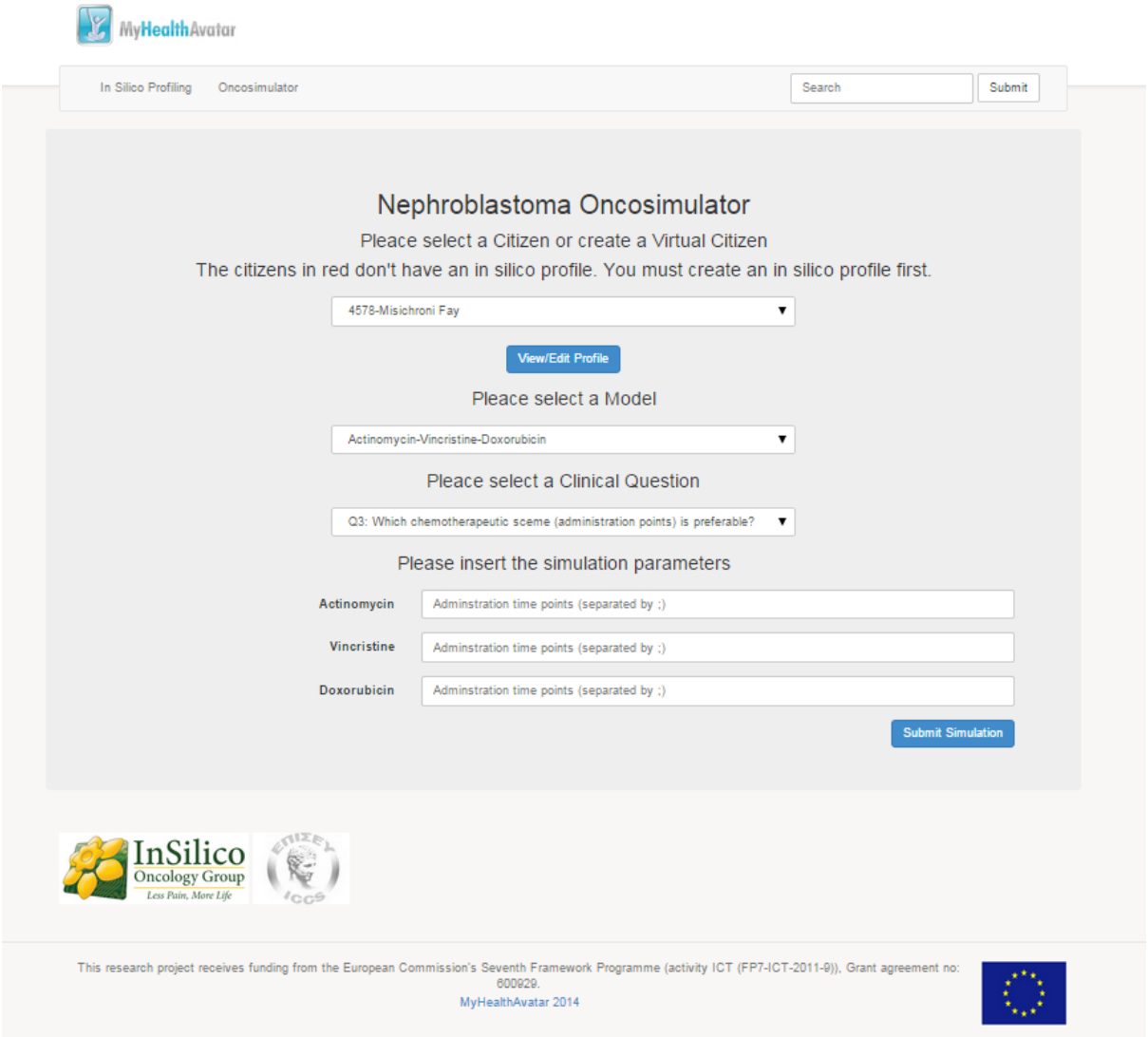


Figure 27. Parameter that is needed for Q3: Which chemotherapeutic sceme (administration points) is preferable? (Actinomycin-Vincristine-Doxorubicin)

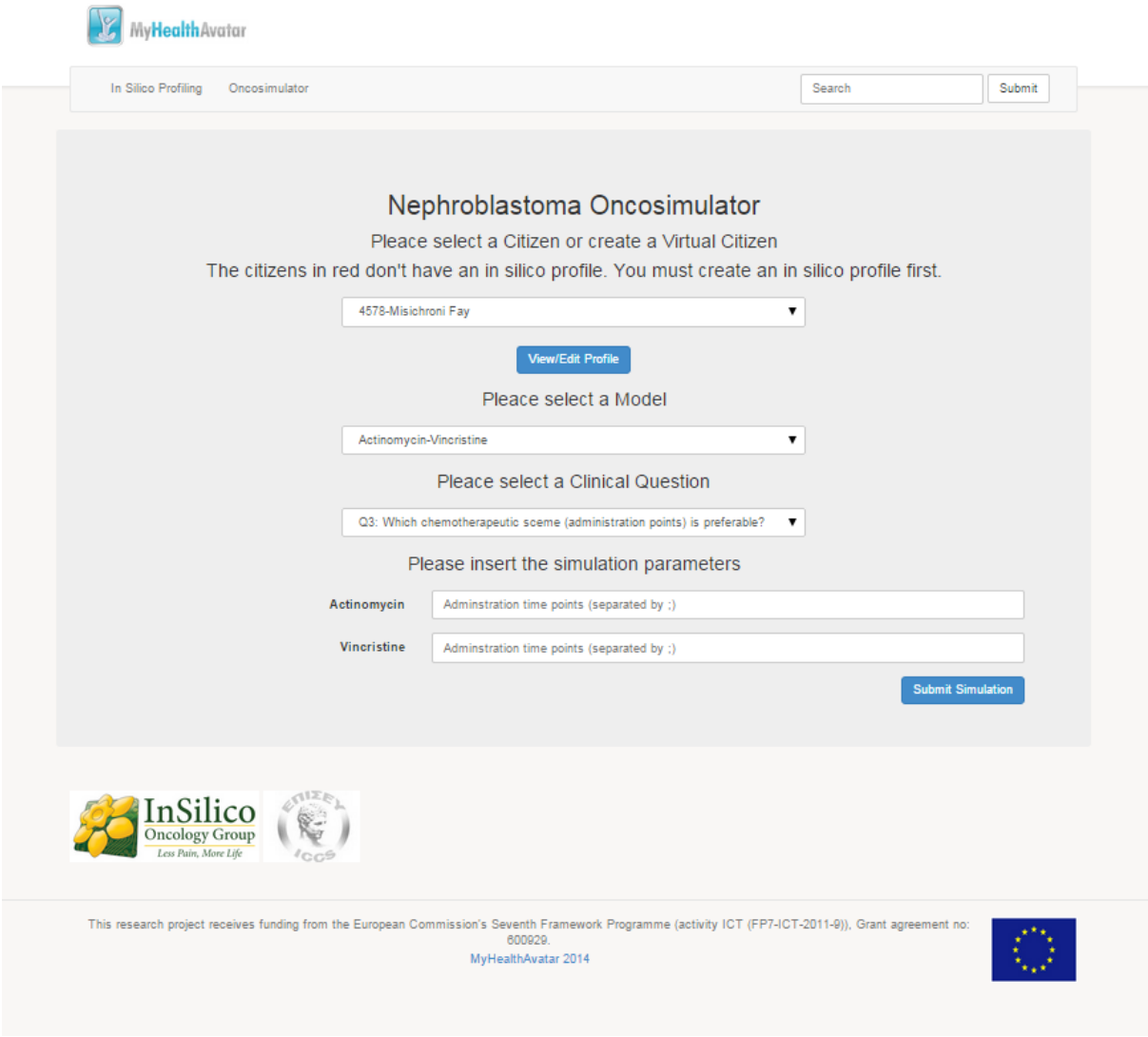


Figure 28. Parameter that is needed for Q3: Which chemotherapeutic sceme (administration points) is preferable? (Actinomycin-Vincristine)

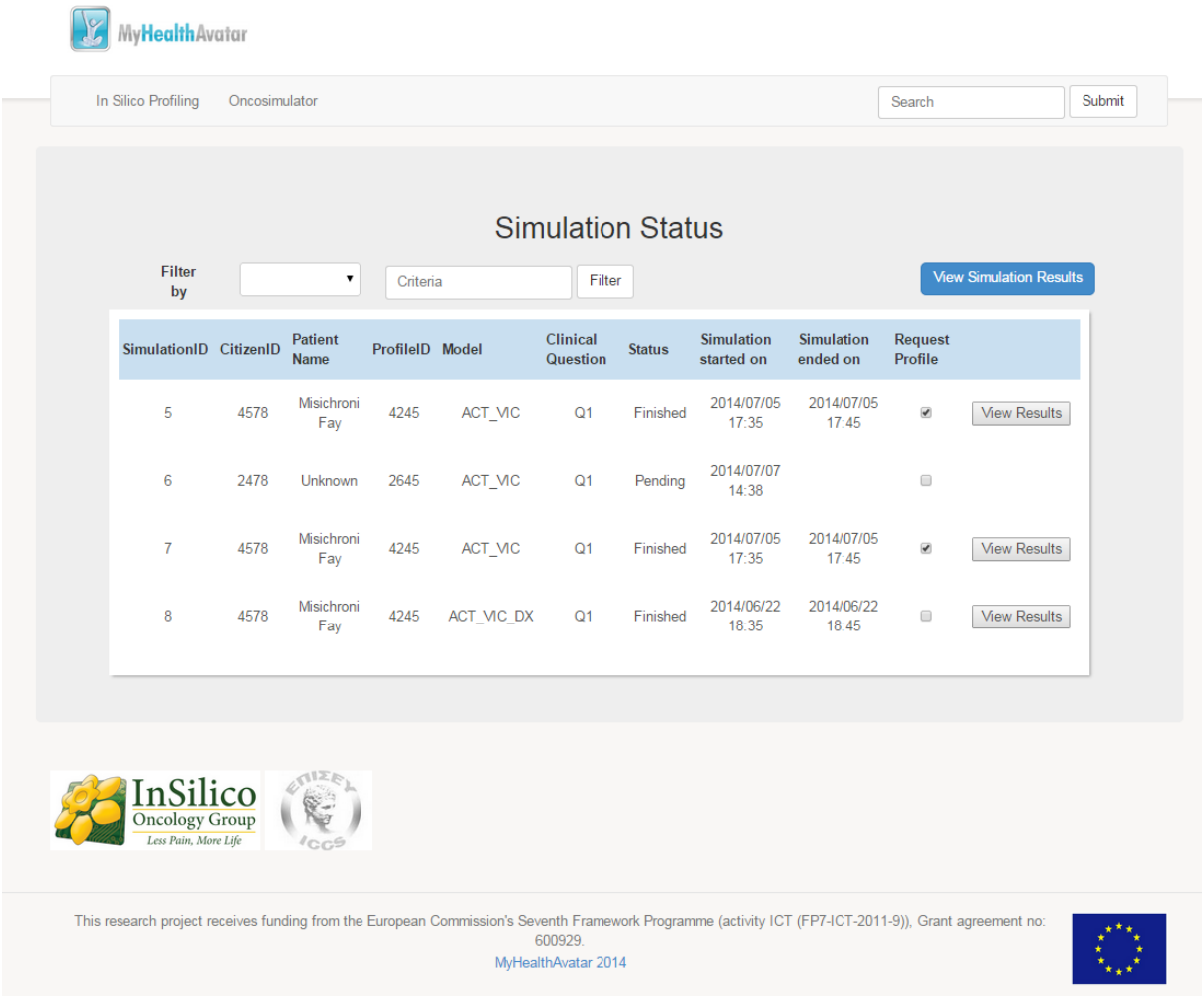


Figure 29. Monitoring of in silico simulations.

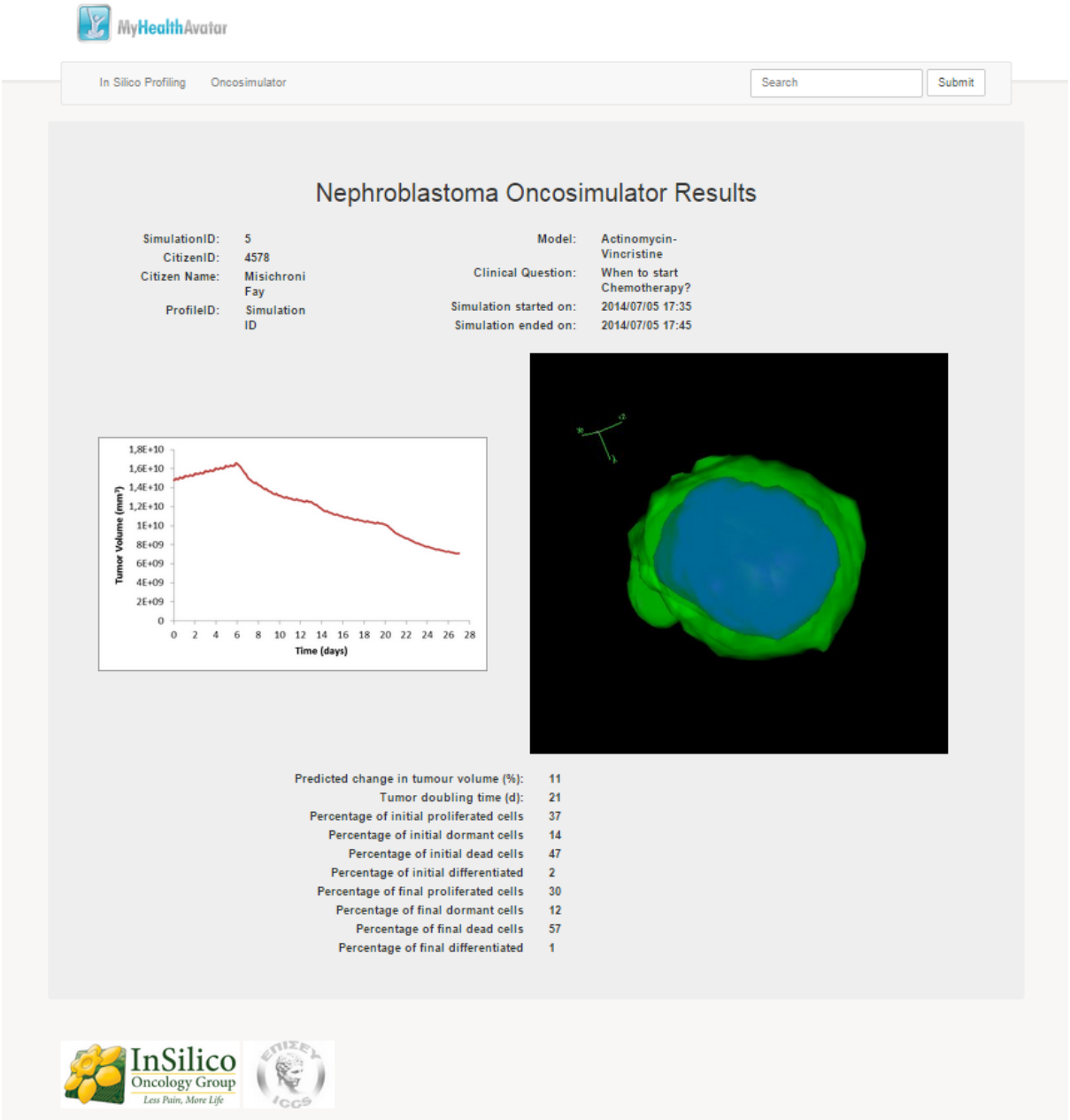


Figure 30. Visualisation of the simulation results.

2.4 Data involved

The clinical partner (USAAR) will record data regarding radiology, histology, biological markers on blood and urine tests and genetic counselling. In addition biomaterial for molecular and genetic research will be available in order to find new biomarkers and targets for new compounds in the future. This will be done by storing and analysing biomaterial by a wide range of molecular and proteomic technologies from patients enrolled in the new nephroblastoma protocol and having given consent for this research.

The aforementioned data will be preprocessed by the VPH modelling partner (ICCS) and transformed appropriately into Wilms Oncosimulator input. More specifically, clinical data, imaging data (MRI at the time of diagnosis and after preoperative chemotherapy) and molecular data (miRNA) will be exploited.

2.5 Added values to the MHA platform

MHA provides a unique platform that empowers different stakeholders to manage lifestyle but also diseases. UC-NEPH will be used by at least 4 different stakeholders as described above.

The nephroblastoma case provides multiple benefits for modellers and clinicians as well. Utilizing data from SIOP trials provides a reliable reference for both developing and validating in silico models. Ultimately, this use case aims at quantitatively predicting the response to preoperative chemotherapy, which would permit to avoid unnecessary treatment in non-responding tumours and apply chemotherapy only to those patients that would benefit most. The entire procedure can also be the basis for a clinical decision support tool for the less experienced clinicians. Furthermore, the 'in-silico profile' created in the first stage, could be further used by clinicians as a tool to provide insight into the biological characteristics of a specific tumour, as an input for future use in the same model, as an input for the use in other models (e.g. within the collaborating CHIC project's platform) and as a statistical tool to categorize patients (by associating their clinical and in silico profiles) and define ranges of model parameter values to guide the process of model adaptation for new patient cases.

Additionally, the scenario will support patients and/or parents by demonstrating them in a visual way how the malignant nephroblastoma will shrink during preoperative chemotherapy. The tool can be also used in that way as a teaching facility. For Oncologists it can help them in individual cases to demonstrate in advance of treatment how the tumour will develop under preoperative chemotherapy. In addition citizens are able to use the tool to get an understanding of what 'in silico' oncology is able to do. In that way MHA platform will help to disseminate new knowledge about 'in silico' oncology.

3. Design & components

3.1 Technology components

The core technology components of this use case are:

- MR: Model Repository.
- Simulation Engine
- DR: Data Repository for storing 'in silico profiles' and predictions.
- Email Notification Service

3.2 Architectural support

This use case is related to the following MHA architecture components:

- MHA portal
- Data repository
- User management and consent
- External link to Hospital Information System (HIS) and CTMS: Clinical Trial Management System.
- Tool/Model repository
- Data collection utilities

3.3 Integration

More information about how the internal and external component interconnect to each other in this use case can be found in:

- Figure 12. Sequence diagram of 'in silico profiling' (NEPH-UC- stage 1) .
- Figure 19. Sequence diagram of prediction simulations (NEPH-UC- stage 2).

3.4 Image Processing

For patients with nephroblastoma, imaging studies (MRI T1, T1 with contrast enhancement, T2 and T2 flair) may be available at the time of diagnosis and after 4 weeks of preoperative chemotherapy. The imaging studies at the time of diagnosis are used for the prediction of tumour shrinkage during and after 4 weeks of vincristine and actinomycin-D chemotherapy.

One of the main inputs into the Oncosimulator is the volumetric data of nephroblastoma. This data may consist of isotropic voxel dimensions in order to facilitate the computation of tumour dynamics simulation. Since MRI slices are usually reconstructed containing highly non-isotropic voxels, interpolation of the binary segmentation volumes is performed.

Segmentation of the tumour is important in order to provide information on the shape and location of the tumour. This process is also important for model validation since it allows quantitative comparison of the simulation predictions with the actual development of the tumour in vivo.

3.5 Other data handling

MicroRNA expression data is under integration into the Oncosimulator.

Further information regarding the basic science and technical aspects of the nephroblastoma Oncosimulator is available on:

- G Stamatakos, Memeber , IEEE , D Dionysiou, A Lunzer, R Belleman, E Kolokotroni, E Georgiadi, M Erdt, J Pukacki, S Rueping, S Giatili, A d`Onofrio, S Sfakianakis, K Marias, Member , IEEE , C Desmedt, M Tsiknakis, Member , IEEE , and N Graf, Member , IEEE "The Technologically Integrated Oncosimulator: Combining Multiscale Cancer Modeling with Information Technology in the In Silico Oncology Context" DOI:10.1109/JBHI.2013.2284276 IEEE J Biomedical and Health Informatics vol.18, No. 3, pp.840-854 2014
- G.S.Stamatakos, E.Ch.Georgiadi, N.Graf, E.A.Kolokotroni, and D.D.Dionysiou, "Exploiting Clinical Trial Data Drastically Narrows the Window of Possible Solutions to the Problem of Clinical Adaptation of a Multiscale Cancer Model", PLOS ONE 6(3), e17594, 2011

4. Implementation

4.1 Tasks and milestones

The tasks and milestones of this demonstration will include:

Task 1: Implementation of simulation platform

M1: Initial version of simulation platform completed

Task 2: Implementation of nephroblastoma simulation models

M2: Initial version of nephroblastoma models completed

Task 3: Integration of nephroblastoma models into the simulation platform

M3: Integration of nephroblastoma models into the simulation platform completed

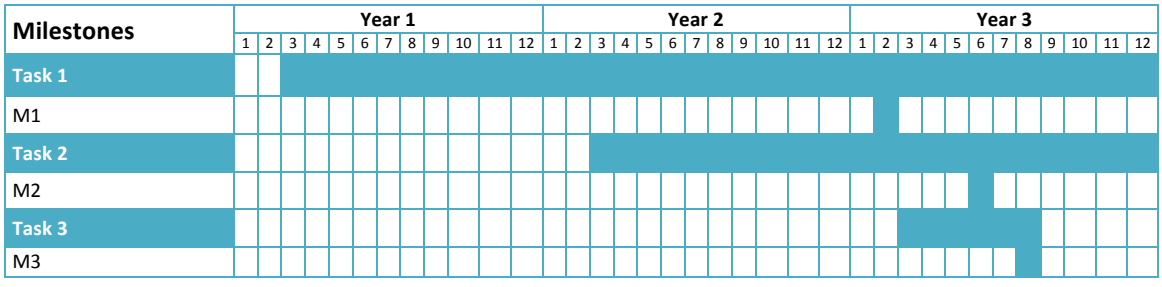
Task 4: Generation of nephrobastoma synthetic patients by compilation of clinical data available from other EU projects (corresponding to MS054 from DoW)

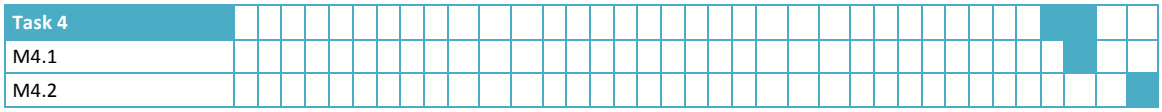
M4.1: Synthetic patients available for in silico studies

M4.2: Final version of nephroblastoma use case demo and simulation platform (D5.2)

4.2 Gantt chart

The implementation Gantt chart is shown in the following diagram:





5. Evaluation

5.1 Participants recruitment

We will carry out evaluation activities by exposing the system to its end-users through their experience gained through their experiments with the mock-ups. The validation of the developed demonstration will be done through a set of volunteers. The evaluations on the technical components will be done via the technical development team, and via the participants of the project.

The participants will be recruited in the following ways:

- Parents of patients with nephroblastoma from the department of Pediatric Oncology at USAAR
- Physicians and surgeons from different hospitals
- Citizens and other volunteers
- Researchers and technology experts from the MHA consortium
- Medical professionals from the MHA consortium

5.2 Evaluation activities

The evaluation activities will include:

- Questionnaire: this involves a set of written questions to evaluate the high-end scenario;
- Workshop: this is a way to help the multiple stakeholders understand the system design process and hence to deeply involve the end-users in the system development. The presentations and face-to-face discussions in the workshops allow good communications between the end-users and the system designer, leading to the forming of partnership for co-design.

5.3 Evaluation outcome analysis

We will analyse the information gathered in Section 5.2.

- User feedback analysis: This will analyse the strength and weakness of the system by looking into the feedback from the participants.
- Conclusions: This will put together the outcome from the above analysis to draw conclusions on the evaluation outcomes.

4 Conclusions

The previously reported activities and results from WP7 allowed us to elaborate, define and present the final set of high end clinical demos. Close to it we are very grateful and proud to acknowledge the support and contribution received from MHA project partners (BED, ICCS, FORTH).

Each demo is close related and associated not only to a specific tool or application but as well to a set of specific Use Cases / Scenarios. All are defined within complex but very concrete and focused clinical contexts. The demos, at this stage, have already the potential to demonstrate the clear benefits for MHA end-users.

A progressive and additional achievement of this document is the 'in advance' presentation of demos' mock-ups and the expected evaluation activities.

The description of all demos will allow all project partners to have a well-defined focus on next activities according to the elaborated Gantt charts summarised below (Tasks and milestones description is available in Chapter 3).

Diabetes and Emergency Demo (DIAB-EME)

Milestones	Year 1												Year 2												Year 3											
	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
Task 1																																				
M1																																				
Task 2																																				
M2																																				
Task 3																																				
M3.1																																				
M3.2																																				
Task 4																																				
M4.1																																				
M4.2																																				

Personalized CHF Related Risk Profiles and "Real-Time Monitoring" Demo (CHF)

Milestones	Year 1												Year 2												Year 3											
	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
Task 1																																				
M1																																				
Task 2																																				
M2																																				
Task 3																																				
M3.1																																				
M3.2																																				
Task 4																																				
M4.1																																				

Osteoarthritis Demo (OST)

Milestones	Year 1												Year 2												Year 3											
	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
Task 1																																				
M1																																				
Task 2																																				
M2																																				
Task 3																																				
M3																																				

Nephroblastoma (Wilms Tumour) Simulation Model and Clinical Trial (UC-NEPH): In-silico Profiling of Patients and Predictions

Milestones	Year 1												Year 2												Year 3											
	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
Task 1																																				
M1																																				
Task 2																																				
M2																																				
Task 3																																				
M3																																				
Task 4																																				
M4.1																																				
M4.2																																				

Appendix 1 – Abbreviations and Acronyms

CHF	Congestive Heart Failure
DoW	Description of Work
EHR	Electronic Health Record
ICT	Information and Communications Technology
MHA	MyHealthAvatar
PHR	Personal Health Record

Appendix 2 – The Final Set of MHA Scenarios / Use Cases

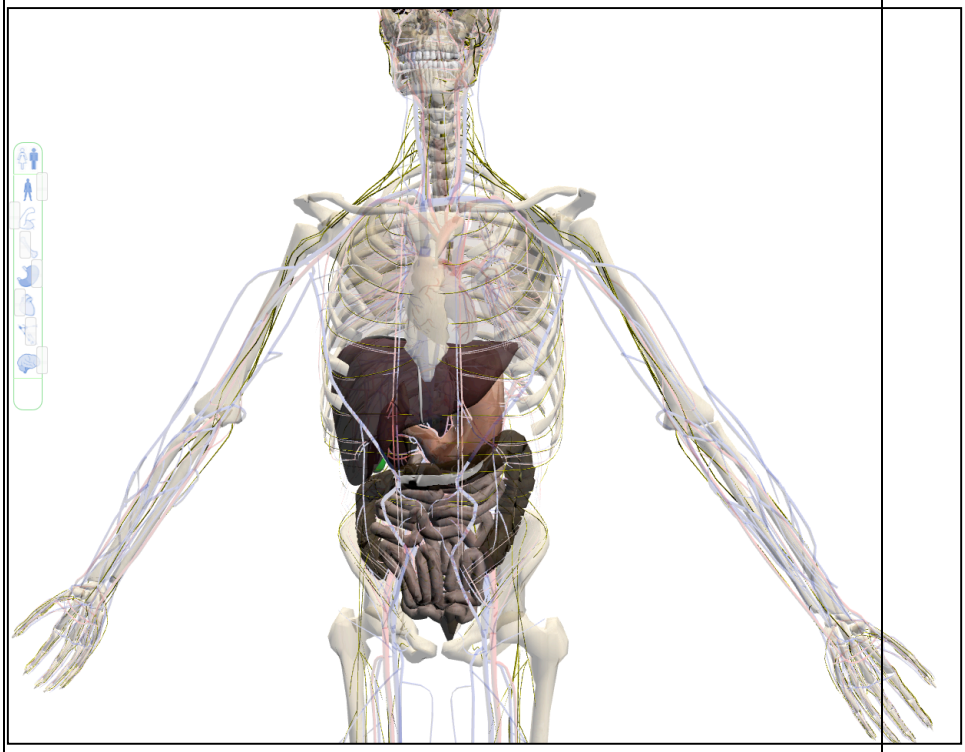
MHA User Accounts (UC-UAC)

Use Case ID:	UC-UAC		
Use Case Name:	MHA User Accounts		
Technical Collaborators:	BED, FORTH, ICCS	**Clinical Collaborator:**	USAAR
Description:	Users (citizens) will be able to log onto the system using their username and password. New users will be able to sign up to the system by creating basic personal information including security questions. Informed consent and privacy: Users will need to accept the privacy policy and the "terms and conditions" of using the MyHealthAvatar platform. Upon log into the system, users will be able to enter, browse their data, explore medical information, communicate with other fellow patients. Users will be able to view and interact with an avatar - a 3D representation of the human body. It will allow the End User to click with the computer mouse on a particular part of the avatar "body" to trigger a search of medical records to retrieve relevant information MyHealthAvatar is a platform for End-Users who want to share their health information to create collective knowledge about disease, health, and treatments. In order to achieve this goal advanced Informed Consent and Privacy Policy Scenario / Use Case should be implemented. End User has the GUIs, functionalities and tools in the frames of MyHealthAvatar platform to accept, reject, print or revise at any time the Privacy and Informed Consent settings. There will be two types of users, the first type includes patients and citizens for their life time data collection, the second type includes doctors who will be linked to the avatars from citizens/patients for clinical practices and medical research purpose		
Actors:	*Two types of users: Type 1: Patients/citizens* *Type 2: doctors/medical researchers*		
Trigger:	*n/a*		
Preconditions:	*n/a*		
Successful End condition	*n/a*		
Fail End condition	*n/a*		
Basic Flow:	Sign up and log in 1. After press a sign up button, new users will provide basic information (user name, age, gender etc.) and some security questions. They will also have to accept the privacy policy and the "terms and conditions" of using the MyHealthAvatar platform. 2. Upon log in, users will be able to access the system 3. Users will be able to perform the system operations (e.g. data browsing, sharing etc.) Privacy policy setting 1. Successful Log-In (or New account creation) by using Username or Email and Password 2. Click Accept/Revise link named "Privacy and Informed Consent" of your Avatar 3. The Privacy and Informed Consent description with checkboxes is		

	shown. 4. End User has the option to select any checkbox according his/her preferences 5. End User has the option to "Edit", "Save" and "Print" the Accepted "Privacy and Informed Consent" preferences. Note: the sign up interface for patients and doctors will be slightly different.	
Alternate Flows:	*n/a*	
Postconditions:	*N/a*	
Dependencies:	*n/a*	
Required External Resources:	[ ] Data, please specify:	n/a
	[ ] Tools, please specify:	n/a
	[ ] Services, please specify:	n/a
	[ ] Models, please specify:	n/a
	[ ] Other, please specify:	n/a
How this use-case is going to be validated?		
Frequency of Use:		
Who are the users?	*Two types of users: Type 1: Patients/citizens* *Type 2: doctors/medical researchers*	
Special Requirements:		
Assumptions:		
Questions:		

Avatar Visualization (UC-3DS)

Use Case ID:	UC-3DS		
Use Case Name:	3D Avatar Visualization		
Technical Collaborators:	BED	**Clinical Collaborator:**	USAAR
Description:	MyHealthAvatar platform would propose an avatar - a 3D representation of the human body - to allow End Users (e.g. patients, doctors) to visualize patient medical records in a new way. The avatar will be used as a means for presenting general medical knowledge to the citizen users. Users will be able to select individual parts and see related medical information such as anatomy. The information may also include medicine and food. Some individualization of the 3D model is desirable.		

	 **3D Avatar View** *Centre for Computer Graphics & Visualisation University of Bedfordshire, UK* *(18-19 February 2014, Luton Meeting)*
Actors:	*This will be mainly for citizens/patients to view their own data* *The doctors can also load the avatars from their patients to see patient data*
Trigger:	*n/a*
Preconditions:	*n/a*
Successful End condition	*n/a*
Fail End condition	*n/a*
Basic Flow:	The basic steps are: 1. Successful Log-In (or New account creation) by using Username or Email and Password 2. Select your Avatar 3. Click on different parts of the 3-D Avatar of the human body (e.g. kidney) 4. See all the available medical history and information related to that patient's parts of the human body (e.g. text entries, EHR, lab results and/or medical images). 5. Browse the available information with ability to Add, Edit, Save, Change the Privacy Settings, or Delete the existing entries. 6. End messages (e.g. "Success", "Error") in case of any of the above performed actions. 7. Log-Out option with related message
Alternate Flows:	*n/a*
Postconditions:	*N/a*
Dependencies:	*n/a*
Required External	[ ] Data, please specify: n/a

Resources:		
	[ ] Tools, please specify:	n/a
	[ ] Services, please specify:	n/a
	[ ] Models, please specify:	n/a
	[ ] Other, please specify:	n/a
How this use-case is going to be validated?		
Frequency of Use:		
Who are the users?	*This will be mainly for citizens/patients to view their own data* *The doctors can also load the avatars from their patients to see patient data*	
Special Requirements:		
Assumptions:		
Questions:		

MHA Data Browse (UC-DB)

Use Case ID:	UC-DB		
Use Case Name:	MHA Data Browse		
Technical Collaborators:	BED, LIN, FORTH, ICCS	**Clinical Collaborator:**	USAAR
Description:	Upon log in to their own account, users will be able to browse their own data, including all the personal health status data collected through the avatar system, plus medical records and clinical data from the hospitals The avatar system will need to offer tools that support effective data query and search, such as filtering. The 4D avatar will play an important role in presenting the data. Users will be able to select individual parts of the avatar body to view the data associated to the selected parts. Different colours or textures will be assigned to individual parts of the 4D avatar to represent their health status. For example, if the heart has a serious problem it will be highlighted using a unique colour or texture Patients/citizens will use the data browser to view their own data; Doctors will be able to view data from all his/her patients connected to the avatar. The avatar system will also need tools which will help users to analyze medical images		
Actors:	*Patients/citizens will use the data browser to view their own data* *Doctors will be able to view data from all his/her patients connected to the avatar.*		
Trigger:	*n/a*		
Preconditions:	*n/a*		
Successful End condition	*n/a*		
Fail End condition	*n/a*		
Basic Flow:	The basic steps are: 1. Successful Log-In (or New account creation) by using Username		

	and Password 2. Use user interface (menus, dialog boxes etc) to view data 3. Allow to use filters for data selection 4. Allow data presentation at different level of details (e.g. use small text box, large textbox, or even open a new page) 5. View health status through the colours/textures of the 4D avatar 6. Click on individual parts of the avatar to view relevant data 7. For image data browsing: • Select a set of medical images within the avatar • Load and Browse the selected images • Allow zoom in/out at particular areas of the images • Indicate the images at corresponding part of the avatar body • Perform basic image processing, such as Image filtering, and enhancement, etc. • Perform segmentation of region of interests (lesions or anatomies) on selected images	
Alternate Flows:	*n/a*	
Postconditions:	*N/a*	
Dependencies:	*n/a*	
Required External Resources:	[ ] Data, please specify:	n/a
	[ ] Tools, please specify:	n/a
	[ ] Services, please specify:	n/a
	[ ] Models, please specify:	n/a
	[ ] Other, please specify:	n/a
How this use-case is going to be validated?		
Frequency of Use:		
Who are the users?	*Patients/citizens will use the data browser to view their own data* *Doctors will be able to view data from all his/her patients connected to the avatar.*	
Special Requirements:		
Assumptions:		
Questions:		

MHA Virtual Community (UC-VC)

Use Case ID:	UC-VC		
Use Case Name:	MHA Virtual Community		
Technical Collaborators:	BED, FORTH	**Clinical Collaborator:**	USAAR
Description:	This case describes the search framework from end-users' perspective and it is focused on listing all MHA registered end-users with ability to apply advanced search filters: • Age • Gender		

	• Votes (Likes) • Treatment • Symptom • Interests • Country • City • etc. It is important to mention that every end-user should confirm the possibility to visualize his/her profile publically or privately. Only public profiles should be visible in search results. Additionally, the search function is suggested to be accessible only for end-users with public profiles. This case also provides a social media that allows patients to build up a virtual community by sharing their daily activities (e.g. how many exercises they have done), exchanging their experiences. It should also provide a link to Facebook/Twitter. The social media service will be used to allow the interconnection of end users. This social media service, accessible by smart phones, will be used in a dual mode allowing the users to insert information about themselves (like they do in common social media technologies) but also will be a mean of supporting personalized services to them from the system in the form of alerts and guidance (i.e. post therapy monitoring of user's behaviours after orthopaedics operation, cancer patients reaction to treatment, etc.). More specifically, patients will be able to 1) Find patients with similar condition, symptom and treatments 2) Find out symptoms and treatment for their conditions by looking at other fellow patients 3) Find out possible conditions for their symptoms by looking at other fellow patients *4)* Find out possible treatments for their conditions by looking at other fellow patients *5)* Find out "friends" and allow "followers" as in Facebook/Twitter *6*) Share activities, exercise experiences etc with friends and followers. End User has the related tools in the frames of MyHealthAvatar platform to collect, save and share data from third party social networks (Facebook, Twitter, etc.). The interface allows the End Users to attach to his/her own Avatar his/her own Facebook and/or Twitter account. The End-User's Avatar will have the frames to show the last updates, status messages or short texts from the related Facebook and/or Twitter accounts. The Avatar (End-User) has the option to share data to the added (only own!) Twitter and/or Facebook channels
Actors:	*Patients/citizens will use this to build patient communities* *Doctors can also have the option to join in the patient communities*
Trigger:	*n/a*
Preconditions:	*n/a*
Successful End condition	*n/a*
Fail End condition	*n/a*
Basic Flow:	*Upon* successful Log-In (or New account creation) by using Username and Password, users will be able to carry out search among all the users of the

	avatar system for the following purposes: 8. Search for patients with specific conditions, symptoms and treatments 9. Find out symptoms and treatments for specific conditions 10. Find out conditions from specific symptoms. 11. Search for treatments for specific conditions 12. Find out "friends" and allow "followers" as in Facebook/Twitter 13. Share activities, exercise experiences etc with friends and followers.	
Alternate Flows:	*n/a*	
Postconditions:	*n/a*	
Dependencies:	*n/a*	
Required External Resources:	[ ] Data, please specify:	n/a
	[ ] Tools, please specify:	n/a
	[ ] Services, please specify:	n/a
	[ ] Models, please specify:	n/a
	[ ] Other, please specify:	n/a
How this use-case is going to be validated?		
Frequency of Use:		
Who are the users?	*Patients/citizens will use this to build patient communities* *Doctors can also have the option to join in the patient communities*	
Special Requirements:		
Assumptions:		
Questions:		

Self Data Collection (UC-DCU)

Use Case ID:	UC-DCU		
Use Case Name:	Self Data Collection		
Technical Collaborators:	BED, FORTH	**Clinical Collaborator:**	USAAR
Description:	This case seeks new solutions for increasing the quality and sustainability of future healthcare systems by actively engaging citizens in monitoring their own health through self collection of lifelogging data. The development and treatment of many diseases are affected by our life styles and environment. A long term monitoring of these factors, especially through the self-involvement of patients, is extremely valuable in supporting individualised health prediction and treatment. Many studies have shown compelling needs in self-lifelogging and self monitoring of patients, which has great potential in leading to preventive medicine, cost saving and enhanced quality in future healthcare. We aim to create a symbiotic relationship of available technology today and MyHealthAvatar platform. The goal is to respond to the fast growing		

	demand for developing new technologies and services for self monitoring for supporting wellness, fitness and prevention of the most common chronic diseases (i.e. cardio-vascular and stroke, diabetes, rheumatic problems, respiratory problems and COPD, etc.). Mobile applications will monitor user's "health-status", "lifestyle" and "wellness" and upload data to the MyHealthAvatar system for close monitoring of health conditions and prevention of many diseases. The system then will be able to analyse user's lifestyle and medical data. Special "alerts" will be applied to support end users with feedback supporting and assisting their daily activities and well-being. An interface for patients writing a diary is very helpful to collect patient specific data related to their disease. This can be partly structured: e.g. body weight, heart rate, blood pressure, temperature, medicine taken, etc. It can also include structured data of scoring systems, e.g. physical and/or psychological and/or emotional status. In addition free text entry needs to be allowed. More specifically, we explores various ways for the data collection in the avatar to monitor users' health-status, lifestyle and wellness. These include: • Web interface for data entry • Sensors (e.g. blood glucose, blood pressure, heart rate, locations, steps, sleep) • Mobile apps For example, users uses a glucose meter and MyHealthAvatar platform to monitor his/her blood sugar levels. The data is saved that maintains the Avatar's long-term history and looks for possible abnormal events. If the saved data is unusual, or the End-User skips a test, the MyHealthAvatar platform automatically generates an alert message Mobile apps will be used to monitor the health status of the users (e.g. mood, food). We will also explore the possibility to extract health related information from electronic cards (e.g. purchase of food and drink, daily exercises in gyms), as well as from social network. We will also look into the possibility of implementing an advanced Patient Devices Software Development Kit (SDK or "devkit"). A SDK will represent a set of software development tools that will allow healthcare it professionals the creation of applications for MHA able to access and strore data from any patient monitoring device. Patient Devices SDK may be something as simple as an application programming interface (API) in the form of some files to interface to a particular programming language or include sophisticated hardware to communicate with MHA platform. SDK may also include sample code and supporting technical notes or other supporting documentation to help clarify points from the primary reference material.
Actors:	*Patients/citizens*
Trigger:	*n/a*
Preconditions:	*n/a*
Successful End condition	*n/a*
Fail End condition	*n/a*
Basic Flow:	The basic steps are: For manual data entry: • Successful Log-In (or New account creation) by using Username and Password • Click relevant section from your Avatar

	• The interface is shown with ability to enter and or visualize data by date, week, month, year. • End User has the option to select any date or any diary entry with possibility to update it (in case of updates the update date is shown) • Some diary entries could be in linkage with avatar appearance. • End User has the option to "Edit", "Save", "Print" or "Share" the Diary info. For automatic data collection 1. Login in and select "remote monitoring devices" 2. End-User has the option to "Add" the monitoring device, at the initial stage only a glucose meter could be added 3. The monitoring devices parameters (Bluetooth or USB) are settled. 4. Users should be able to switch on/off the automatic data collection 5. User has the option to visualize the collected data 6. Collected data could change the appearance of the Avatar and/or alert messages are sent if the End-User skipped a test	
Alternate Flows:	*n/a*	
Postconditions:	*N/a*	
Dependencies:	*n/a*	
Required External Resources:	[ ] Data, please specify:	n/a
	[ ] Tools, please specify:	n/a
	[ ] Services, please specify:	n/a
	[ ] Models, please specify:	n/a
	[ ] Other, please specify:	n/a
How this use-case is going to be validated?		
Frequency of Use:		
Who are the users?	*Citizens/patients*	
Special Requirements:		
Assumptions:		
Questions:		

MHA Toolbox (UC-TOOL)

Use Case ID:	UC-TOOL		
Use Case Name:	MyHealthAvatar Toolbox		
Technical Collaborators:	ICCS, FORTH	**Clinical Collaborator:**	USSAR
Description:	**<u>Remote Monitoring</u>** The Remote Monitoring tool/frame collects and processes patient care information from supported healthcare devices that conform to standards (preferably selected by the Continua Health Alliance). End User uses a glucose meter and MyHealthAvatar platform to monitor		

	his/her blood sugar levels. The MyHealthAvatar platform reminds to check the blood sugar regularly during the day, and the glucose meter should be able seamlessly to transmit the measurements to the Avatar after each use. The data is saved that maintains the Avatar's long-term history and looks for possible abnormal events. If the saved data is unusual, or the End-User skips a test, the MyHealthAvatar platform automatically generates an alert message. The monitoring data will be made available through the citizen self-monitoring case (which is another use case). To allow for remote monitoring from the doctors using the avatar system, we need to link the avatar system to the hospital information system (which is again another use case). This will subsequently allow the transfer of the avatar data into the hospital records. **Simulation** End-User has the GUIs, functionalities and tools in the frames of MyHealthAvatar platform to create and execute a biological simulation scenario. End-User selects one of the biological simulation models available in the Model Repository and one of the sets of clinical data available in the Clinical Data Repository (or uploads a set from his computer). Afterwards he/she executes a biological simulation. Finally he/she retrieves the results of the simulation and proceeds to their evaluation. **Knowledge discovery** Patients are interested in the most recent and personalized information about their disease, treatment and prognosis. MHA platform could contain a ontology-based Knowledge Discovery (KD) module able to connects highly heterogeneous data and textual information. The semantic framework could be based on gene, tissue, disease and compound ontologies (important for drugs and clinical research frames). This framework could contain information from different organisms, platforms, data types and research areas that is integrated into and correlated within a single searchable environment using search algorithms. It could provide a unified interface for all MHA users to formulate, explore and identify new information (according to specific preferences and needs) across vast collections of available experimental and research data. KD module could combine classical keyword-based search with text-mining and ontologies to navigate large results sets (internal & external) and facilitate information and/or knowledge discovery. End users could be provided with an advanced ontology based (Gene Ontology (GO) and Medical Subject Headings (MeSH)) 'Table of Contents' in order to access, explore, structure (quickly) the millions of available resources (PubMed abstracts, news, clinical trials info) according to the predefined topics of interest (Allergy, Cancer, etc.).
Actors:	*Remote consultation: doctors (GPs) and patients* *Simulation: researchers, clinicians, patients* *Knowledge discovery: medical researchers, doctors*
Trigger:	**Simulation:** • User accesses the section "Simulation Interface". • User "clicks" on a specific area of the 3-D avatar of the human

	body, for example the kidney, is directly or indirectly (by a menu) redirected to the "Simulation Interface" and is guided to the proper biological simulation model/-s (for example the kidney simulation model/-s
Preconditions:	**Simulation:** • The User has to Log-in or to create a New Account (New Avatar). • The option to "perform simulations using biological models" must be enabled in the user's profile. • The user must have the proper access rights in order to use a biological simulation model from the Model Repository. • The biological simulation model must be already imported to the Model Repository. • The user must have the proper access rights in order to use a set of clinical data from the Clinical Data Repository. • The clinical data that the biological simulation model needs in order to run must be already imported into the Clinical Data Repository or it must be provided (uploaded) by the user just before the start of the simulation. • The clinical data must be compatible, in terms of format and content, with the selected biological simulation model. • The user must have the proper access rights to a computational platform. • The computational platform must have enough available resources in order for the simulation to be performed successfully
Successful End condition	*n/a*
Fail End condition	*n/a*
Basic Flow:	The basic steps in case of **simulation** are: 1. Successful Log-In (or New account creation) by using Username or Email and Password. 2. Select the Avatar. 3. The flow ends here if the End-User doesn't have the option "Perform simulations using biological models" enabled. 4. The flow continues if the End-User has the option "Perform simulations using biological models" enabled. 5. End-User creates a biological simulation scenario, by selecting a simulation model from the Model Repository and a set of data from the Clinical Data Repository. 6. End-User starts the simulation process. 7. When the simulation is completed, the proper ending code is displayed, either a success message or an erroneous message. 8. End-User user has the possibility to download the results of the simulation to his computer, either the simulation ended successful or with errors".
Alternate Flows:	The alternative flows in case of **simulation** are: 1. In step 5 of the basic flow, the selection of the simulation model can be guided by narrowing the available simulation models to only the ones related to a specific part of the human body, by clicking on the 3-D representation of human body. *2.* In step 6 of basic flow, End-User can upload a set of data from his computer instead of using a set of data provided by the Clinical Data Repository
Postconditions:	*N/a*
Dependencies:	**Simulation:**

	• The option to perform simulations using biological models must be enabled in the user's profile. • The user must have the proper access rights to the Model Repository. • The user must have the proper access rights to the Clinical data repository. • The user must have the proper access rights to a Computational Platform.	
Required External Resources:	[ ] Data, please specify:	Clinical data (already preprocessed), ready to be used by the simulation models
	[ ] Tools, please specify:	• Model Repository • Clinical Data Repository (related to simulation models)
	[ ] Services, please specify:	• Query the Model Repository for available models. • Query the Clinical Data Repository (related to biological simulation models). • Copy a selected model to the computational platform. • Copy a set of selected preprocessed data to the computational platform. • Execute the simulation scenario (by sending a computational job to the computational platform). • Retrieve the result of the execution of a simulation model.
	[ ] Models, please specify:	Simulation Models
	[ ] Other, please specify:	Computational Platform: Can be either a personal computer, a cloud virtual machine, a High Performance Computer (HPC) or any other system able to perform computational simulations.
How this use-case is going to be validated?		
Frequency of Use:	*Medium*	
Who are the users?	*Remote consultation: doctors (GPs) and patients* *Simulation: researchers, clinicians, patients* *Knowledge discovery: medical researchers, doctors*	
Special Requirements:		
Assumptions:	**Simulation:** • The biological simulation model is already imported in the model repository. • A set of clinical data compatible with the aforementioned	

	biological simulation model is already imported in the clinical data repository. • Appropriate computational resources are available for running the simulation. • The security framework is responsible for controlling the access to the model repository, the clinical data repository and the computational platform.
Questions:	Although the biological simulation model (nephroblastoma) planned to be used in the MyHealthAvatar demonstrator doesn't use proprietary software, what if a model uses proprietary software, like a model developed in Matlab (licensing issues)?

Link MHA to HIS and CTMS (UC-HIS)

Use Case ID:	UC-HIS		
Use Case Name:	Link MHA to HIS (Hospital Management System) and CTMS (Clinical Trials Management System)		
Technical Collaborators:	FORTH, ICCS	**Clinical Collaborator:**	USAAR
Description:	End User has the GUIs, functionalities and tools in the frames of MyHealthAvatar platform to enter, import, store and export personal medical data with hospital information systems. One option is to use ObTiMA as a dummy system to mimic external hospital system. ObTiMA, an ontology-based clinical trial management system, has been developed 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) project. ObTiMA has a modular architecture with a core basic module for data management of clinical trials. Different other modules are under development in the frames of p-medicine project. The data stored in ObTiMA are relevant for the Health Avatar to enhance the system with relevant clinical trial data. On the other hand the info stored in MHA might be of relevance for a clinical trial. As result, the bidirectional data upload from MHA to ObTiMA is needed. This Scenario / Use Case describes the bilateral linkage between ObTiMA and MHA by being focused on the Operational Data Model (ODM). There are also a few other dummy systems available at FORTH, which can be used to mimic the external hospital system.		
Actors:	*Patients/citizens will see their own health records from the hospitals* *Doctors will be able to see patient data in their avatars*		
Trigger:	*n/a*		
Preconditions:	*n/a*		
Successful End condition	*n/a*		
Fail End condition	*n/a*		
Basic Flow:	The basic steps are: • Access the data export/import interface • Specify data export/import from ObTiMA (or other dummy systems)		

	• Specify data export/import from MHA • Confirmation message of data/export	
Alternate Flows:	*n/a*	
Postconditions:	*N/a*	
Dependencies:	*n/a*	
Required External Resources:	[ ] Data, please specify:	eCRF with filed in data from ObTiMA Health Avatar with clinical trial related data (i.e. laboratory results, pre-operative state, etc.)
	[ ] Tools, please specify:	ObTiMA platform
	[ ] Services, please specify:	n/a
	[ ] Models, please specify:	The Operational Data Model (ODM) is designed to facilitate the archive and interchange of the metadata and data for clinical research, its power being fully unleashed when data are collected from multiple sources.
	[ ] Other, please specify:	n/a
How this use-case is going to be validated?		
Frequency of Use:		
Who are the users?	*Patients/citizens will see their own health records from the hospitals* *Doctors will be able to see patient data in their avatars*	
Special Requirements:		
Assumptions:		
Questions:		

Personalized CHF Related Risk Profiles and "Real-Time Monitoring" Services (UC-CHF)

Use Case ID:	UC-CHF		
Use Case Name:	Personalized CHF Related Risk Profiles and "Real-Time Monitoring" Services		
Technical Collaborators:	FORTH	**Clinical Collaborator:**	University of Crete, Faculty of Medicine
Description:	A major challenge related to caring for patients with chronic conditions is the early detection of exacerbations of the disease that may be of great significance. In this scenario we focus on methodologies that would facilitate the prevention, monitoring, and treatment of heart disease on a daily basis. Generally, cardiovascular disorders as chronic diseases require a continuous everyday record for patient's status. The proposed scenario is built on the following pillars:		

	1) Real-time patient monitoring In addition to the above the dedicated clinical personnel should be contacted immediately and possibly intervene in time before an acute state is reached, by changing medication, or any other interventions, in order to ensure patient safety. There is a need to support real-time remote monitoring of patients diagnosed with congestive heart failure and MHA, enhanced with semantic technologies, may host personalized, accurate and up-to-date clinical information. To this end we built a real-time patient/ doctor alarming will be built according to rule-based alarms enabling intelligent alerting of the dedicated physician in case of an emergency. The alarming process will be based on vital signs monitoring and specifically Heart Rate (HR), Pulse Oximetry, and Blood Pressure acquisition, adapted according each specific patient's medical history and age, and even risk predictor's outcome (described below). *2) CHF Risk Assessment* In order to tailor the proposed system to the patient's profile and assist physicians in selecting people who are predisposed by coronary disease, hypertension, or valvular heart disease; we build a CHF related risk profile based on a risk appraisal function that is based on the diagnostic criteria [i.e. the Framingham Heart Study (486 heart failure cases during 38 years of follow-up)]. The predictors used are based on Age, Coronary heart disease and Valve disease status provided by the patient Electronic Health Record (EHR), as well as on HR, on blood pressure and on Body Mass Index (BMI) provided by the pulse oximeter, the blood pressure monitor and the weight scale, respectively. The calculated risk probability may be used to alter the default threshold values (higher risk probability adds more constraint on the physiological patterns). Furthermore, we present what else data regarding patients' health status could be embed into the platform towards the creation of a profile with necessary information for both patient and treating physicians. To this respect an approach of presenting data regarding demographic, physiology, diagnostic test results and disease management (i.e. prescribed drugs) is provided. *3) Comorbidities and Drug Interaction* There are many cases where more than one medications are prescribed due to disease progression or due to the wide appearance of both cardiac and non-cardiac co-morbidities (respiratory comorbidities, renal dysfunction, cognitive dysfunction, depression and in some cases arthritis). To this respect, there is an urgent need for providing information in both the treating physicians, but also the patient him/ herself regarding negative drug interactions.
Actors:	Avatar1 (Doctor), Avatar2 (Patient)
Trigger:	Patient is diagnosed with CHF according to: • Patient's physiological, imaging, blood test results data and past diagnoses, uploaded in patient's electronic health record or during creation of patient's Avatar in MHA platform. • Patient physical examination and confirmation with differentiating diagnostic tests (i.e. echocardiography)
Preconditions:	The major precursor of all cardiovascular diseases is attributed in congenital or acquired factors that lead to atherosclerosis disorders and in some cases to complications from diabetes, kidney disease and hypercholasterolaemia. Heart failure is caused by any condition, which reduces the efficiency of the myocardium, or heart muscle, through damage or overloading. As such, it can be caused by a diverse array of conditions, including myocardial infarction (in

	which the heart muscle is starved of oxygen and dies), hypertension (which increases the force of contraction needed to pump blood) and amyloidosis (in which protein is deposited in the heart muscle, causing it to stiffen).
Basic Flow:	Basic steps 1. Generation of patient's avatar o Register life style factors (i.e. diet habit, alcohol, smoking) o Register of physiology, pathology, genetic information (i.e. pharmacogenomics) regarding patient's health ▪ Age ▪ Height ▪ Weight ▪ Body Mass Index(BMI)/Body Surface Area (BSA) ▪ Blood pressure ▪ Pulse (possible need for creating time graphs) o Register life style factors (i.e. diet habit, alcohol, smoking physical activity) 2. Embed in Avatar platform of patient's examination results o Update of patient's basic examination outputs regarding cardiovascular system (blood test results, blood pressure, EEG results, imaging and physical exam) 3. Diagnosis of the heart failure and classification of patient according to one (or if possible more) categories (i.e. Framingham and or NYHA) o Matching of possible co-morbidities or setting alarms for possible complications due to disease progression (i.e. kidney function) 4. Record of patient's drug prescription (dose regiments) provided by the treating physician 5. Record of patient's compliance regarding provided treatment o Update avatar during last drug prescription for other diseases and alarm for possible interactions between medications (i.e. antibiotic medicines that could interact with cardiovascular treatments) 6. Real-time patient vital signs and data updates (if available) and processing to detect possible deviations from normal values
Alternate Flows:	Alternative flows will be followed if patient data are not provided in full.
Postconditions:	• Remote monitoring of patient health status after diagnosis. • Risk assessment and update data in MHA platform. o Creation of graphs with data values in time (i.e. BP, pulse, time of drug administration etc.) • Basic information for patient regarding health status during treatment. • Information regarding administration of other medications prescribed regarding drug-drug interactions and also in cases of over-the-counter medication that can be taken from the patient etc.
Dependencies:	This case tries to integrate information from the potential architecture of the platform including data from ontologies (linking of information regarding disease progression, side effects, drug interactions, genomic data, environmental factors, regulatory organizations guidance etc.) This use case includes or is part of the following use cases: • Utilization of personal genomic information for the individualization of MHA platform • Decision making tools regarding emergency situations in clinical practice. The example of anti-platelet & anticoagulation therapy in the

<table>
<tr><td></td><td colspan="2">pre-operative patients
To achieve a good functionality as proposed in this set the following device and technologies should also be available:
• Wireless or wearable medical devices and sensors acquiring patient's vital signs. In our reference implementation the supported measurements are:
○ Heart Rate (HR), SpO2, body weight and real time ECG monitoring.
• Monitoring application recording the aforementioned bio signals and hosting risk assessment algorithms to enable the alerting process.
• Ontology-driven application intelligence capable of reasoning on the patient's and drug data.</td></tr>
<tr><td rowspan="2">Required External Resources:</td><td>[ ] Data, please specify:</td><td>• Patient's data
○ Demographic
▪ Gender
▪ Age
▪ Height
▪ Weight
▪ BMI/BSA
○ Genetic
▪ CHF related genome data
▪ Pharmacogenomic data
○ Physiology- Pathology
▪ Blood pressure
▪ Cardiac flow (BP and pulse)
▪ Kidney function
▪ Blood test results
▪ Coagulation factors
▪ Atherosclerosis level
• Differentiating tests
• Associated diseases
• Physical examination
• Imaging
• Electrocardiography
• Echocardiogram
• Protocols/References regarding disease diagnosis/treatment
○ Available regimens for prescription and potential alternatives
○ Medline references
○ Patients hand out from regulatory organizations for disease management</td></tr>
<tr><td>[ ] Tools, please specify:</td><td>For Physician
• PC hosting MHA platform with access to EHR
• Links of Avatar's internal organs with diagnostic tools (i.e. linking of heart with ultra-sound image of the patient or ECG)
• Medline references
○ i.e. drug interactions</td></tr>
</table>

		• Availability to store part of the data as case study For Patient • PC hosting MHA platform with access to EHR • Smartphone with MHA interface capable of updating necessary data (i.e. daily diet) • Wireless vital signs monitoring devices Information on disease progression with/without compliance (i.e. visualization of heart function)
	[ ] Services, please specify:	Links with EHR and PACS Links with external databases (i.e. DrugBank)
	[ ] Models, please specify:	1. Risk Assessment model 2. Real Time Alarming model 3. Visualization models 4. Disease progression models
	[ ] Other, please specify:	
Frequency of Use:	The proposed application can be used even in real time or selected time intervals, depending on the patient's initial diagnosis. Frequency of use can be categorized in two parts: 1) Patient's information regarding health status, disease progression, improvement etc. 2) Any treating physician which is going to prescribe a specific treatment for the patient and has access to MHA platform	
Special Requirements:	Familiarity of doctors and generally of the medical staff with MHA technologies Linking of MHA data between research and medical organizations and personnel applying MHA technological tools and services.	
Assumptions:	Some basic assumptions are: • Necessary physiological and clinical data to run the model. • Detailed patient's health history record • Linking of MHA platform with hospitals as well as research institutions that contribute in the health care system • Linking of the platform with external resources for providing information regarding CHF diagnosis and treatment • Monitoring Devices/ Sensors, if available • Patient's compliance in keeping update information in MHA platform • Doctor's compliance in updating patient's examination info in MHA platform • Full and detailed patient's health history record.	
Questions:		

Osteoarthritis (UC-OST)

Use Case ID:	*UC-OST*		
Use Case Name:	Osteoarthritis		
Technical Collaborators:	FORTH	**Clinical Collaborator:**	University of Crete,

			Faculty of Medicine
Description:	Osteoarthritis (OA) is a disabling degenerative joint disease leading to joint pain, stiffness and loss of function predominantly in the knees, hips, hands, and spine. The major histological finding in OA is degeneration and loss of the articular cartilage that acts as a protective cushion between bones within a joint. Imaging methods including weight bearing radiographs and in selected cases Magnetic Resonance Imaging (MRI,) may be used to study morphological and inflammatory changes occurring in the articular cartilage, menisci, extra-articular soft tissues and the subchondral bone marrow. Health care professionals support assessment and management of patients with OA in order to modify their nutrition and exercise lifestyle behaviour. Hereditary factors (genetic) increase the risk for developing OA. It is worth pointing out that an estimated 75% of adults over the age of 65 years have OA resulting to impaired quality of life, and considerable healthcare costs. Moreover, about 100% of adults over the age of 80 years old have OA. The avatar system will monitor patient's daily diary and ambulatory activity and warn the patient, if she/he does not meet the special medical guidelines. The monitoring will rely on techniques of self-life logging, enhancing the patient engagement. Also, the platform will function as a supportive system to the patients by means of offering advice and assistance. Moreover, the avatar system will offer a useful input to doctors, as the related heterogeneous data (i.e. imaging and semi-quantitative data) will be properly visualized and presented using interactive, multi-scale visualization techniques. This will help doctors for data reasoning and for carrying out personalized healthcare. Advanced personalized healthcare will also be enhanced by existing genomic predisposition evaluation and health risk estimation. Thus, this use case is strongly related with the UC-09 (MHA Personal Genomic Information).		
Actors:	*Doctors and citizens/patients*		
Trigger:	1. *A citizen is diagnosed with Osteoarthritis* 2. *Avatar platform reveals for a citizen an increased risk of developing OA*		
Preconditions:	*n/a*		
Successful End condition	*n/a*		
Fail End condition	*n/a*		
Basic Flow:	1. The patient visits the doctor complaining for knee joint pain, stiffness, particularly after rest, crepitus, and swelling (soft from joint effusion or hard from osteophyte formation). The diagnosis of OA is based on the: a. History including pre-existing disorders such as previous		

	serious injury, b. Clinical examination, c. Imaging studies, primarily radiographs and in some cases MRI, d. Additional semi-quantitative metrics are collected for diagnosis and follow up: • A number recorded with regard to a certain pain-scale • Range of motion of the knee joint (in degrees), e. Genetic predisposition evaluation for examining if an increased risk of developing OA exists (according to available genomic data). The above data, imaging and evaluation metrics, are collected and stored through the avatar system, which has novel ways for representing this multi-scale and heterogeneous information to medical professionals. **Self-care:** The treatment includes drugs and in more severe cases local injections, use of knee braces and knee replacement surgery. In addition, the doctor advices patient to modify or change the lifestyle. This includes weight reduction, exercise (quadriceps muscle strengthening, resistance training, aerobic exercise-walking, and flexibility exercise) and aquatic exercise. Too little movement can lead to stiffness and weak joints, whereas strong muscles protect joints. An OA management plan also involves following a healthy diet, managing stress and depression, and getting a good balance of rest and activity each day. **Monitoring:** The avatar system will monitor patient's daily dietary and ambulatory activity (using activity trackers) and warn the patient, if he does not meet the special medical guidelines (e.g. losing weight, exercise etc.). The monitoring will rely on techniques of self-life logging, which will monitor a wide range of daily activities and behaviours of the patients, including their locations, movements, diet, quality of life, environment, and other symptoms, etc. Visual analytics will be used to display individual/aggregated data items to allow easy interpretation of the data from the patients. With the search bar of the system, the users can easily send queries about their activities, movements, diet, etc. **Patient education:** The avatar system will also allow patient education on the knowledge of the diseases. It will also test the knowledge of the patients. It is expected that a good knowledge of the disease will lead to enhanced patient behaviours. 2. The patient visits the doctor again complaining for recurrence and deterioration of symptoms. a. The semi-quantitative metrics are collected again and compared with the previous ones stored through the avatar system. b. A new weight baring radiograph is taken.

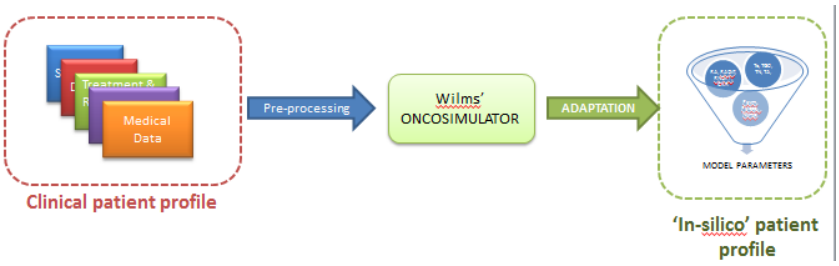
	c. The doctor examines if the patient was compliant with the treatment guidelines. If the radiograph reveals severe structural changes, the doctor will discuss the surgical replacement of the joint. If the radiographic findings do not explain the clinical symptoms, a new MRI is required to explore other than internal derangement causes, such as insufficiency fracture of the subchondral bone. Due to the temporal nature of the data the representation is obtained by "animating" the visualization over time. Each frame will display the value of each parameter at a given time point.	
Alternate Flows:	1. *Avatar system reveals for a citizen an increased risk of developing OA through comparison to existing genomic predisposition data and warns the patient.* 2. *Avatar system advices citizen to modify or change his lifestyle. This includes weight reduction, exercise (quadriceps muscle strengthening, resistance training, aerobic exercise-walking, and flexibility exercise) and aquatic exercise.*	
Postconditions:	-	
Dependencies:		
Required External Resources:	[ ] Data, please specify:	• Patients' data from MyHealthAvatar, including patient's history, imaging data, genomic data, semi-quantitative metrics, daily activities, exercises, diet over the time
	[ ] Tools, please specify:	• Multi-scale visualization & visual analytics tools for the visual representation of the multi-scale, heterogeneous data related to OA • Genomic analysis tools for evaluating the genomic predisposition and health risk
	[ ] Services, please specify:	• Links to data repository for retrieving the patients' clinical data
	[ ] Models, please specify:	•
	[ ] Other, please specify:	• Visualization server for performing the multi-scale data representation: can be either a personal computer or a high performance computer
How this use-case is going to be validated?	*By citizens with OA and medical experts*	
Frequency of Use:	*When a citizen is diagnosed with OA or has an increased risk of developing OA*	
Who are the users?	*Doctors and citizens/patients*	
Special Requirements:	-	
Assumptions:	-	
Questions:	-	

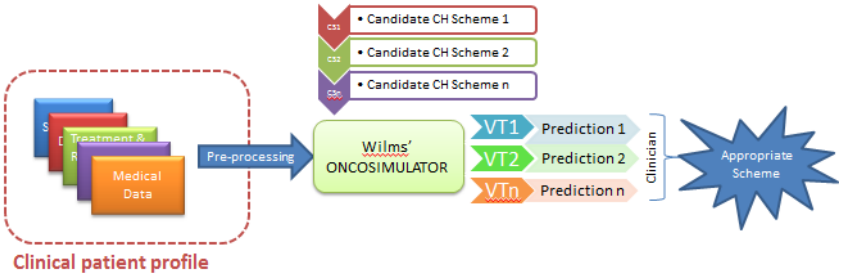
Pre-Diabetes (UC-DIAB)

Use Case ID:	UC-DIAB		
Use Case Name:	Pre-Diabetes		
Technical Collaborators:	BED	**Clinical Collaborator:**	
Description:	Diabetes is the world's fastest growing disease with substantial costs at individual and social economic level. It is estimated diabetes affect more than 32 million EU citizens (nearly 10% of the total EU population), and an additional 32 million citizens have not yet been diagnosed, or with pre-diabetes. Globally, the main risk factors for chronic disease, such as diabetes, are hypertension, tobacco use, high cholesterol, low fruit and vegetable intake, overweight and obesity, sedentary lifestyle and alcohol abuse. Strategies for tracking chronic disease include prevention and early detection; people with high risk of developing diabetes are suggested to carry out many self-care behaviours. These include dietary change, exercise, regular self-medication , and regular attendance at clinic and for screening programmes. If diagnosed with diabetes, additional care, such as insulin injection, self-manage of blood glucose, and insulin dose adjustment are needed. Self-management means that people can take a more active role in decisions about their own treatment and about healthy lifestyle. It is a shared responsibility between individuals and service provider. Service providers recognise the individual's role in managing their health and well-being. MyHealthAvatar provides a unique citizen/patient empowered system that can be used, in particular for pre-diabetes care where the citizens with high risk of diabetes but not yet been diagnosed, and therefore not yet been known to the health care system. The functionalities of MyHealthAvatar provides a one-stop service for citizens in terms of data collection, and self-management services, such as monitor, record, and education. The avatar system will support the storage the behaviours and daily activities of citizen. The platform will function as a supportive environment from healthcare providers to the individual by means of offering advice, assistance and assessments; and by means of allowing for health promotion.		
Actors:	Doctors and citizen/patient		
Trigger:	Citizen takes risk analysis, and has been predicted with high risk		
Preconditions:			
Successful End condition			
Fail End condition	-		
Basic Flow:	The avatar system will include: • **Personal Diary:** Storage and management of the health status of the individual and their behaviours. This will rely on techniques of self-lifelogging, which will monitor a wide range of daily activities and behaviours of the citizen/patient, including their locations, movements, diet, quality of life, environment, mood, blood pressure, glucose, alcohol, smoking, and other symptoms, etc. Visual analytics will be used to display individual/aggregated data items to allow easy interpretation of the data from the patients. With the search bar of the system, the users can easily send		

	queries about their activities, movements, diet, etc. • **Intervention:** allowing for multi-modal intervention of lifestyle in a shared decision manner between the doctor and citizens/patients. In the case of pre-diabetes, MyHealthAvatar will be able to demonstrate to the citizens/patients the relations between the outcomes of the self-management/treatment using prediction models. . "Behaviour prescription" will be issued based on clinical guidelines and trusted sources (such as NICE), which is expected to include a set of targets in terms of daily activities, calorie intake and energy consumption, etc. • **Monitoring:** allowing for the progress review of the individual by comparing the personal diary with the behaviour prescription as mentioned above. • **Warning:** The avatar system will send reminder messages at various priorities in one of the following occasions: medication reminder, due hospital visit (for screening etc.), sign of change of conditions, early sign of one of developing diabetes with constant scored as high risk. • **Complication:** The avatar system will have patients' clinical records and history, which will facilitate the management of complications from other possible conditions. The long term records will also help define personalised care plan.	
Alternate Flows:	-	
Postconditions:	-	
Dependencies:	-	
Required External Resources:	[x] Data, please specify:	Citizen/Patients' data from MyHealthAvatar, including daily activities, exercises, diet, mood, etc.
	[x] Tools, please specify:	Visual analytics tools for data visualization & analysis Statistical tools for computing standard indexes & charts (e.g. BMI, SAD) Prediction tolls for 'good' or 'bad' behaviours.
	[ ] Services, please specify:	
	[x] Models, please specify:	Statistical tools for computing standard indexes & charts(e.g. BMI, SAD)
	[ ] Other, please specify:	
How this use-case is going to be validated?		
Frequency of Use:		
Who are the users?	Citizen/patients	
Special Requirements:		
Assumptions:		
Questions:		

Nephroblastoma (Wilms Tumour) Simulation Model and Clinical Trial (UC-NEPH)

Use Case ID:	UC-NEPH		
Use Case Name:	Nephroblastoma (Wilms tumour) Simulation Model and Clinical Trial: In-silico profiling of patients and prediction simulations		
Technical Collaborators:	ICCS	**Clinical Collaborator:**	USAAR
Description:	Nephroblastoma diagnosis is based on a variety of multiscale data. These data can be used in the creation of a clinical multiscale profile of the tumour. After the necessary pre-processing of the available data, the data are fed into a nephroblastoma simulation model. The nephroblastoma simulation model is a predominantly discrete, clinically-oriented multiscale model of solid tumour response to treatment. Preoperative chemotherapy is the simulated form of treatment. A ''top-down'' simulation approach is adopted. The simulation method starts from the macroscopic imaging data, representing a high biocomplexity level, and proceeds towards lower biocomplexity levels. Clinical orientation of the model has been a fundamental guiding principle throughout its development. Available medical data (imaging, histopathological, molecular) can be exploited, in order to strengthen patient individualized modeling. **Stage 1 (in-silico profile of patients):** Semi-automatic adaptation of the model parameters could be conducted in case of efficient availability of clinical data (many data sets at different time points). The determined model parameters serve as a patient record for in silico tumor characteristics and form the 'in-silico profile' of the patient.  **Stage 2 (prediction simulatations):** The paediatric oncologist using the 'in-silico profile' of the patient runs a number of experiments in silico (= on the computer), to simulate the most likely response of the tumour to the most relevant candidate chemotherapeutic schemas. The outcomes of the simulations (predictions) help the oncologist decide the appropriate treatment plan. The 'in-silico profile' could be further used from clinicians as a tool to provide insight into individualized biological characteristics of the tumor, an input for future model use and an input for the use of other models. It could also serve as a statistical tool to categorize the patients (by associating their clinical and in silico profiles) and define a range for model parameters to lead adaptations of new patients.		

	 References: • G.S.Stamatakos, E.Ch.Georgiadi, N.Graf, E.A.Kolokotroni, and D.D.Dionysiou., Exploiting Clinical Trial Data Drastically Narrows the Window of Possible Solutions to the Problem of Clinical Adaptation of a Multiscale Cancer Model. 2011, PLOS ONE • Georgiadi EC, Stamatakos GS, Graf NM, Kolokotroni EA, Dionysiou DD et al., Multilevel Cancer Modeling in the Clinical Environment: Simulating the Behaviour of Wilms Tumour in the Context of the SIOP 2001/GPOH Clinical Trial and the ACGT Project. in. : Proceedings of the 8th IEEE International Conference on Bioinformatics and Bioengineering. 8-10 Oct 2008. Athens, Greece. CFP08266, ISBN: 978-1-4244-2845-8, Library of Congress: 2008907441, Paper No. BE-2.1.2. • Graf N, Hoppe A, Georgiadi E, Belleman R, Desmedt C et al., In Silico Oncology for Clinical Decision Making in the Context of Nephroblastoma. Klinische Paediatrie , Vol. 221, pp. 141-149.
Actors:	End User & MyHealthAvatar platform
Trigger:	Stage1: Enrich the patient record with an "in silico" profile Stage2: Prognosis is needed for nephroblastoma response to treatment.
Preconditions:	• The availability of clinical data that is compatible, in terms of format and content, with the nephroblastoma simulation model. • The availability of sufficient computational resources in order for the simulation to be performed.
Successful End condition	-
Fail End condition	-
	The basic steps for stage 1 are: 1. The End-User places the already preprocessed data to the location where the model expects to find them. 2. The Technical partner adapts the model parameters according to the available clinical data 3. The End-User starts the simulation process. 4. When the simulation is completed, the End-Users use the appropriate

	tools in order to read or/and visualize the outcome of the simulation. 5. The End-Users evaluate the adaptation by comparing simulation results with clinical reality. 6. In case of a succesful adaptation, the defined model parameters are recorded by the End Users and form the "in-silico patient profile" 7. In case of not satisfying adaptation, steps 2-5 are repeated. The basic steps for stage 2 are: 1. The End-User places the already preprocessed data to the location where the model expects to find them. 2. The End-User starts the simulation process. 3. When the simulation is completed, the End-User uses the appropriate tools in order to read or/and visualize the outcome of the simulation.	
Alternate Flows:	-	
Postconditions:	Stage 1: The in-silico profile of the patient is recorded. Stage 2: A treatment plan is drawn.	
Dependencies:	This use case will be used as test case for UC-TOOL (MHA Toolbox).	
Required External Resources:	[x] Data, please specify:	Clinical data (already preprocessed), ready to be used by the simulation model. The SIOP 2001/GPOH clinical trial, including microRNA data, if available, will be used.
	[x] Tools, please specify:	Open source tools (e.g. ImageJ) can be used for visualization purposes.
	[ ] Services, please specify:	
	[ ] Models, please specify:	
	[ ] Other, please specify:	
How this use-case is going to be validated?	Technical validation of the use case will be performed by the responsible technical partner.	
Frequency of Use:	When a prognosis in needed for nephroblastoma patients.	
Who are the users?	Clinicians, Researchers	
Special Requirements:	-	
Assumptions:	-	
Questions:	-	

Emergency Contact (UC-EME)

Use Case ID:	UC-EME		
Use Case Name:	MHA Emergency Contact		
Technical Collaborators:	BED, USAAR	**Clinical Collaborator:**	USAAR

Description:	This use case describes the situation where a patient is unconscious in Accident and Emergency Units in hospitals. The patient is not able to authorize the doctors to access his data in the avatar. However, some of the information within the avatar can be crucial for the clinical decisions by the doctors. For example, the doctor needs to know a health profile of the patient, including his previous medical history, etc. We envisage a Europe-wide MHA service centre is needed to offer a solution to this case. Each avatar user will have the option to sign an agreement to authorize the data access to doctors, who may treat him/her under a future emergency circumstance. For the signed users, doctors can contact the MHA service centre to obtain their data in the MHA for the treatment purpose under an emergency situation.	
Actors:	Doctors at emergency units in hospitals Patients Worker in the MHA service centre	
Trigger:	n/a	
Preconditions:	n/a	
Successful End condition:		
Fail End condition:		
Basic Flow:	Users 1. New users will grant access to the doctors for emergency data access during the sign up process. 2. The users can also log in the existing account first and then to grant the access 3. The users can change their decisions at anytime 4. The users will be informed about their legal rights and risks for giving or not giving the access In an emergency situation where 1. The doctors will contact the MHA service centre 2. The IDs of the doctors and the hospital will be checked 3. The service centre will search for the patient information in the MHA system according to the patient information provided by the doctors 4. The patient information will be provided to the doctors by either direct download, or granting access to the account	
Alternate Flows:	n/a	
Postconditions:	n/a.	
Dependencies:	n/a	
Required External Resources:	[ ] Data, please specify:	n/a
	[ ] Tools, please specify:	n/a
	[ ] Services, please specify:	n/a
	[ ] Models, please specify:	n/a
	[ ] Other, please specify:	
How this use-case is going to be validated?	We will create a virtual citizen who will provide the authorization during his MHA amount, and will simulate the case where a doctor contact the MHA service centre and will be checked and granted access to the patient data by the service centre.	
Frequency of Use:	Only in medical emergency	
Who are the users?	Patients who give authorization through their user account Doctors from emergency units The MHA service center staff	

Special Requirements:	no
Assumptions:	The authorization from the users will be given
Questions:	n/a

Brain Trauma (UC-TBI)

Use Case ID:	*UC-TBI*		
Use Case Name:	*Brain Trauma*		
Technical Collaborators:	LIN	**Clinical Collaborator:**	*BED*
Description:	A pre-injury clinical profile of patient is a critical aide that can help the clinicians by providing a better insight and possibly improve the clinical outcomes by circumventing the barriers imposed by the heterogeneity of traumatic brain injuries. Individualized treatment and targeted therapies based on patients' data are imperative both from the patients' perspective and also from the clinicians point of view and can ensure more promising outcomes and better prediction and prevention. Such a profile can be used to establish models of pathphysiologic mechanisms significant to pathoanatomic presentations of brain injuries. A clinical phenotype of the patient has to be developed based on pre-injury characteristics. The patients' past medical history, drug history, demographic information, family history, socioeconomic status and life style and habits contribute significantly towards accurate assessment and management in case of brain trauma or cerebrovascular accident. In cases requiring surgical intervention, pertinent medical history can provide information about any co-existing brain lesions or any medical condition that contra-indicates general anesthesia or surgery e.g., patients on anticoagulation therapy. Studies show that prognosis after TBI is strongly correlated to the medical history of the patient and characteristics like age, alcoholism, drugs, cardiac problems, hypertension, liver dysfunction, diabetes and renal impairment etc. can affect the treatment regimen and morbidity and mortality. For example, subdural haematomas (SDH)can be difficult to differentiate from extradural haematomas (EDH) if the size is small, however, the aetiology, management and outcomes can be significantly different. History of repeated brain injury, e.g., sports related, can exacerbate the symptoms. Small children and old people are prone to falls and history of head trauma may be difficult to identify, while road traffic accidents are more common in young and middle aged people with associated skull fractures. Family history of brain aneurysms is an important consideration for suspected subarachnoid haemorrhage (SAH). Junior doctors in A&E who do not have adequate experience in interpreting ct scans can sometime misdiagnose and this undertriage or overtriage can lead to a treatment which is different than what is required. An automated system providing second opinion to the radiologist can help improve the sensitivity and specificity of diagnoses and reduce inter-observer variability. The data repository available within MyHealthAvatar can allow researchers develop mathematical and computational models based on gender, race, ethnicity categories, age, lifestyle, education and medical data and this can significantly contribute to innovative healthcare practices. These data from MyHealthAvatar combined with presenting complaints at the time of admission, history of presenting illness, clinical and neurological findings such as the Glasgow Coma Scale, pupil reactivity, loss of consciousness, vomiting episodes, ENT bleeding, fits, headaches and vital signs can be		

	combined with image features from CT scans and Marshall CT Classification to develop a prognostic model for traumatic brain injuries (TBI).	
Actors:	Doctors and patients .	
Trigger:	Prognosis is needed for patients with suspected brain injury.	
Preconditions:	The availability of demographic data, past medical history, drug history, clinical phenotypes (from clinical and neurological examination) and image phenotypes (from neuroimaging modalities like CT scans)	
Successful End condition	Differential diagnosis of the type of injury and prognosis for traumatic brain injuries are reported. The information is updated in MyHealthAvatar.	
Fail End condition	-	
Basic Flow:	The basic steps include: 1. The patients share their avatar data with the doctors. The pre-injury profile of the patient is developed including life style factors, medical history, drug history and clinical examination data like age, height, weight, vital signs and neurological assessment. 2. The doctor accesses the data of the patient to identify life style, habits, existing or suspected medical conditions, drug usage and/ or occupational hazards which can affect the prognosis and outcome in case of brain injury. The assessments by the doctors are updated in the MyHealthAvatar system. 3. The doctor accesses the clinical and image data of the patient from the hospital system (e.g. PACS) when a patient with suspected brain injury comes to A&E. The physical mechanism of injury, presenting complaints, clinical and neurological examination results and imaging interpretation are combined with the MyHealthAvater data to derive differential diagnosis e.g., ischaemia, EDH, SDH, SAH, contusion, IVH or DAI etc., and a management plan is drawn for targeted therapy and surgical intervention. 4. The doctor assesses the patients' condition using a prognosis model such as Rotterdam Scale or Glasgow Outcome Scale to ascertain possible outcomes. A second opinion is provided by the automated system in MyHealthAvatar.	
Alternate Flows:	-	
Postconditions:	• A management, surgical intervention and targeted treatment plan is developed • Future monitoring of the patient after injury and discharge from hospital • Risk assessment and prediction of long-term outcomes of TBI including pathoanatomic and pathophysiologic sequelae • Classification of patients in cohorts with common characteristics likely to benefit from a given targeted intervention	
Dependencies:	The patients are registered to the avatar system and their medical history and other characteristics data are available in their avatars.	
Required External Resources:	[ ] Data, please specify:	• Patients' data from MyHealthAvatar • Clinical and neurological examination data at the time of admission to hospital • Related studies on patient cohorts, such as IMPACT, CRASH
	[ ] Tools, please specify:	• Prognosis models, data mining tools and image segmentation tools for doctors

		• MyHealthAvatar access for the doctors and patients
	[ ] Services, please specify:	• Links with PACS and electronic health records • Links with TBI databases like TARN and FITBIR • Related studies on patient cohorts, such as IMPACT, CRASH, ADNI
	[ ] Models, please specify:	• Prognosis and outcome models such as Rotterdam Scale and Glasgow Outcome Scale • Risk assessment model for predisposition to and outcomes from TBI
	[ ] Other, please specify:	• Normal values and ranges of clinical and neurological assessments • Neurological atlas for image interpretation and segmentation tools
How this use-case is going to be validated?	*By experts with clinical background in BED*	
Frequency of Use:	*When a prognosis is needed for patients with suspected brain injury*	
Who are the users?	*Doctors and patients*	
Special Requirements:	*Creating awareness and familiarizing doctors and patients with the MyHealthAvatar services*	
Assumptions:	• *Patients' clinical and neurological data are available* • *Patients' imaging data and interpretations are available*	
Questions:		

Anti-Platelet & Anticoagulation Therapy in the Pre-Operative Patients (UC-APLA)

Use Case ID:	UC-APLA		
Use Case Name:	Decision making tools regarding emergency situations in clinical practice. The example of anti-platelet & anticoagulation therapy in the pre-operative patients		
Technical Collaborators:	FORTH	**Clinical Collaborator:**	FORTH
Description:	Hemostasis disorders can develop due to a deficiency or defect in an individual's platelets or clotting mechanisms. Dysfunctions can lead either in bleeding disorders (hemophilia) or in over-clotting disorders such as thrombosis. Dysfunctions that lead in thrombus formation can be related with morbidities such as cardiovascular disorders (coronary disease, heart attack, angina, congestive heart failure and valve disease), pulmonary embolism, stroke and transient ischemic attacks, deep vein thrombosis, peripheral vascular disease (PVD), phlebitis and in some cases obesity. Patients that are diagnosed with over-clotting deficiencies are treated with anticoagulant or anti-platelet therapies as a preventive care. Several single nucleotide polymorpshisms (SNPs) are known regarding drug-targets or metabolizing		

	enzymes (mainly of Cytochrome P450 family) of anti-platelet and anticoagulant therapies. Some well-known examples are the Vitamin K epoxide reductase complex subunit 1 (VKORC1) where specific gene mutations have been related with deficiencies in Vitamin-K-depedent clotting factors and the response to anticoagulant therapies of warfarin and acenocoumarol. In addition, regarding the metabolizing enzymes of P450 family, CYP2C19 is the main metabolic enzyme for the activation of the anti-platelet agent clopidogrel. The latter, is a pro-drug activated in the liver by cytochrome P450 enzymes, mainly CYP2C19. Genetic polymorphism (CYP2C19*2, CYP2C19*3 and CYP2C19*17) exists for CYP2C19 expression, with approximately 5% of Caucasian and 20% of Asian populations being poor metabolizers with no CYP2C19 function. Due to the above, anti-platelet and anticoagulant agents that are administered in clinical practice, appear to have a wide inter-subject variability in their pharmacokinetics and thus in pharmacodynamics. Antiplatelet and anticoagulation therapies are typical examples where therapeutic drug monitoring is applied for every patient as well as pharmacogenomics information are taken into account and several algorithms have been created in order to integrate data and improve pharmacotherapy. Moreover, there are emergency cases such as pre-operative status, where an adjustment in dose should be applied for patients following anti-coagulation and anti-platelet therapies in order to avoid bleeding problems during surgery or during recovery. Summarizing the above information there are cases where additional information are needed but not easily attainable due to lack of clinical data. To this respect in silico approaches (such as Physiologically-based pharmacokinetic/pharmacodynamic modeling) seem capable in providing evidence regarding possible treatment outcomes and organized in order treating physicians will be able to avoid as much as possible “guesswork” for a specific patient. The availability of creating “virtual cohorts” of patients and in silico approaches can assist in generating predictive approaches towards improved personalized medicine. A typical use-case scenario: "A male 55 years old that follows anti-platelet therapy, needs to go on surgery. The doctor has to re-adjust the administration of the anti-platelet therapy for the up-coming surgery and needs to schedule the operation as soon as possible. General guidelines are known for pre-operative care but how could the doctor avoid any guesswork and apply a personalized approach for this patient but also for future patients?"
Actors:	Avatar1(Doctor),Avatar2 (patient), (Avatar3) Research staff for in silico clinical trials platforms, genome information platform/tool, MyHealthAvatar platform
Trigger:	Upload of diagnosis in patient’s electronic health record or during creation of patient’s Avatar in MHA platform. Alternative the use case can be triggered after the medical examination and the decision that patient should go on surgery.
Preconditions:	The facts that are true in this case are: i) Anti-platelet therapy may lead in bleeding during the perioperative or the postoperative period ii) Anti-platelet and anti-thrombotic agents that are administered in clinical practice, appear to have a wide inter-subject variability in their pharmacokinetics and thus in pharmacodynamics due to genetic and epigenetic factors. iii) Anti-platelet therapy is a clinical case in which personalized medicine tools are essential. Therapeutic drug monitoring is usually followed for the proper adjustment of the applied treatment

	iv) There are not many data available regarding the time that the treatment will stop being active after the discontinuation v) Clinical trials regarding the above situation cannot be performed
Basic Flow:	Basic steps: 1. Gathering all the necessary data required from patients health records. This step can run during the therapeutic drug monitoring and dose adjustment prior to the emergency situation. Also this step can run during utilization of personal genomics (Use-case 12) 2. Creating of MyHealthAvatar profile for this patient 3. Embed results of pharmacogenomics information in MHA profile for patient 4. Clustering patients in appropriate cohorts and creation of "virtual population" based on demographic, physiology and genomic data 0. The creation of "virtual population" is based in the distribution of the several parameters and the relation with each other (i.e. weight modeled against height) according to specific algorithms followed by a platform for in silico clinical trials 1. Distribution of pharmacogenomics data in the population of patients 5. Export of "virtual population" in appropriate in silico clinical trials platform 6. Development of a workspace in a platform for in silico clinical trials The basic required information are: I. Drug data regarding the pharmacokinetic and/or pharmacodynamic parameters including toxicity II. Population data including demographic, genetic, biochemical and physiological parameters – Patient's genetic data of drug-metabolizing enzymes which can influence drug concentrations in the body should be considered. – Data for (I) and (II) could be available from literature and can be in the default parameters of the platform or can be enriched from patient's data – Data for (II) can be created from clustering of MyHealthAvatar profiles of patients with same or similar disease profile III. Clinical trial protocol and design. In this case the clinical trial will need to estimate the drug concentrations in the body for a period of time following the last administration (i.e. 48 hours) 7. Simulation of virtual clinical trials in the specific "virtual population" 8. Embed results in an appropriate worksheet or in a different platform 9. Matching and identification of the Avatar from MHA with the "virtual patient" from the "virtual population" of the simulated clinical trial 10. Identification of the time that anti-platelet's drug concentration is below the minimum effective concentration 11. Evaluation for the time needed after the sub-therapeutic concentrations of the drug in order the clotting activity to start returning to the default values. 12. Evaluation of the obtained results and decision of the time that the patient will be ready for surgery 13. Surgery performing and re-introduction of the anti-thrombotic treatment

	Note: This basic flow can be created during therapeutic drug monitoring of patient's status after the diagnosis of clotting-deficiency	
Alternate Flows:	Alternative flows will be followed if the patient is receiving treatments for other co-existing diseases in order to assess any interactions and/or any modulations regarding the basic flow. Alternative flows can be considered, taking into account the adding therapies applied after or during surgery for this patient (e.g. antibiotics, analgesics, sedatives, antacids, anticoagulants administered subcutaneous or intravenous such as heparin etc.)	
Postconditions:	Monitoring of patients status after surgery. Evaluating results and update data in MHA and in clinical trial simulator platform. Re-adjust the therapy on the recovery stage Embed results in MHA platform so both patient and physicians could have access in necessary information. • Example dose adjustment was based in the pharmacogenomics data regarding metabolizing enzyme CYP2C19. In case of modulation of dose the concentration-time profile for this Avatar (patient) is expected to follow this trend (show graph).	
Dependencies:	This case refers to the administration of drugs in emerging situations in the clinical setting of the preoperative and ICU patients. However it represents a typical example of how data can be created and organized through in silico clinical trials approaches particularly in clinical cases where clinical trials cannot be performed. It also attempts to represent how personalized information regarding drugs, diseases and health status information can be introduced and exploited through MHA in order to create decision making tools and approaches. Dependencies of this case can be related with use cases 1, 2, 3 and 5. This case follows and it is related with the use case-12 and utilization of personal genomic information for the individualization of MHA platform	
Required External Resources:	[ ] Data, please specify:	• Drug data ○ Pharmacokinetic properties ○ Pharmacodynamic properties • Population data ○ Demographic ○ Genetic ○ Physiology ○ Pathology • Clinical trials protocols and parameters (as they described in regulatory organizations FDA and EMA)
	[ ] Tools, please specify:	• MHA platform • Genomic platforms/tools • Bio-informatics tools • PCs with related software installed regarding in silico clinical trials ○ PB/PK/PD platforms with license of use
	[ ] Services, please specify:	Links with databases: Genomic databases (see use-case 12)

		Drug databases (PharmKGB, Pubmed, DrugBank) Links with internal/external research laboratories providing data regarding PB/PK/PD and TDM
	[ ] Models, please specify:	• Physiologically-Based Pharmacokinetic/Pharmacodynamic models • Therapeutic drug monitoring models
	[ ] Other, please specify:	Normal values of hemostatic factors in general and/or specific population
Frequency of Use:	The in silico application of virtual clinical trials can be used in every emergency case where a following treatment may influence the post-operating recovery of a patient after surgery. The development of databases and generation of data prior to the emergency situation could be more helpful regarding the faster fitting of the patient with Avatar. End-users of this approach are physicians and research personnel focusing to in silico clinical trials approaches. Especially for physicians it could provide them with results through in silico approaches of treatment outcomes in patient group that fit with the patients that are monitoring and not with a general "virtual population". This approach and the data provided could be benefit for the treating physicians giving them tools of decision making options towards an improved personalized medicine approach. End-users will also be the patients with MHA profile since they can have access to information regarding the provided treatment and the modulations that could be occurred. It could be possible also to provide them with explanations and answers regarding different treatment outcomes in patient groups that would be able to participate through MHA platform. Moreover, under their approval, they could be able in providing their MHA profile in research facilities towards creating of in silico research approaches in drug development processes and therapeutic drug monitoring as they would do if they would choose to participate in a clinical trial process.	
Special Requirements:	Familiarity of doctors and generally of the medical staff with MHA technologies Linking of MHA data between research and medical organizations and personnel applying MHA technologies	
Assumptions:	Some basic assumptions are: • Necessary drug data for the generation of the in silico clinical trials are available in the literature and easily accessed • Full and detailed patient's health history record • Platforms used for in silico clinical trials have been evaluated with clinical results from other studies (Validity of the platform) • Continuous development and simulation of clinical trials from in silico platforms in order to create databases for patient's avatar fitting	
Questions:	The new era in health care towards the "stratified medicine" and personalization of treatment demands the development of approaches and tools such as MHA platform. The question that rises is how an education program could be introduced for medical society (especially staff that work in the point of service such as hospitals etc) in order to get familiar with user-friendly platforms and tools and also stay up to date with these approaches?	