OraMod

VPH based predictive model for oral cancer reoccurrence in the clinical practice

TITLE	**D2.3 Technical design**		
Deliverable No.	D2.3		
EDITOR	ONETONET		
Contributors	Guy Kouaga, A.Ruggeri, G.Scoponi		
WorkPackage No.	WP2	**WorkPackage Title**	Usage specifications and system design
Status[1]	FINAL	**Version No.**	6
Dissemination level	PU		
DOCUMENT ID	OraMod D2.3 Technical design		
FILE ID	OraMod_D2_3		
Related documents	OraMod_D2 2_final.pdf – Usecases and user needs OraMod _D2 4_final.pdf - Technical standard position paper		

Distribution List

Organization	**Name of recipients**
UNIPR	T. Poli
VUMC	R. H. Brakenhoff, M van de Wiel
Fraunhofer	F. Jung, S. Steger, S. Wesarg
ST- Italy	Sarah Burgarella, Marco Cereda
VCI	G. Nikitas, G. Aristomenopoulos
OneToNet	A. Ruggeri, G. Scoponi, S. Copelli
UDUS	K. Scheckenbach
VTT	M. Kulju
European Commission	EC Officers and experts

[1] Status values: TOC, DRAFT, FINAL

Revision History

Revision no.	Date of Issue	Author(s)	Brief Description of Change
1	20/04/2014	A. Ruggeri	schema
2	30/06/2014	A. Ruggeri, G.Scoponi	ToC, first draft
3	02/07/2014	E.Martinelli	Some comments and indication
4	06/07/2014	A. Ruggeri, G.Scoponi, G. Kouaga	System Components added
5	15/07/2014	A. Ruggeri, G. Kouaga	Deployment Diagrams added
6	22/07/2014	A. Ruggeri, G.Scoponi	General revision and editing - APPROVED BY COORDINATOR

List of abbreviations and definitions

ADT	Admission, discharge, and transfer system
CDA2	Clinical Document Architecture, release 2
CIS	Clinical Information System
DICOM	Digital Imaging and Communications in Medicine
EHR	Electronic Health Record
GUI	Graphical User Interface
HIS	Hospital Information System
HL7	Health Level 7
LIS	Laboratory Information System
PACS	Picture Archiving and Communication System
qRT-PCR	Quantitative real-time polymerase chain reaction
RFID	Radio-frequency identification
RIS	Radiology Information System
SaaS	Software as a Service
UML	Unified Modeling Language

Table of Contents

1 Preface 8

1.1 Purpose of this document 8

1.2 Overview 8

2 Introduction 9

2.1 Scope 9

2.2 UML Definitions, Acronyms and Abbreviations 10

3 System Overview 11

3.1 System Characteristics 13

3.2 System Architecture 14

4 System Context and External Interfaces 17

5 System Design Methods 19

5.1 Design Method and Standards 19

5.2 Documentation Standards 19

5.3 Software development tools 19

6 Component System Design Description 20

6.1 Decomposition Description (General Logical View) 20

6.2 Interactive Visualization and Simulation Environment 20

6.2.1 Prediction Tool System 21

6.2.2 Data Visualization System 28

6.2.3 Tumor Board System 32

6.3 Multilayer Data Acquisition System 41

6.3.1 Manual data input system 41

6.3.2 Search past patient 41

6.3.3 Hospitalization 42

6.3.4 Out-patient Encounter 43

6.3.5 Statistical data management 45

6.3.6 Report Management 46

6.3.7 Oral Cancer Documentation Management 47

6.4 Image Processing Tool 47

6.4.1 Image analysis 48

6.5 qRT-PCR Device 51

6.5.1 The qRT-PCR state diagram 51

6.6 Oral Cancer Predictive Model Generator 55

List of figures

Fig. 1 - User view of OraMod in the Hospital 11
Fig. 2 – Scheme of OraMod interactions with the Hospitals applications 12
Fig. 3 - The overall OraMod environment 13
Fig. 4 - The 3 OraMod layers 14
Fig. 5 - OraMod system *in-hospital* deployment diagram 15
Fig. 6 - OraMod system geographical deployment diagram 16
Fig. 7 - HL7 Interaction Communication Diagram 17
Fig. 8 - Fraunhofer PACS Communication Diagram 17
Fig. 9 - General logical overview of the OraMod system 20
Fig. 10 - Use Case diagram of Prediction tool system 21
Fig. 11 - Perform Prediction Calculation state diagram 22
Fig. 12 - Perform Prediction Calculation sequence diagram 23
Fig. 13 - Browse List of saved result state diagram 24
Fig. 14 - Browse and saved result sequence diagram 24
Fig. 15 - Print result sequence diagram 25
Fig. 16 - Ask recalculation sequence diagram 26
Fig. 17 - Delete saved result sequence diagram 27
Fig. 18 - Compare saved result sequence diagram 27
Fig. 19 - Data visualization Use case diagram 28
Fig. 20 - Visualization of relevant clinical data sequence diagram 29
Fig. 21 - Navigation on interative clinical data sequence diagram 30
Fig. 22 - An example of the representation of navigation on interactive clinical data 30
Fig. 23 - Some examples of macroscopic anatomic clinical data (from OraMod D2.2 document) 31
Fig. 24 - Use case diagram of the Tumor Board 32
Fig. 25 - Open Board State Diagram 33
Fig. 26 - Open board sequence diagram 34
Fig. 27 - Add Physician State diagram 35
Fig. 28 - Add physician sequence diagram 36
Fig. 29 - Participate discussion state diagram 36
Fig. 30 - Participate discussion sequence diagram 37
Fig. 31 - Participate Audio/video Conference state diagram 38

Fig. 32 - Participate audio/video conference sequence diagram 39
Fig. 33 - Close board state diagram 39
Fig. 34 - Close board sequence diagram 40
Fig. 35 - Manual data input use case diagram 41
Fig. 36 - Search Past Patient State Diagram 42
Fig. 37 - Hospitalization State Diagram 43
Fig. 38 - Our Patient Encounter State Diagram 44
Fig. 39 - Statistical Data Management State Diagram 45
Fig. 40 - Report Management State Diagram 46
Fig. 41 - Oral Cancer documentation Management State Diagram 47
Fig. 42 - Image Processing Tool Use case diagram 48
Fig. 43 - Image Analysis Online Modeling Sequence diagram 49
Fig. 44 - Image Analysis Off-line Modeling Sequence diagram 50
Fig. 45 - Result Image and Data Storage Sequence diagram 50
Fig. 46 - qRT-PCR Device system use case 51
Fig. 47 - qRT-PCR Device system state diagram 52
Fig. 48 - qRT-PCR Device system sequence diagram 53
Fig. 49 - Association Patient-Test cartridge Sequence diagram 54
Fig. 50 - Analyze specimen sequence diagram 55

1 Preface

1.1 Purpose of this document

This document is the Technical Design document for use by OraMod Project. It provides guidance and template material which is intended to assist both the technical staff and management in producing project - specific technical documents. It is also a useful background reading for anyone involved in developing or monitoring the IDA Management System (IDA-MS), as much as it follows IDA Architecture Guidelines[2].

1.2 Overview

Section 1 outlines the purpose of this document.

Section 2 is the introduction and includes a description of the project, with a specific remind to UML diagrams.

Section 3 provides a system overview.

Section 4 contains the system context with the external interfaces.

Section 5 describes the system design method, standards and conventions.

Section 6 contains the component system design.

[2] Cfr. D2.4 Technical standard position paper, Standard #1 IDA Programme.

2 Introduction

This document defines the technical architecture and the design of the OraMod platform and of its components, the data sharing and interoperability protocols and standards required for usage in clinical settings, according to the proposed design. The document relies on the results of "D2.1 Clinical Study protocol and measurements" and "D2.2 Use cases and user needs" and has been jointly run to the definition of technical standards and requirements ("D2.4 Technical standard position paper" document).

The designed architecture is SaaS based, to comply with the EU guidelines and country laws on patient privacy. We have adopted a distributed design to keep a strict separation between sensitive patient's data (localized in each Healthcare Enterprise and accessible only by operators of the hospital) from the Master Patient and Events Record Index, internet-based, that will contain only the database keys to address the patients and their specific clinical events. The architecture will be designed to ensure integration of standalone software components and devices (image processing tools, qRT-PCR device) and full interoperability with legacy IT systems. We have defined and adopted the specific IHE patterns and HL7 as "common language" in order to make all the system components totally independent and easily exploitable in the real commercial world of the IT for healthcare industry.

2.1 Scope

The object of this document is to define the technical design of the OraMod platform.

It describes how the different components interact, with which modality the various information passes among systems and the impact that OraMod environment will have in the Hospitals.

Here we have translated the various cases identified in *D2.2 - Use cases and user needs* documents in UML language, understandable by technicians; for each use case described in that document, we have created the analogous Use Case Diagram: in such manner we will be able to implement the user needs through software.

In this document we describe in more depth how the interfaces used by clinicians shall work, giving all the necessary information to search, identify, obtain and present clinical data.

In particular we will present the Use Case Diagrams, Sequence and in some case State Diagram, describing the Virtual Patient Presentation & Simulation Tool. We also analyze in detail how the Image Processing Tool interacts with OraMod framework, also presenting a deployment solution, not contemplated in the current Fraunhofer environment. This solution – that provides a PACS system integrated into the OraMod environment – has been agreed between partners.

The connections between HIS systems and OraMod framework are declared in terms of dataset to exchange, using HL7 – CDA2 languages, messages and paths. However is not the scope of this document to declare how this exchange will happen and which data will be sent; these details will be described in the final system documentation report (D6.5). We here however provide some details regarding the data exchange between OraMod platform and the qRT-PCR device.

Moreover we explain how the information must flow to be recorded both in the local OraMod database and in the central Multilayer Data Acquisition System, that is the core of the project.

This document constitutes the reference for the technical development and integrations foreseen in the project technical tasks. Each specific partner contribution has been considered in order to implement the best solution for the OraMod platform.

2.2 UML Definitions, Acronyms and Abbreviations

This section defines the terms, acronyms and abbreviations used in this document, specific to the application.

Terms covering the development of software using the Unified Modeling Language (UML) approach are included for completeness.

Class Diagram	Describes the structure of a system
Object Diagram	Expresses possible object combinations of a specific Class Diagram
Statechart Diagram	Expresses possible states of a class (or a system)
Activity Diagram	Describes activities and actions taking place in a system
Sequence Diagram	Shows one or several sequences of messages sent among a set of objects
Collaboration Diagram	Describes a complete collaboration among a set of objects
Use-case Diagrams	Illustrates the relationships between use cases
Component Diagram	A special case of a Class Diagram used to describe components within a software system
Deployment Diagram	A special case of a Class Diagram used to describe hardware within the overall system architecture
System Block diagram	A diagram showing the major components of the system with its interconnections and external interfaces

Tab. 1. Definitions based on the UML approach to system design

3 System Overview

The OraMod design provides the seamless integration of the system in the hospitals environment.

The OraMod framework consists of two different databases logically interconnected; the first of them is in the hospital, gathering all the necessary information for the project, and presenting the results to the clinicians, while the second one is centrally based and is used to collect anonymous data and to provide raw data to the statistic tools.

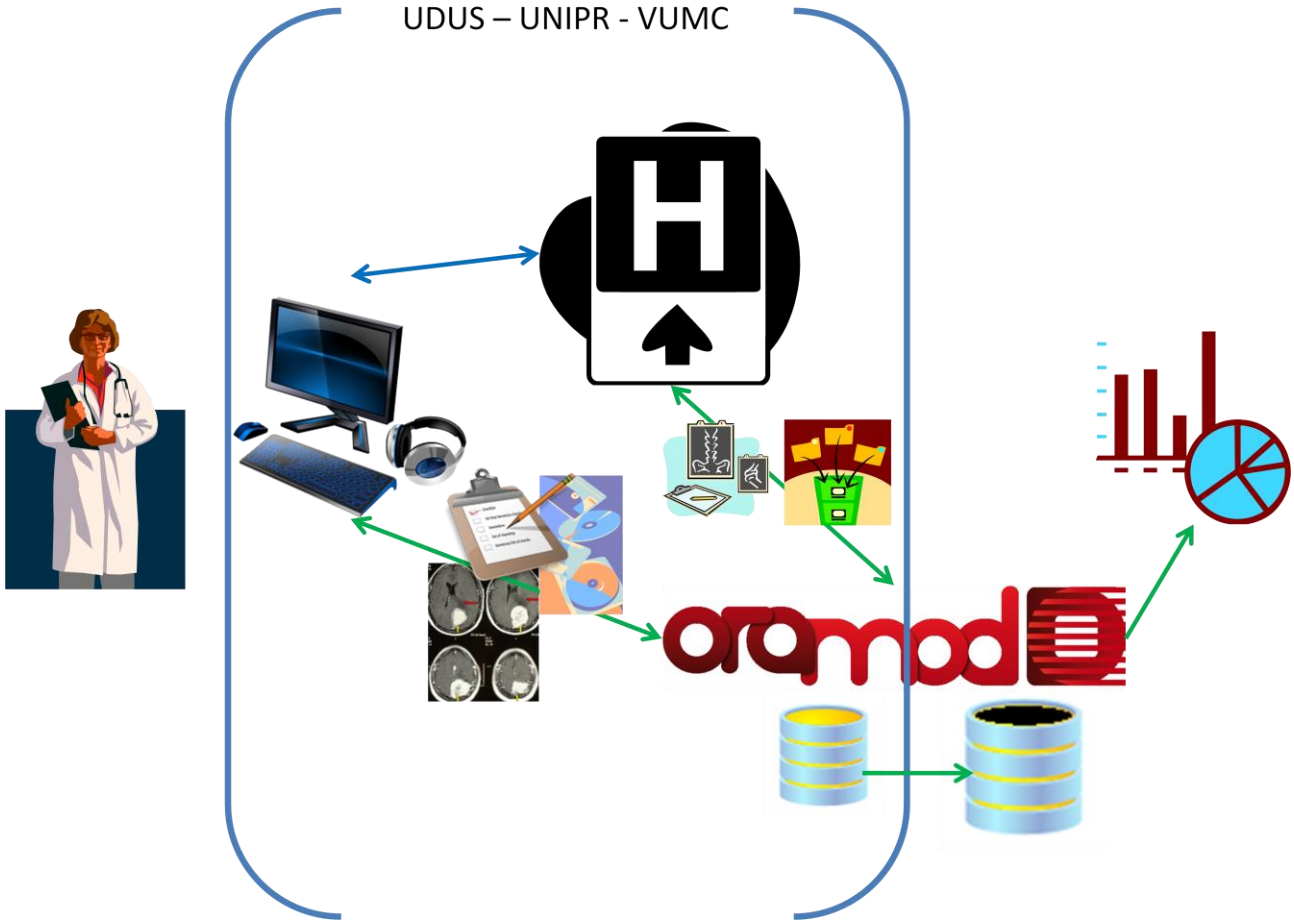

Fig. 1 - User view of OraMod in the Hospital

Each hospital medical personnel authenticated in OraMod can connect using his standard workstation and a browser to access the system, input data, search for information, obtain results and use the model for predictions. He doesn't directly interact with the remote db.

The main idea is to have a separate environment with a series of standard interfaces able to exchange the relevant data.

OraMod needs to gather information from the HIS software (Identity patient db –Demographics, Booking System - Scheduler for the appointments, ADT) and CIS (EHR, Laboratory, Anatomic Pathology and Radiology Systems). Moreover other data are obtained from specific clinical systems and devices (PACS, Image Processing tool, qRT-PCR).

NOTE: The platform can however work also as stand-alone (i.e. independently from HIS components), in case integration with HIS is not possible at the time of implementation in the hospital. In this case, manual input from hospital personnel is required and standard user interfaces are provided by the ClinicalHub software, produced by OneToNet. In this option, the physical interaction and practical planning will prevail over the direct data gathering, thus requiring a specific organizational procedure design to maintain the same levels of data integrity, security and error free transactions.

The figure below depicts how this fits.

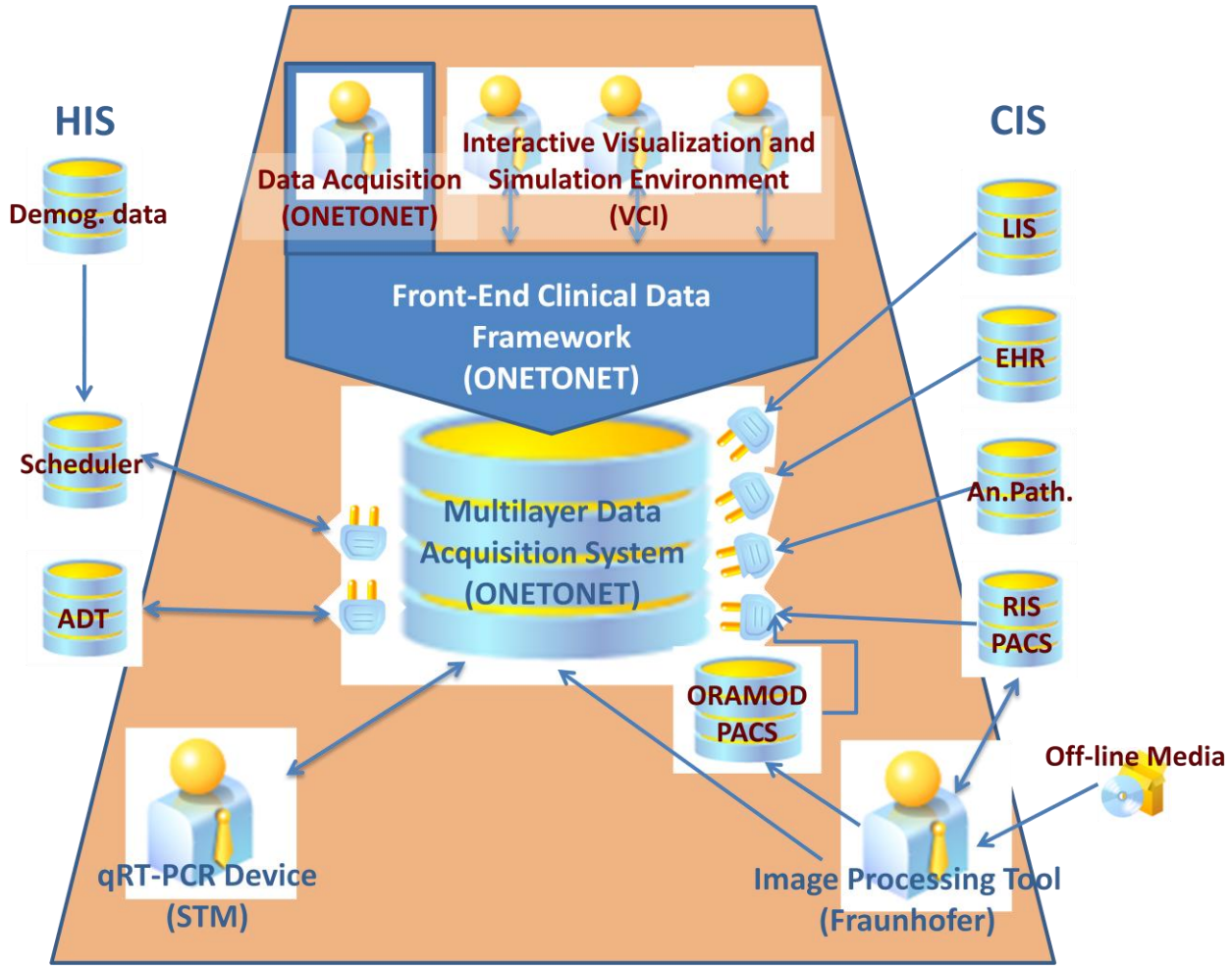

Fig. 2 – Scheme of OraMod interactions with the Hospitals applications

The Multilayer Data Acquisition System is the collector of the OraMod data coming from Demographic data, Scheduler and ADT (HIS – patient information), from the Clinical Systems (LIS, RIS, AP, EHR) and from some specific tools of the OraMod project (qRT-PCR device that collects genomic data and Image Processing Tool, able to compare different kind of images among them).

In the D2.4 - Technical standard position paper are defined the specific interfaces used to communicate between the various systems.

3.1 System Characteristics

For its intrinsic purpose, OraMod has a predictive model component relying on patients' health data. For this reason it is necessary to consolidate relevant data and to anonymize them.

This is obtained by keeping a distinct central database to which all the local OraMod modules send the necessary information, after removing all the personal sensitive data of the patients. The only information useful to combine data for every patient is the Patient_Id, that will be centrally maintained unique for each hospital.

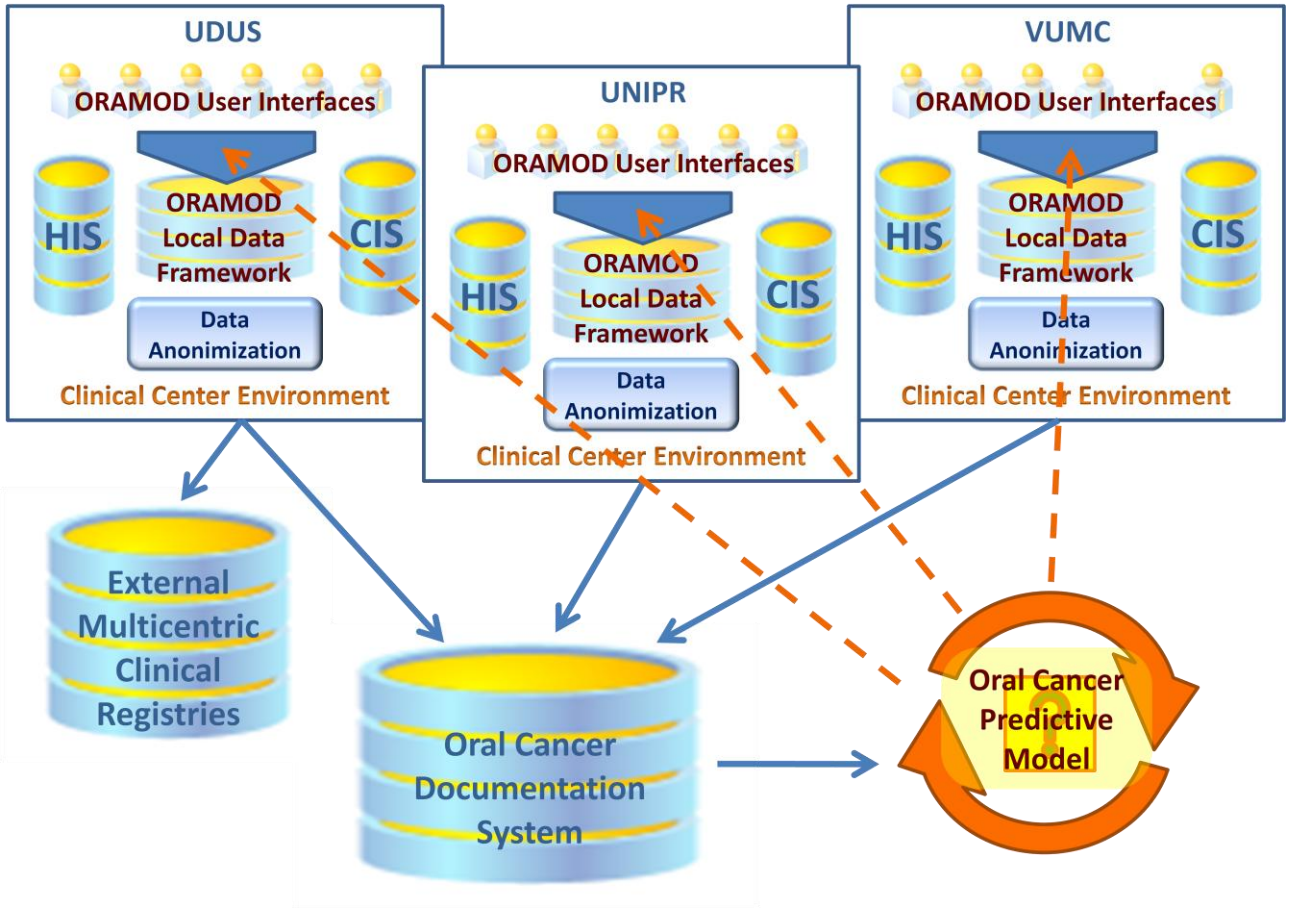

Fig. 3 - The overall OraMod environment

The Oral Cancer Predictive Model uses the anonymized data collected in the central db, not located in any hospital, to produce graphs and statistics that can be shared in each local db. Access to this environment follows the same rules to log-on to local OraMod.

The system is also predisposed to address the need raised by UDUS (a Nordrehin-Westfalen land requirement) to automatically update the Multicentric Clinical Registry [Epidemiologisches Krebsregister NRW[3]].

OraMod is designed to gather a wide variety of data, so, once the information which needs to be transmitted to the Registry is assessed, we will define the rules for the data transfer.

[3] http://www.krebsregister.nrw.de/

3.2 System Architecture

The architecture of the system can be divided into 3 logical domains:

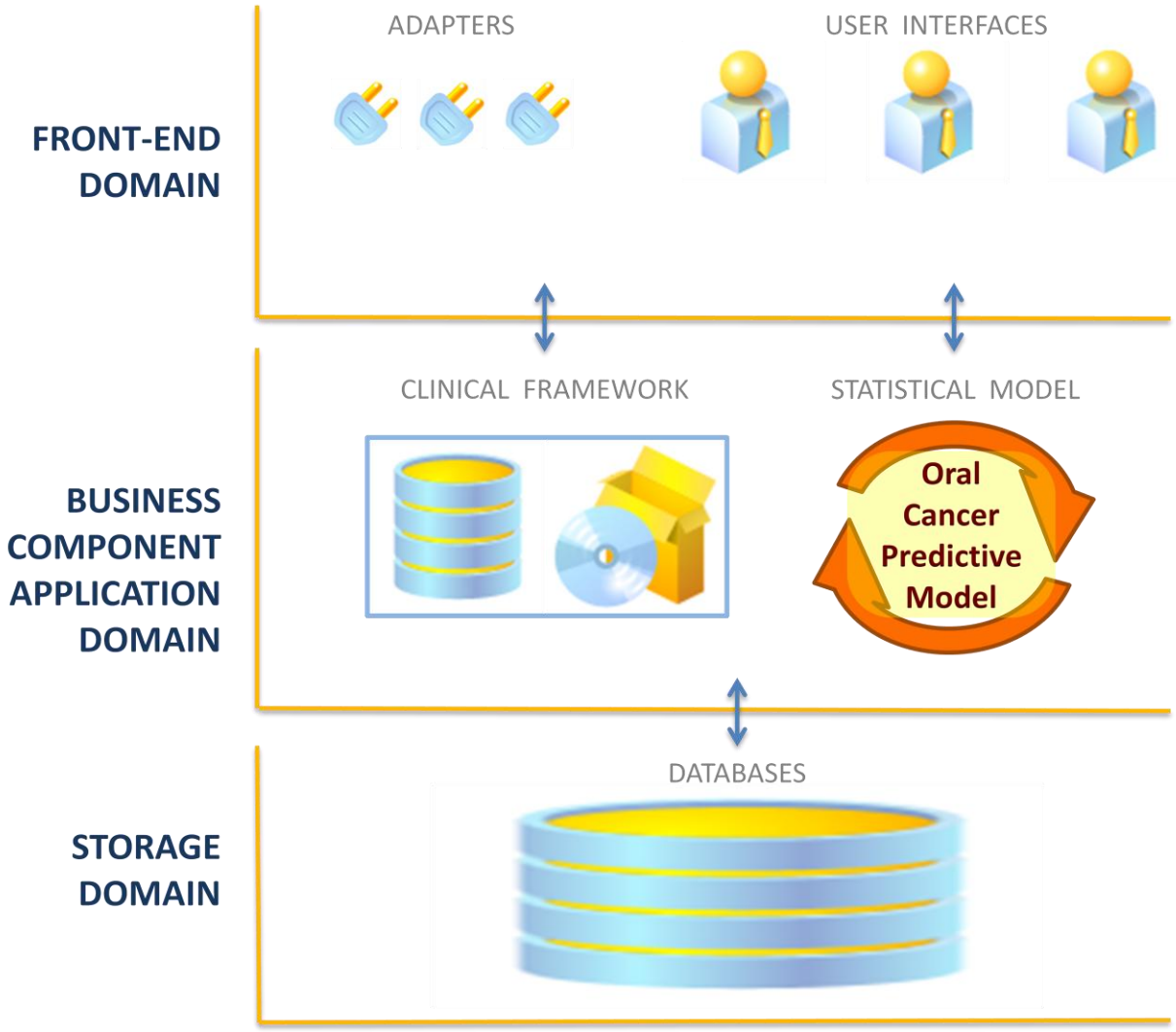

Fig. 4 - The 3 OraMod layers

The front-end domain elements provide the User Interfaces to the Actors of the system. Interfaces can be either software systems or medical devices. All the business logic of the OraMod system resides in the Business Component Application domain. The most relevant item of this layer is the Oral Cancer Predictive Model, while the Clinical Framework has a more subsidiary role providing to the model a huge amount of clinical data to be analyzed. The Predictive Model is the main goal of the OraMod project and will potentially provide to the clinicians a new tool to evaluate the patient's prognosis.

The last tier, obviously, is the storage domain, which providesan effective and flexible multidisciplinary data container.

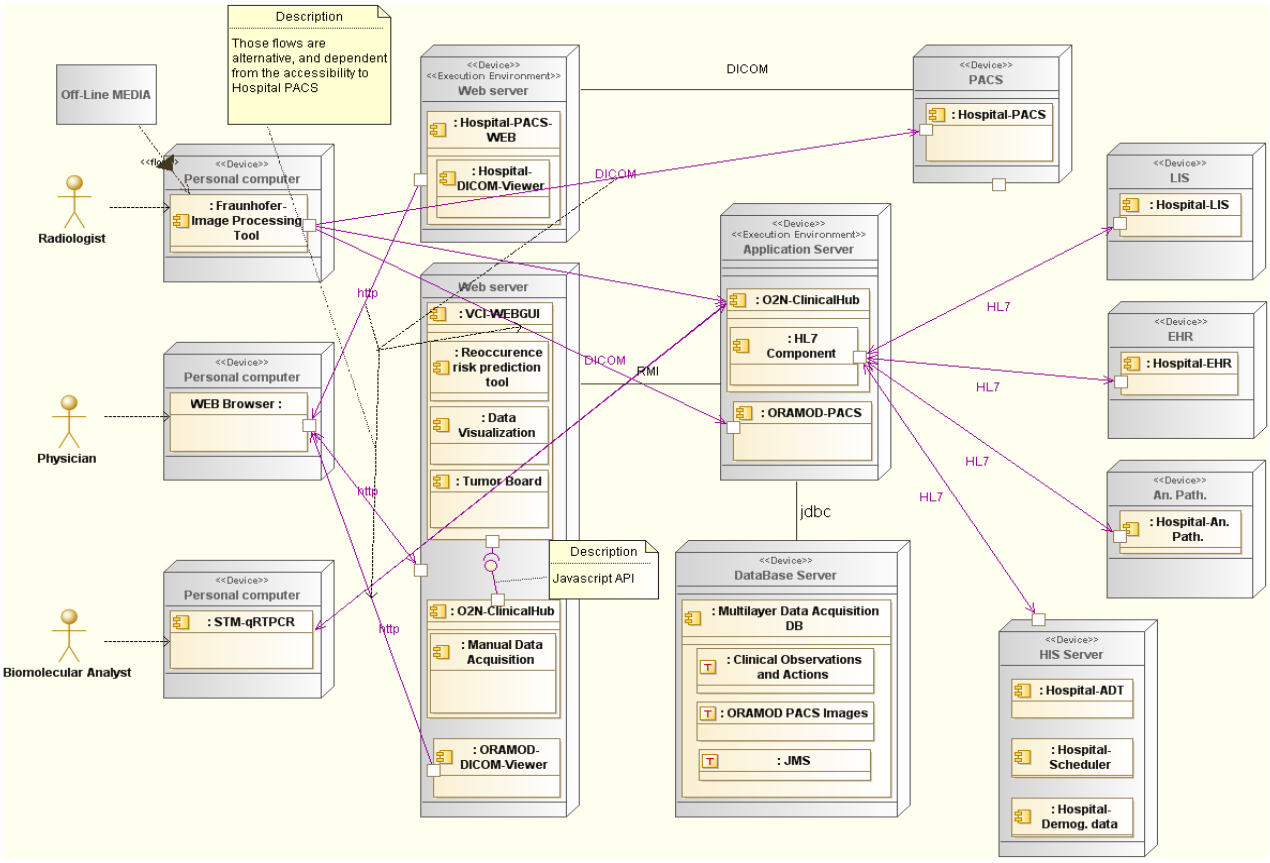

Fig. 5 - OraMod system *in-hospital* deployment diagram

The figure above presents the deployment diagram of the OraMod System inside a single hospital. The diagram shows the physical representation of the OraMod architecture defining the nodes (Execution Environment Nodes), the components running in every single node, the communication ports and the connections between the various components. Please note that usually the physical nodes (Device Nodes) are not specified, thus allowing every single hospital IT to allocate the Execution Environment Nodes in an adequate number of virtual or real servers.

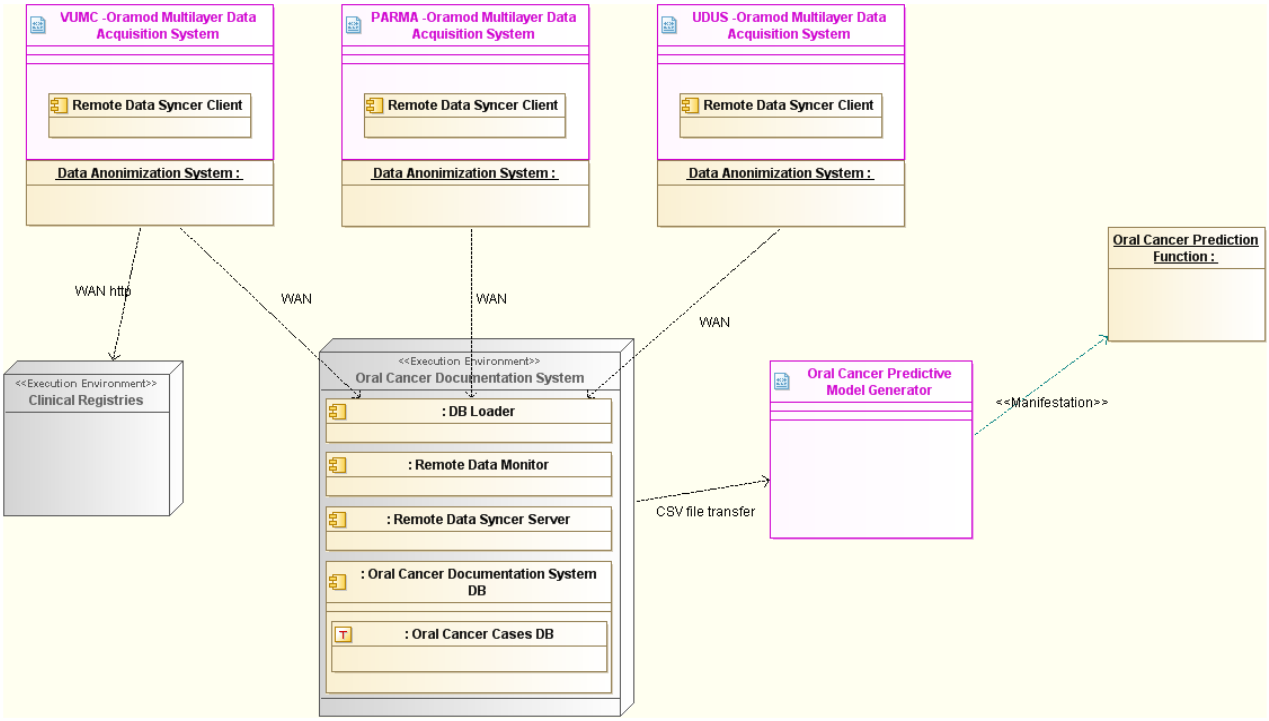

Fig. 6 - OraMod system geographical deployment diagram

This is the physical general architecture of the OraMod System showing the communication and interactions between the three clinical centers and the OraMod Oral cancer Documentation System, as well as the generation of the Oral Cancer Predictive Model/s. Obviously this architecture can be widened and include as many hospitals as required or even be downsized and be tailored for a single hospital.

4 System Context and External Interfaces

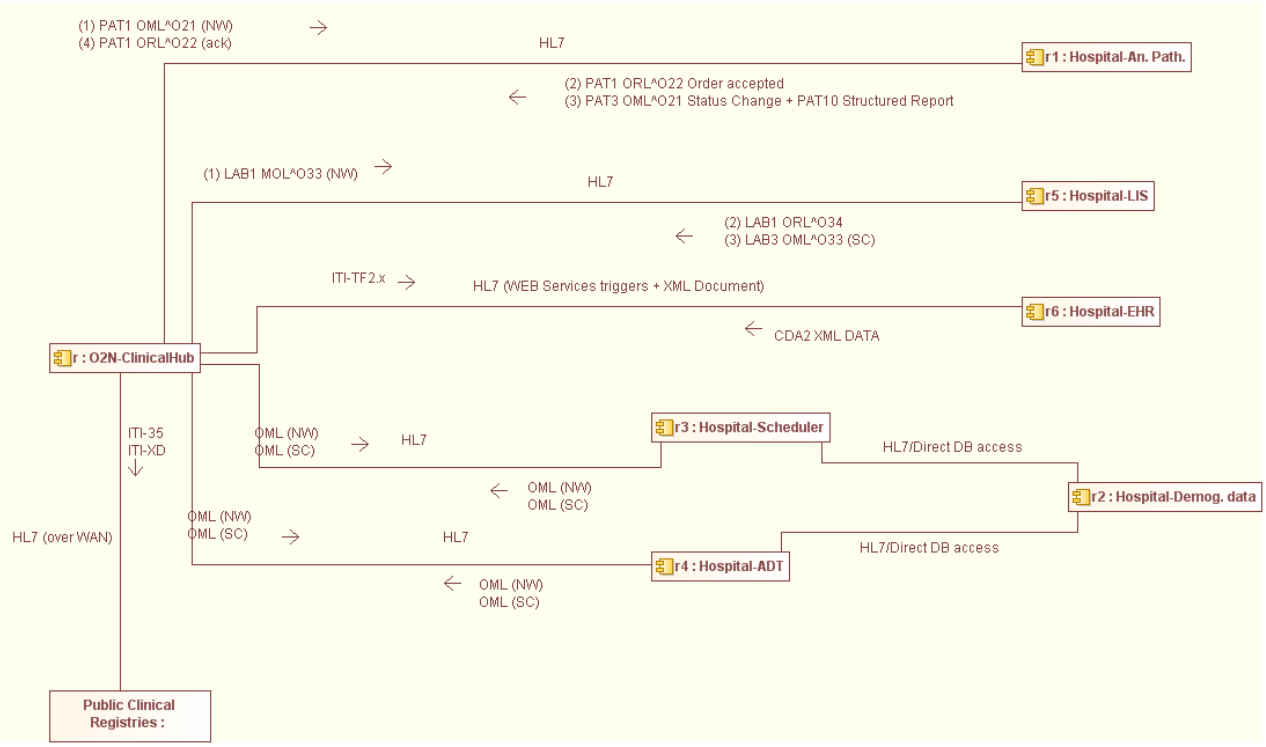

Fig. 7 - HL7 Interaction Communication Diagram

The above picture describes all the HL7 communications inside the single hospital and cross-enterprise transactions for data transfer to public cancer registries.

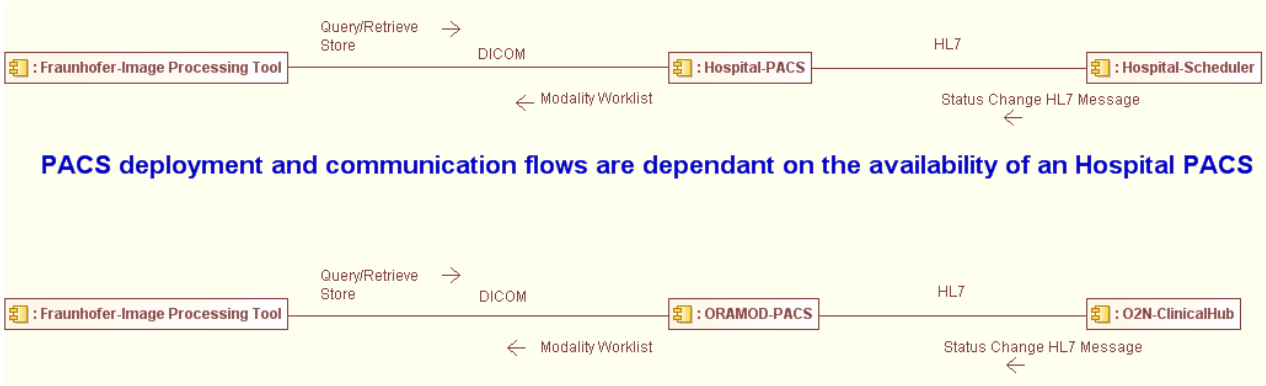

Fig. 8 - Fraunhofer PACS Communication Diagram

The image above shows the communication path between the Fraunhofer Image processing tool and the Hospital or OraMod PACS. Please note that the communication to and from the PACS are alternative: we will primarily try to instance a communication with the Hospital PACS for Modality Worklist, Query/Retrieve

functions or Storage, if this communication will be unavailable we will switch to Offline Media data retrieve and Storage to the OraMod PACS installed on the Multilayer Data Acquisition Application Server.

The communication channels are also showing the common messages sequences and their respective direction within the flow. Specific IHE, HL7and DICOM standard documents used are listed and described in deliverable D2.4.

5 System Design Methods

5.1 Design Method and Standards

Design Methods and Standards are covered in the document D2.4 –Technical standard position paper. Please refer to Appendix II-IV-VI-VII of the above document.

5.2 Documentation Standards

Design Methods and Standards are covered in the document D2.4 –Technical standard position paper. Please refer to Appendix I of the above document.

5.3 Software development tools

Design Methods and Standards are covered in the document D2.4 –Technical standard position paper. Please refer to the Appendix III of the above document.

6 Component System Design Description

6.1 Decomposition Description (General Logical View)

This figure describes the major software artifacts and their information flows described in full detail in the next paragraphs.

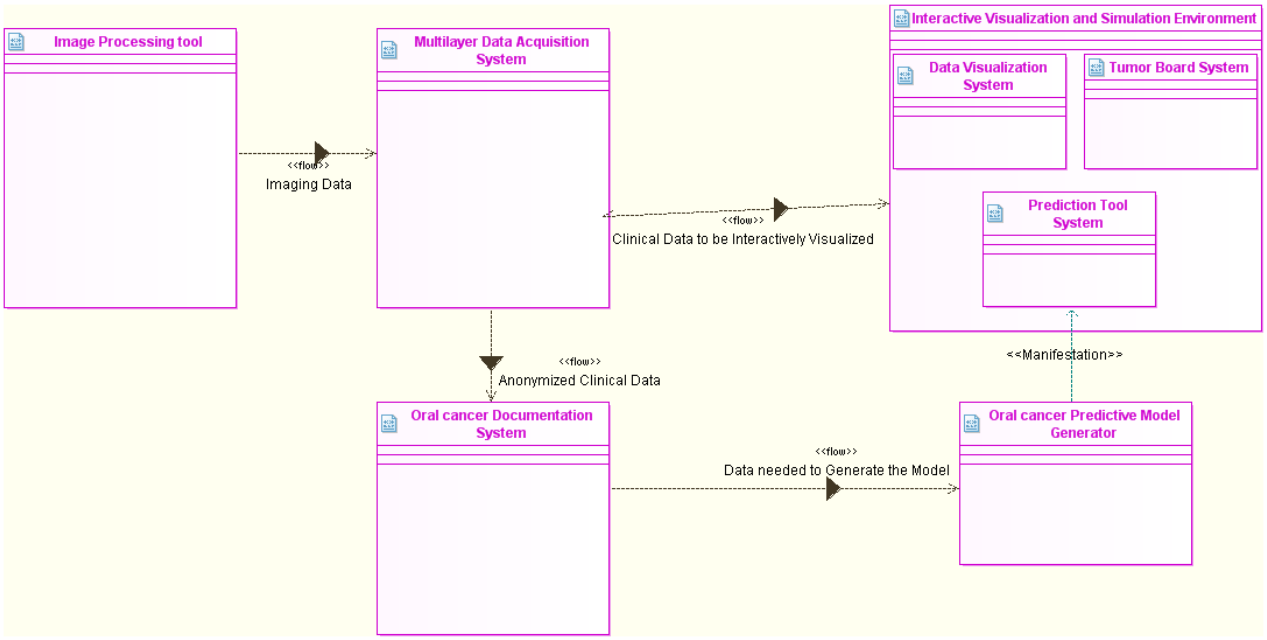

Fig. 9 - General logical overview of the OraMod system

6.2 Interactive Visualization and Simulation Environment

The Interactive Visualization and Simulation Environment is a logical container of three different software components, realizing the most interactive use case regarding patient management, patient prognosis prediction and effective clinical data representation.

6.2.1 Prediction Tool System

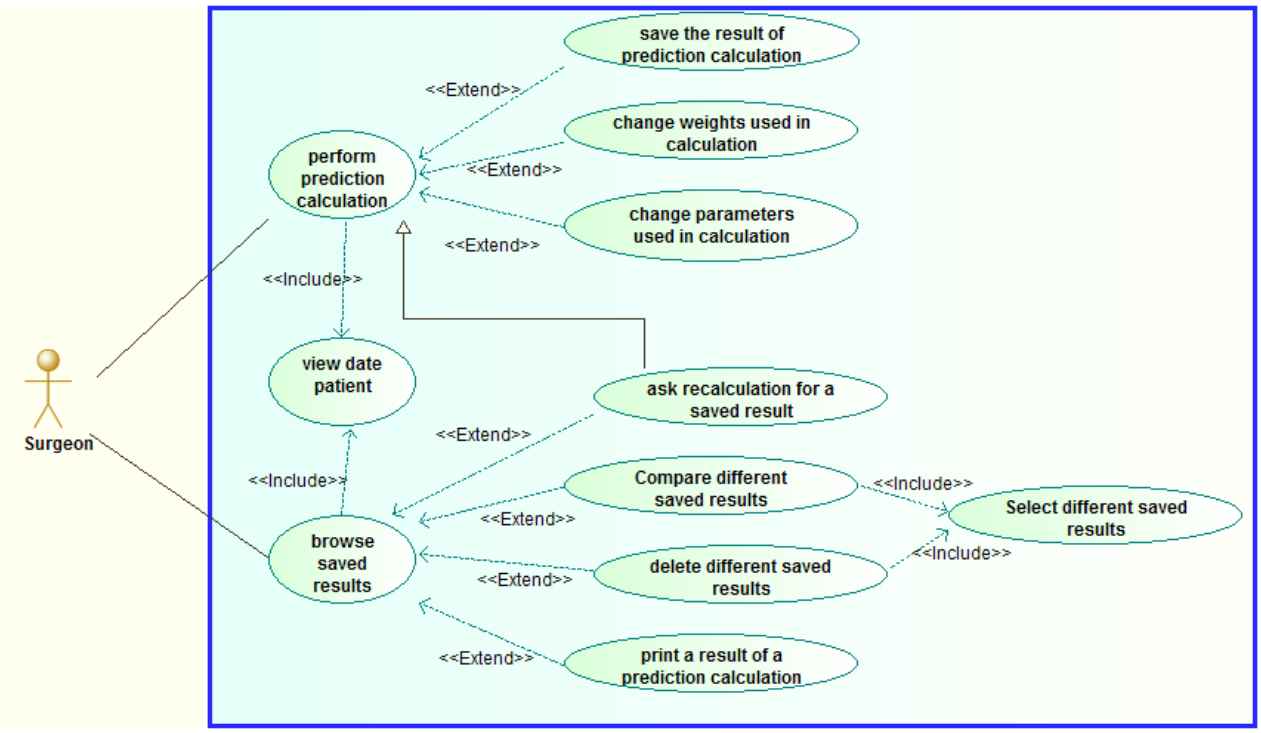

Fig. 10 - Use Case diagram of Prediction tool system

As we can see in the above diagram, our system will provide two different main services requiring access to specific patient data: "**Perform prediction calculation**" and "**Browse saved results**".

6.2.1.1 Perform prediction calculation

The *perform prediction calculation* service requires that all the patient's data (parameter values) and all the mandatory calculation formula items (parameters and weights) are available (not empty). Before calculating the prediction result, as we can see in the diagram, the system will allow the user to change the parameters values, the weights and even select the parameters between those allowed by the prediction calculation formula. After the calculation has been made, the system will allow the user to save the result along with all the variables used to perform the calculation (Parameters, parameters values, weights). All the data will be saved on the Clinical data framework (ClinicalHub).

The next State Diagram presents the prediction calculation specific process.

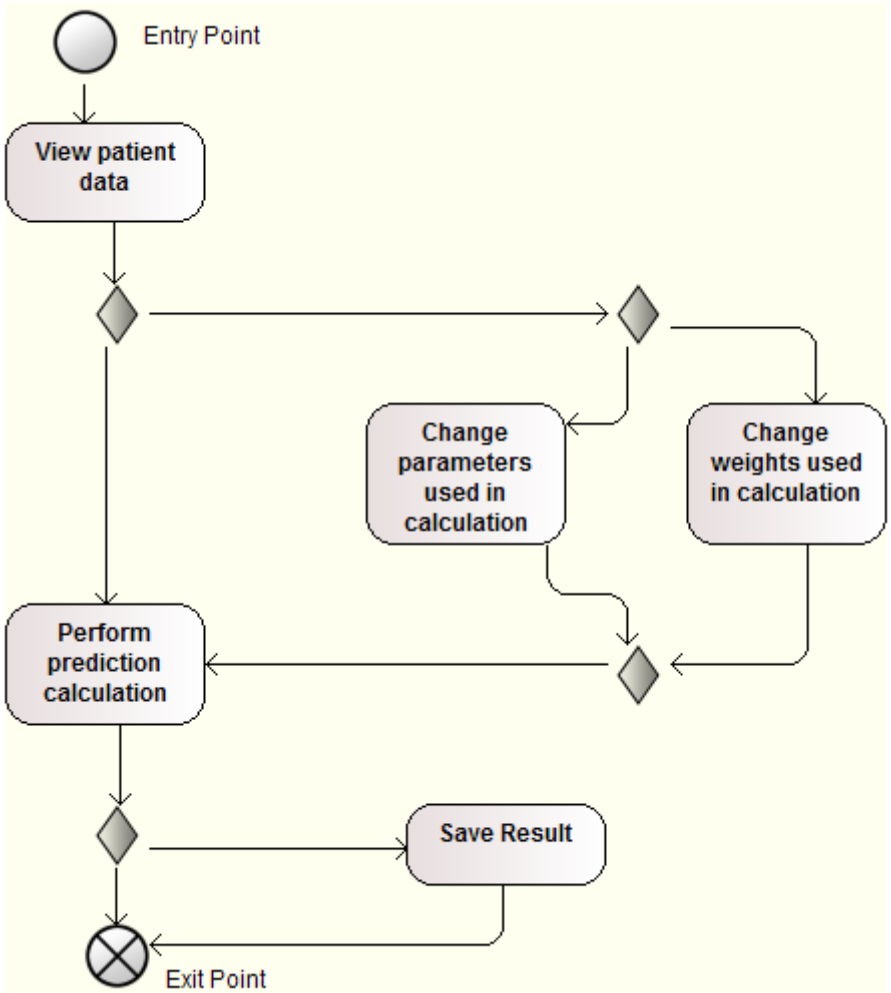

Fig. 11 - Perform Prediction Calculation state diagram

Below we will try, using a sequence diagram, to present any operation provided by our system with the interaction with external agents that may be systems or other actors.

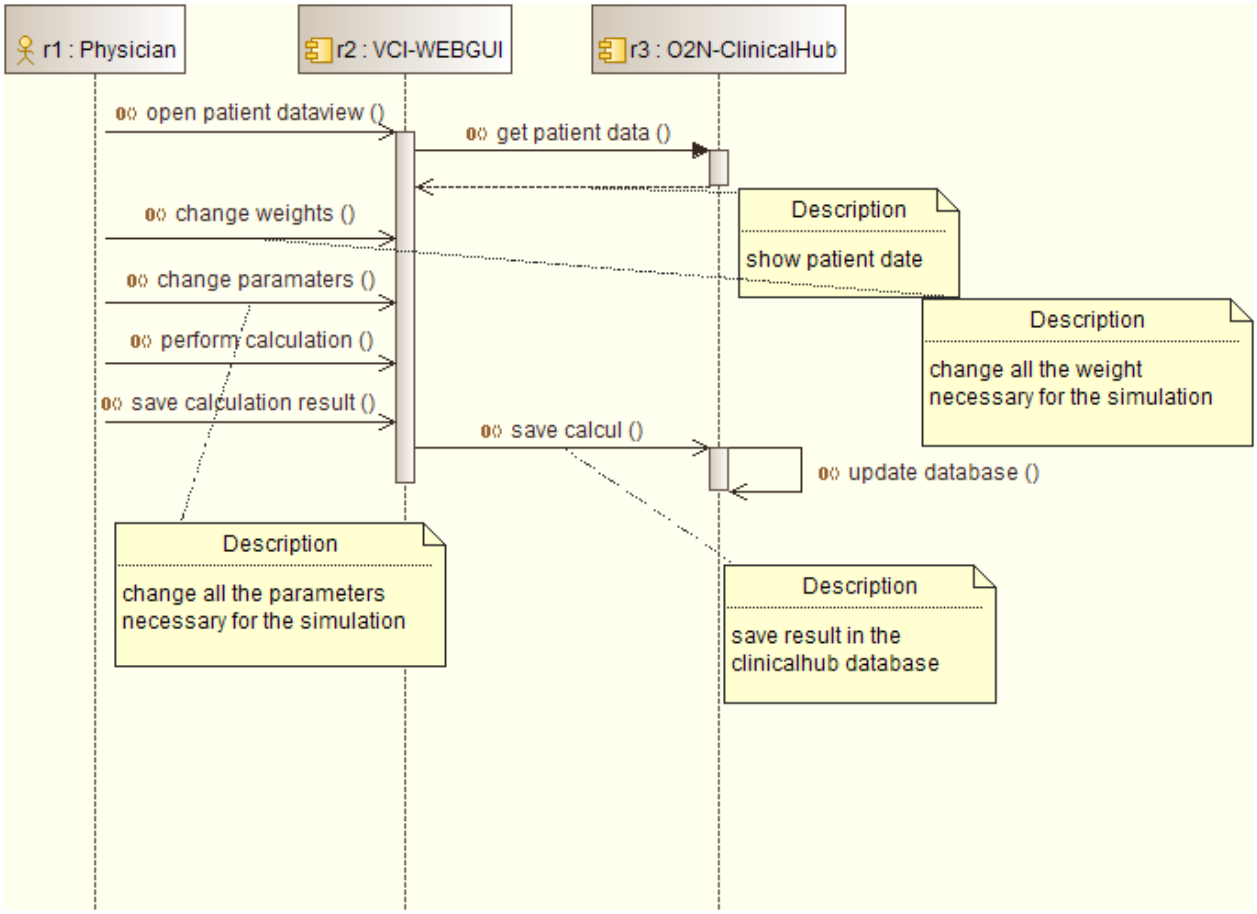

Fig. 12 - Perform Prediction Calculation sequence diagram

6.2.1.2 Browse saved results

The *browse saved results* service manages the list of all the saved calculations results performed on a given patient, designed possibly as a table containing all the single prediction results as well as their respective parameters and weights used in the calculation. This table will provide to the user the different actions potentially performable on the results such as Delete, Compare, Print, (re-)Calculate (Modify). The selection of the rows will allow the access to either the Delete or the Compare services. Print action will print the detailed data of the single row (single result). (re-)Calculate will start a ***perform prediction calculation*** on a selected row (selected result) populating the fields of the prediction interface with the parameters and their values as well as the respective weights.

Saved data visualization could be structured as shown in the following table:

	Patient_ID	Calc_ID	Timestamp	Parameter1	Weight1	P2	W2	...	...		
☐										Print	Calc
☐										Print	Calc
☐										Print	Calc

Delete Compare

The following picture shows the state diagram of the **Browse a list of different saved result** process**.**

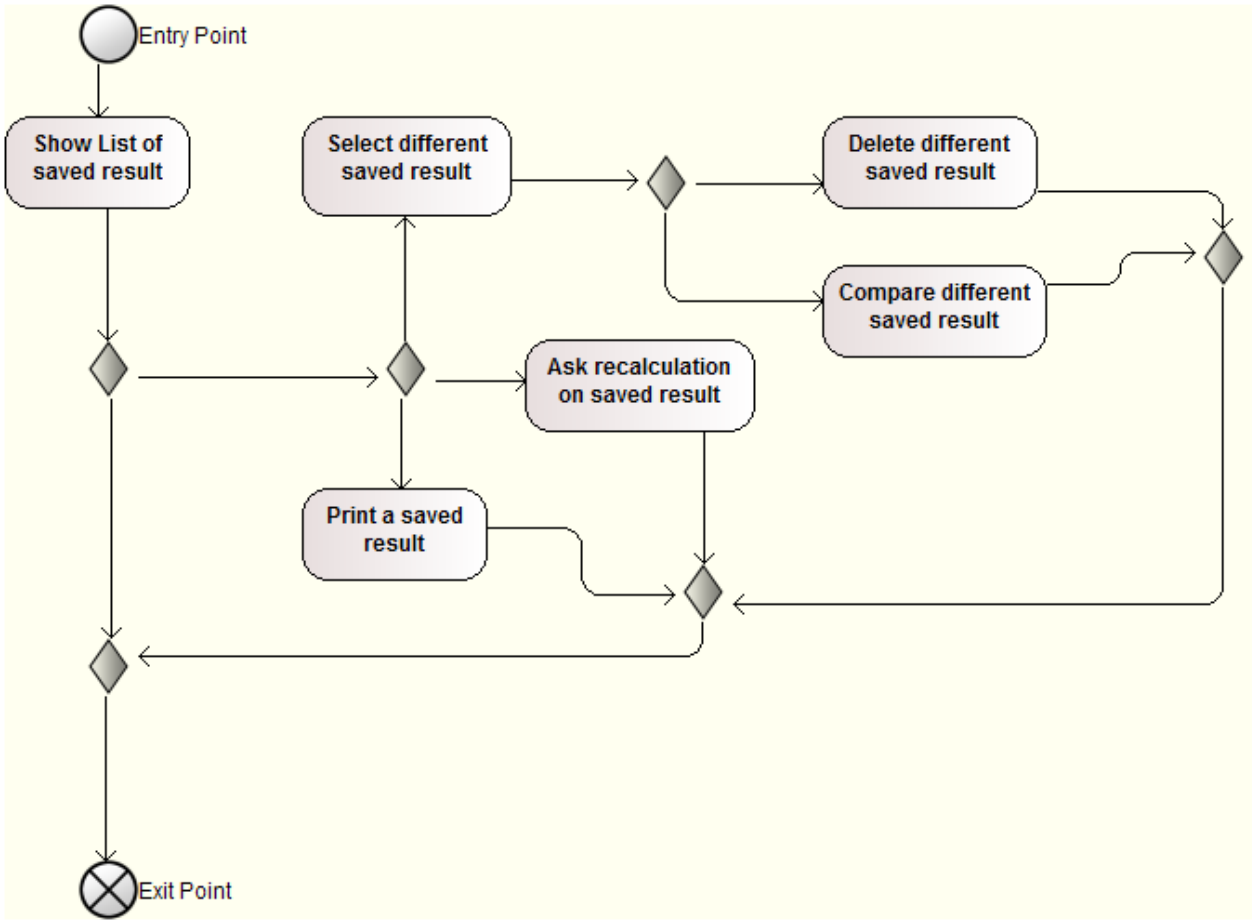

Fig. 13 - Browse List of saved result state diagram

Below we present, using a sequence diagram, any operation provided by our system with the interaction with external agents (either systems or other actors).

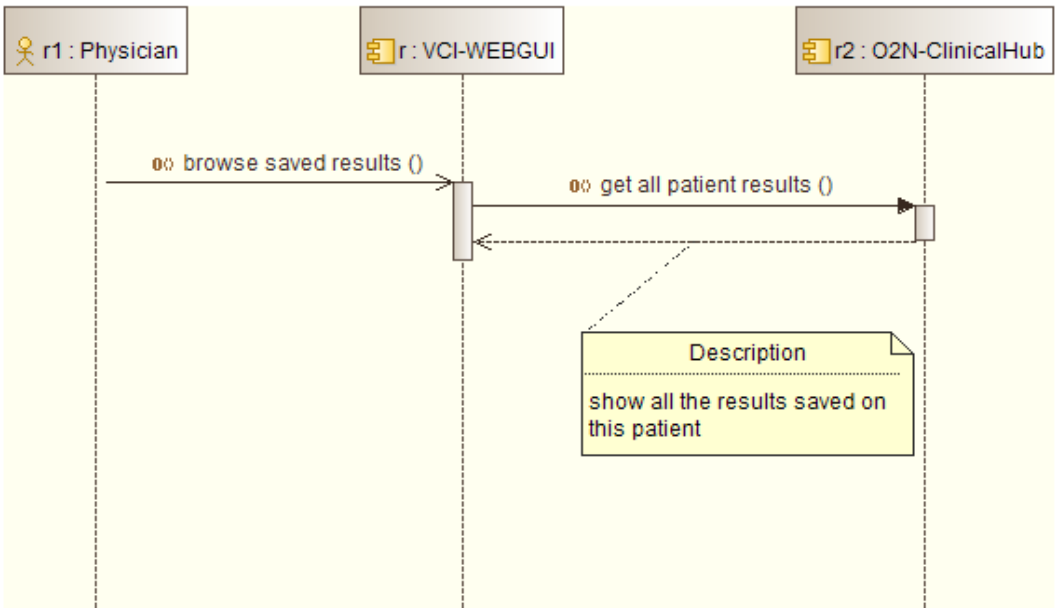

Fig. 14 - Browse and saved result sequence diagram

6.2.1.3 Print a saved result

The **print and saved result** service allows to print a result simply by hitting the button "print" on the respective record/row containing the required result. The printing of such data (Patient_ID, Calc_ID, timestamp, parameter, weight...) should follow a given template (to be defined).

Below we will try, using a sequence diagram, to present any operation provided by our system with the interaction with external agents that may be systems or other actors.

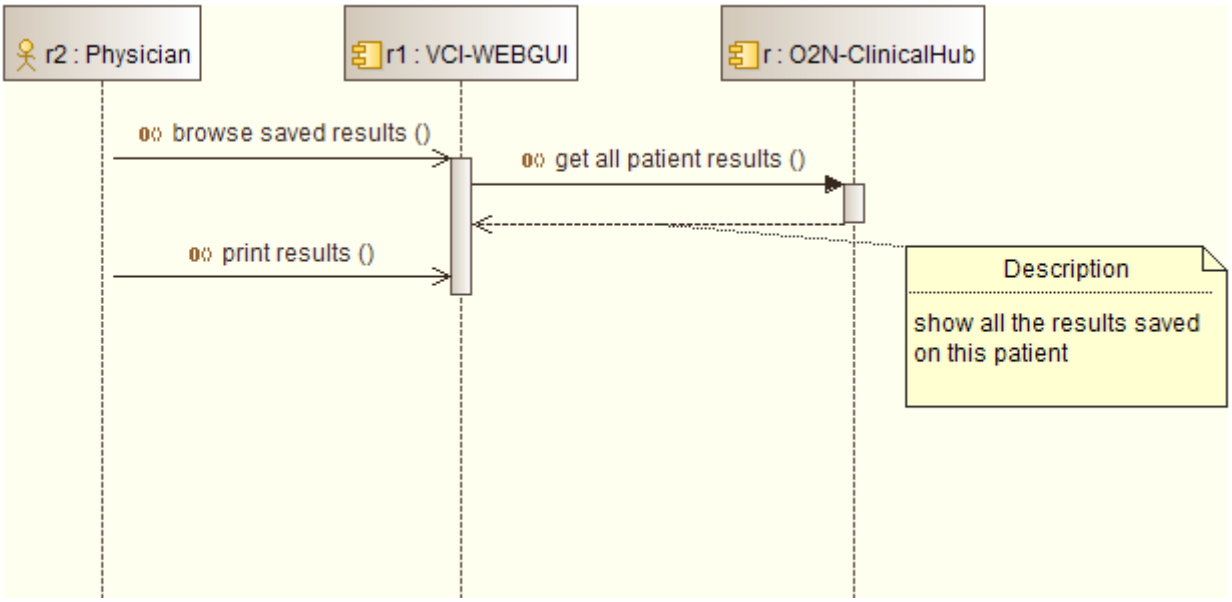

Fig. 15 - Print result sequence diagram

6.2.1.4 Ask recalculation

This function calls back to **Perform prediction calculation** service. In order to perform all the functions available in **Perform prediction calculation** all the fields will be populated with the values of the respective record/row containing the required result**.**

Below we present, using a sequence diagram, any operation provided by our system with the interaction with external agents (either systems or other actors).

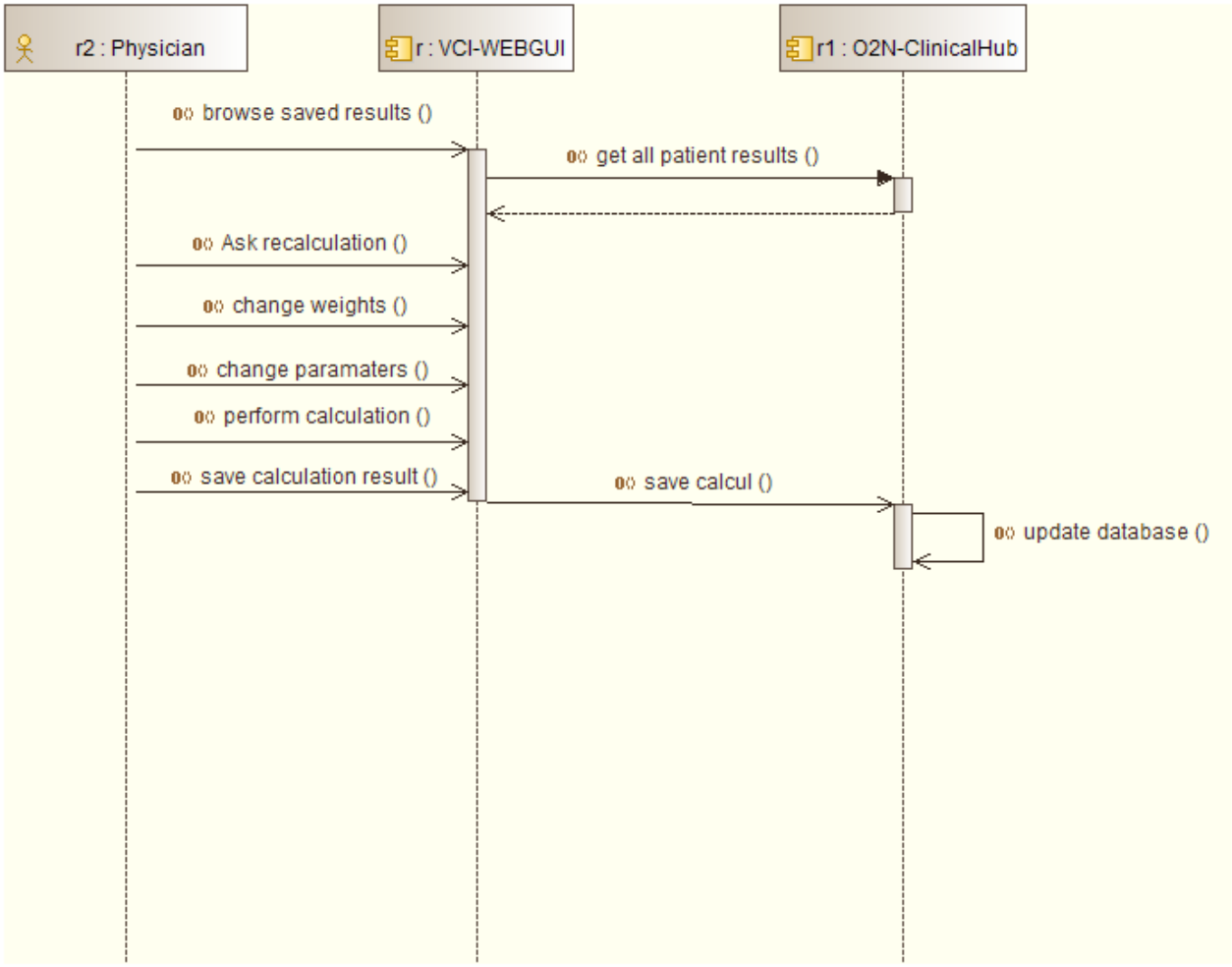

Fig. 16 - Ask recalculation sequence diagram

6.2.1.5 Select saved result

The first column of the table showed in paragraph 6.2.1.2 will contain a checkbox. The selection of the checkbox allows the deletion or comparison of the data contained in the selected row/rows of the table.

6.2.1.6 Delete saved result

The **delete saved result** function needs as a prerequisite the selection of the checkbox of the desired row/rows, after that, pressing the **Delete** button will delete the row/rows and the relative data. Only rows containing simulation data can be deleted.

Below we present, using a sequence diagram, any operation provided by our system with the interaction with external agents that may be systems or other actors.

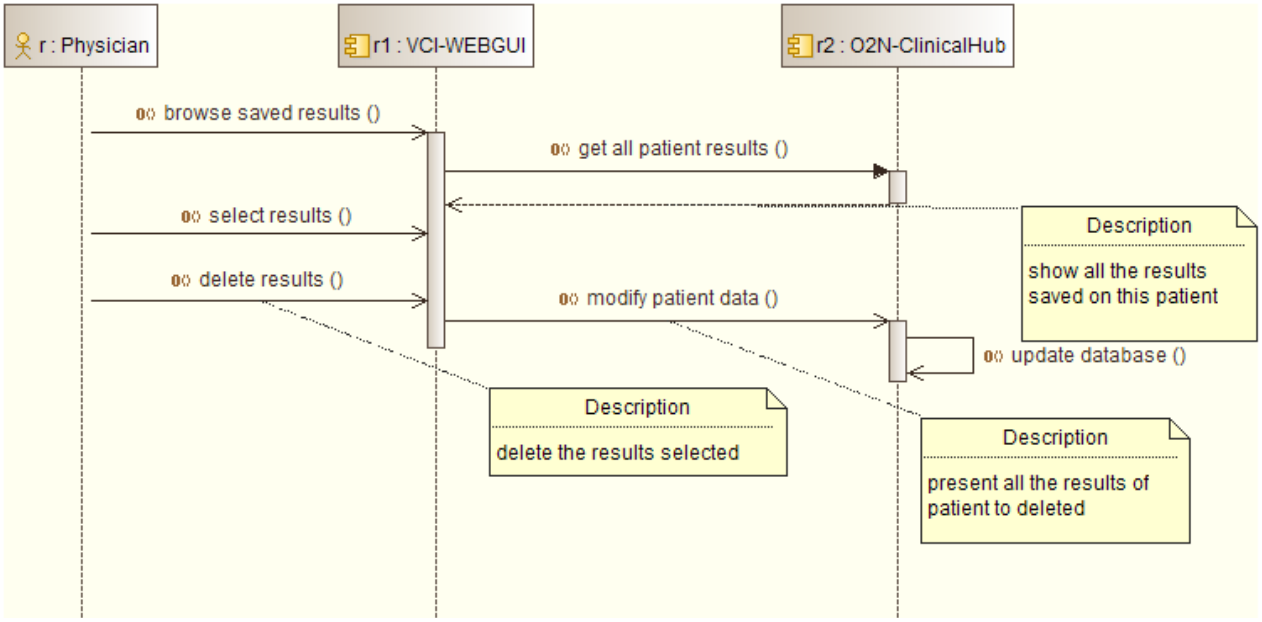

Fig. 17 - Delete saved result sequence diagram

6.2.1.7 Compare saved result

The **Compare saved result** function needs as a prerequisite the selection of the checkbox of the desired row/rows. Pressing the **Compare** button the system will show up selected data with a representation able to compare data sequences.

Below we present, using a sequence diagram, any operation provided by our system with the interaction with external agents that may be systems or other actors.

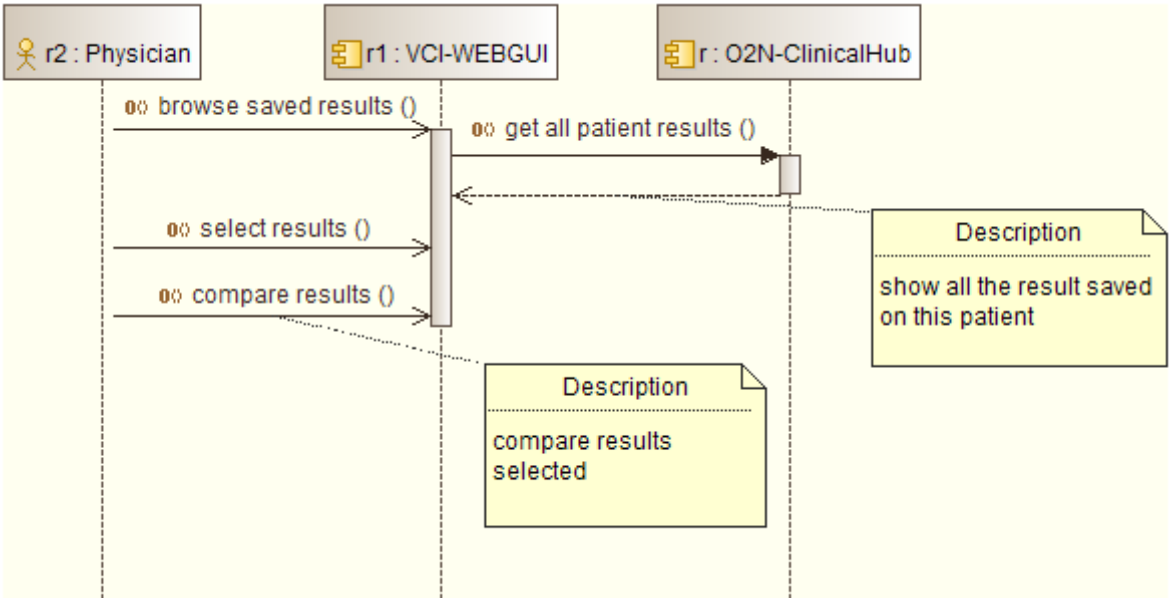

Fig. 18 - Compare saved result sequence diagram

6.2.2 Data Visualization System

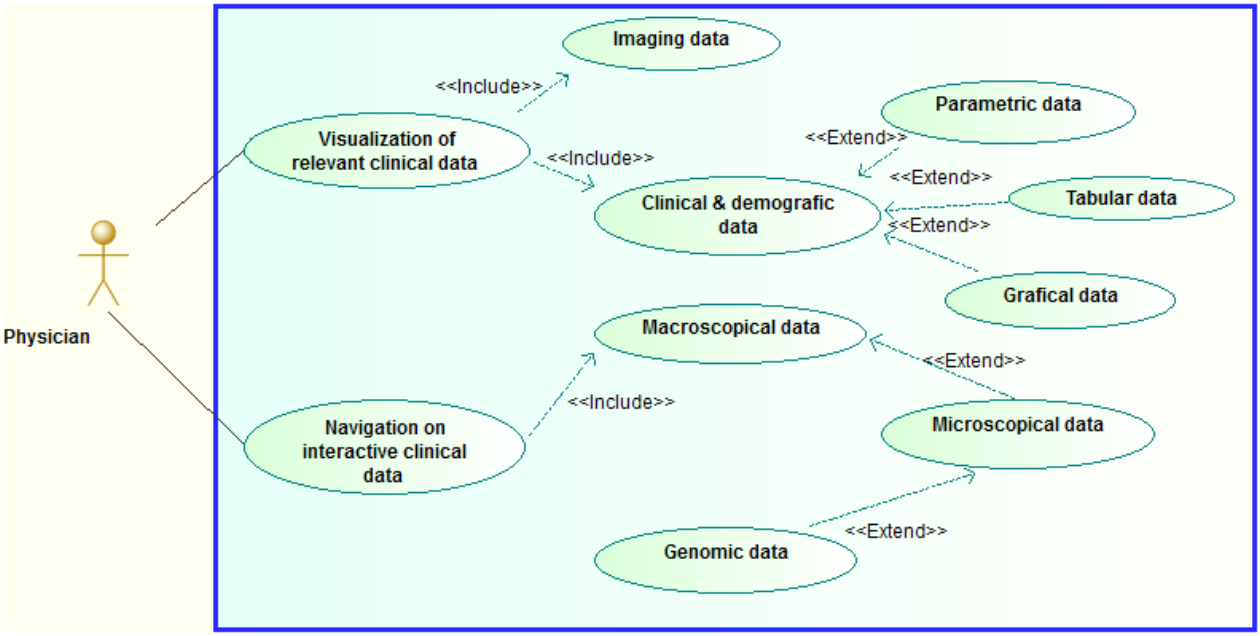

Fig. 19 - Data visualization Use case diagram

6.2.2.1 Visualization of relevant clinical data

This function will help the physician to visualize the more relevant clinical data in a single view. This view will gather both imaging and parametric data in a single page; clinical parametric data should be represented alternatively (or in a combination) in tabular or graphical display. We need Clinicians to specify the most relevant data to be represented.

The following sequence diagram, presents any operation provided by our system with the interaction with external agents that can be systems or other actors.

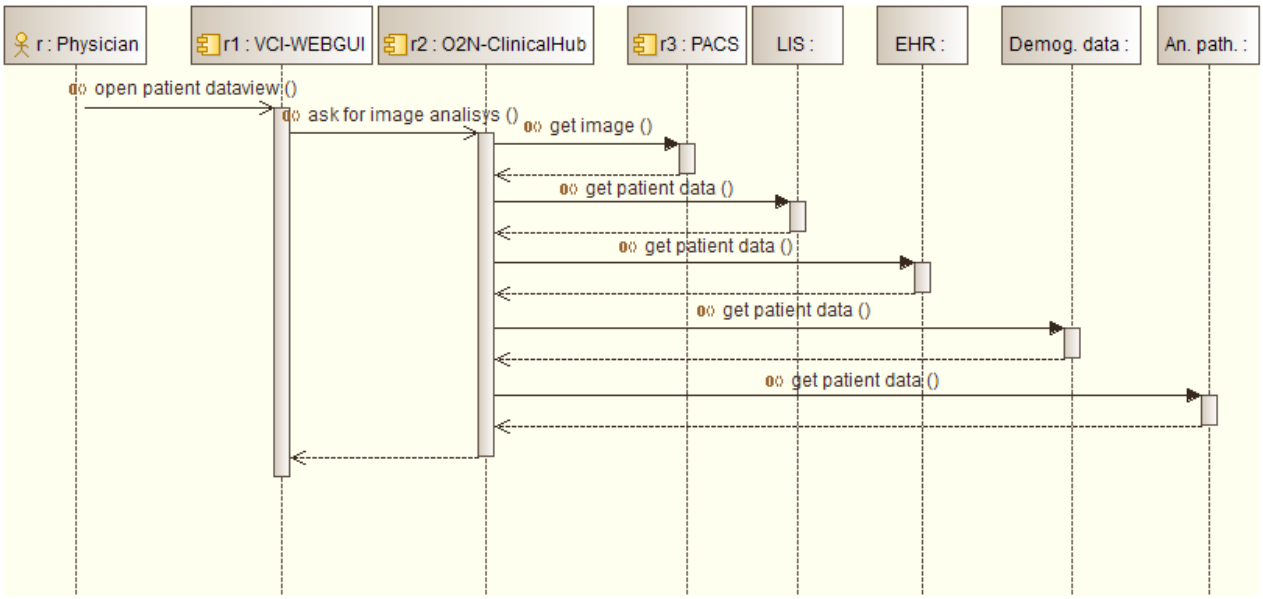

Fig. 20 - Visualization of relevant clinical data sequence diagram

6.2.2.2 Navigation on interactive clinical data

To help the clinicians to visually navigate the data, the function "Navigation on interactive clinical data" will start from a visual representation of macroscopic clinical data (e.g. a picture of the oral cavity with the tumor localization); by zooming (clicking) on a specific point of the macroscopic image you will get the detail of the microscopic anatomical data (e.g. Anatomic Pathological preparations and results); by further zooming (clicking) you will obtain genomic data visualization. A most effective presentation would translate the images into logical maps containing the values (or links to values) of relevant anatomically related parametric values.

The following sequence diagram, presents any operation provided by our system with the interaction with external agents that may be systems or other actors.

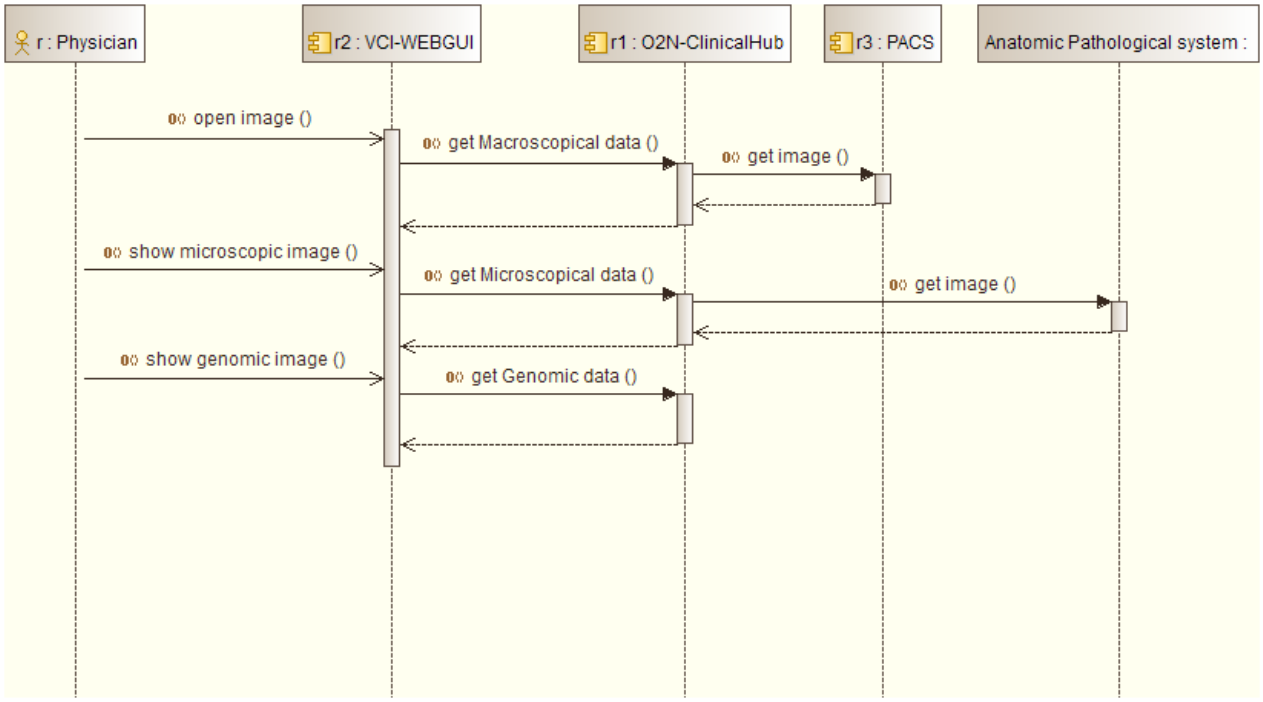

Fig. 21 - Navigation on interative clinical data sequence diagram

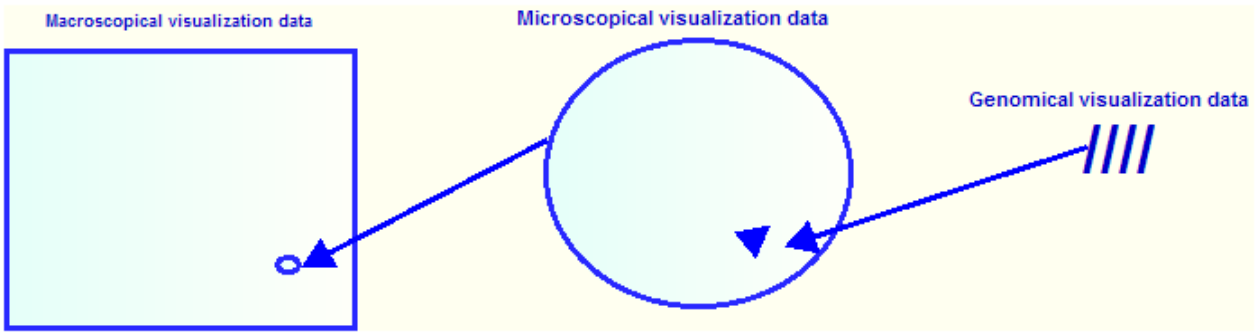

Fig. 22 - An example of the representation of navigation on interactive clinical data

As you can see from the above picture, the ***navigation on interactive clinical data*** starts from an image of a macroscopic anatomic representation of clinical data, by clicking on a detail of the macroscopic image the physician will visualize the related microscopic clinical data and so on till the genomic data.

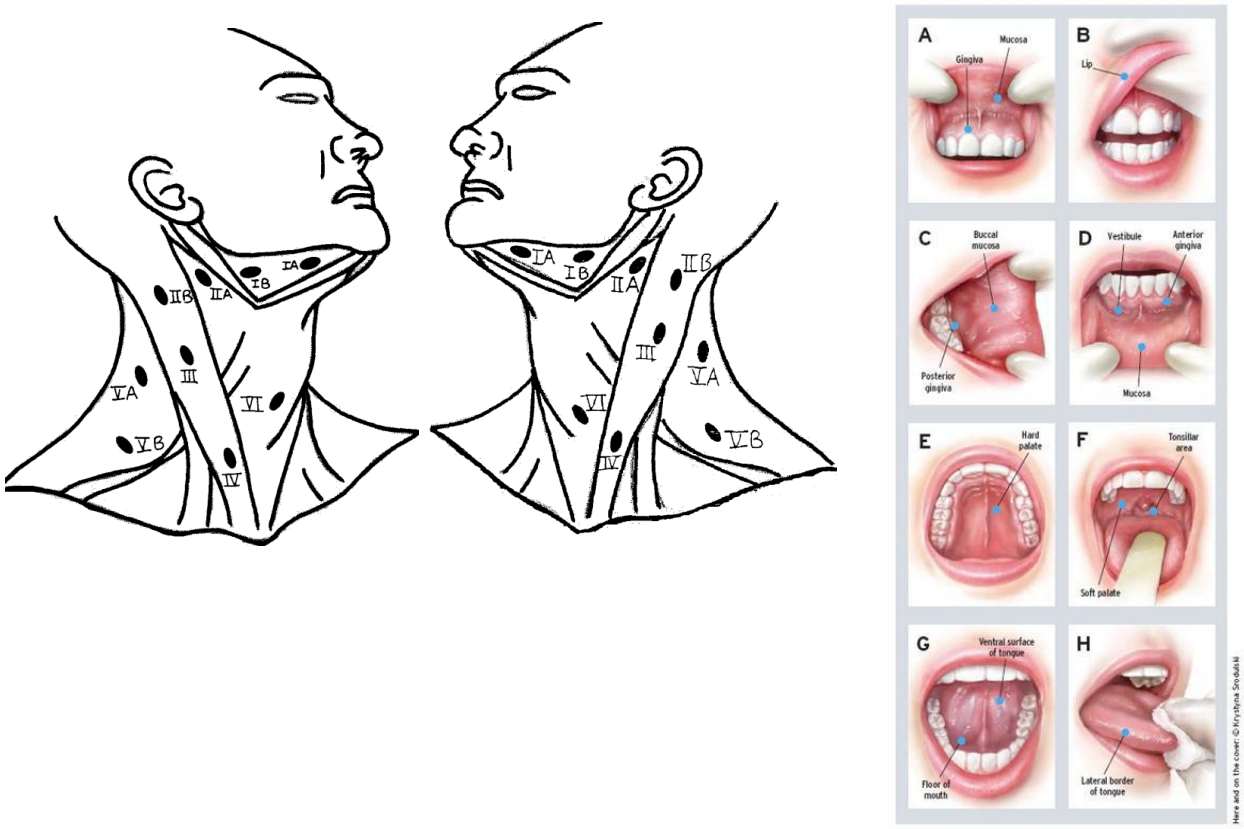

Fig. 23 - Some examples of macroscopic anatomic clinical data (from OraMod D2.2 document)

6.2.3 Tumor Board System

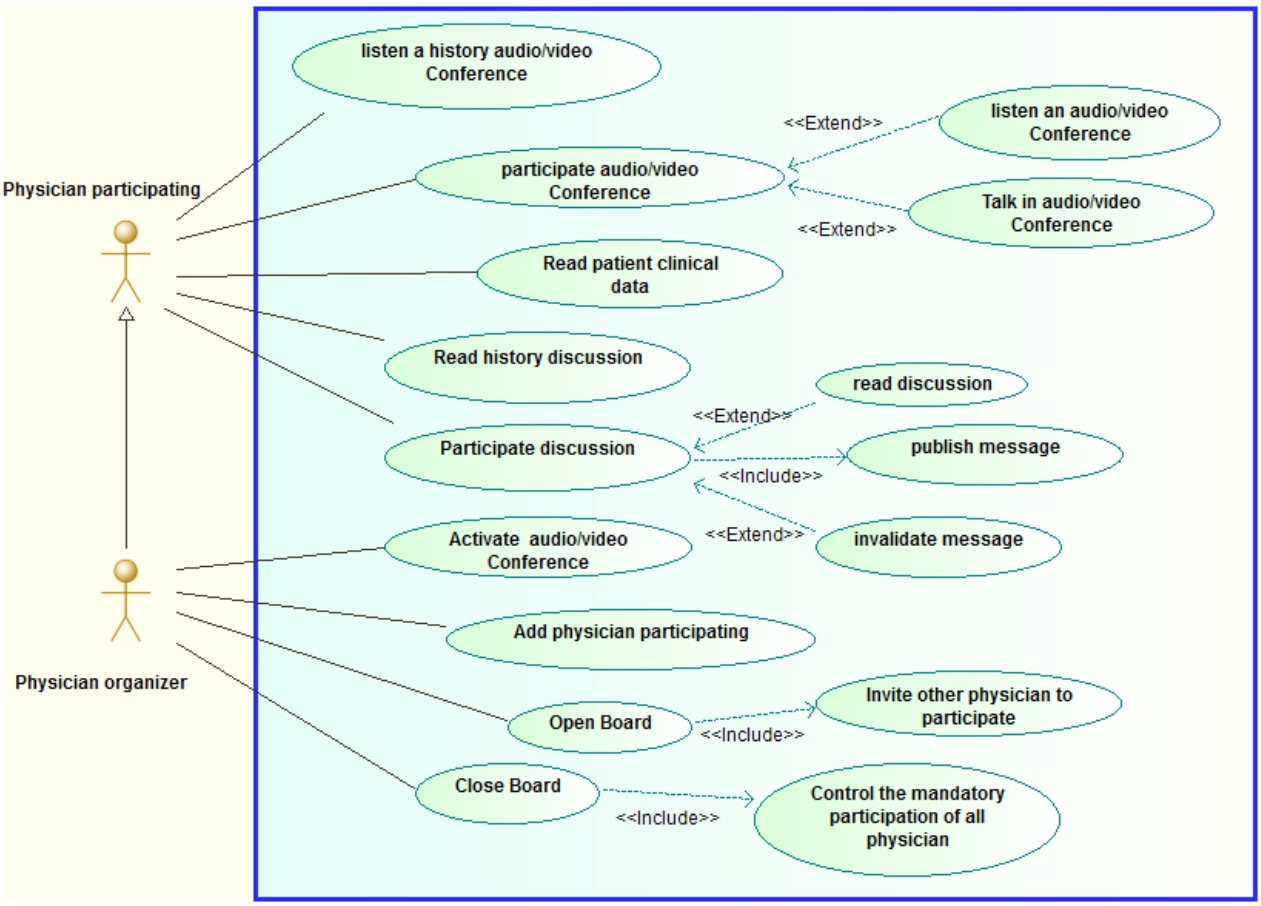

Fig. 24 - Use case diagram of the Tumor Board

As you can see from the above picture the system interacts with two different actors: the **physician organizer**, activating and organizing the board, and the **physician participating**, who can participate in the tumor board under exclusive invitation of the Physician organizer.

Actor 1: **Physician organizer**

This actor has more roles than other participants at the board. This actor chooses the patient, activates the tumor board, defines the title and the topic of the Board, invites other physicians participating and closes the Board. He can plan and invite participants to a synchronous audio/video conference. This actor is unique for every specific board. Physician Organizer has the same active role of all the participants, can add new participants to the Board and when he gets all the exhaustive answers from others participants he can close the Board writing a closing summary.

Actor 2: **Physician participating**

This is the actor invited to the Tumor Board, he can accept or refuse to participate to the board. Lately he can access patient clinical data, read/listen/view all the messages or previously recorded audio/video conferences/chats, he can write messages and accept to participate to audio/video conferences, invalidate his previous messages. He cannot invite other participants, neither activate synchronous audio/video conferences or close the board.

6.2.3.1 Open Board

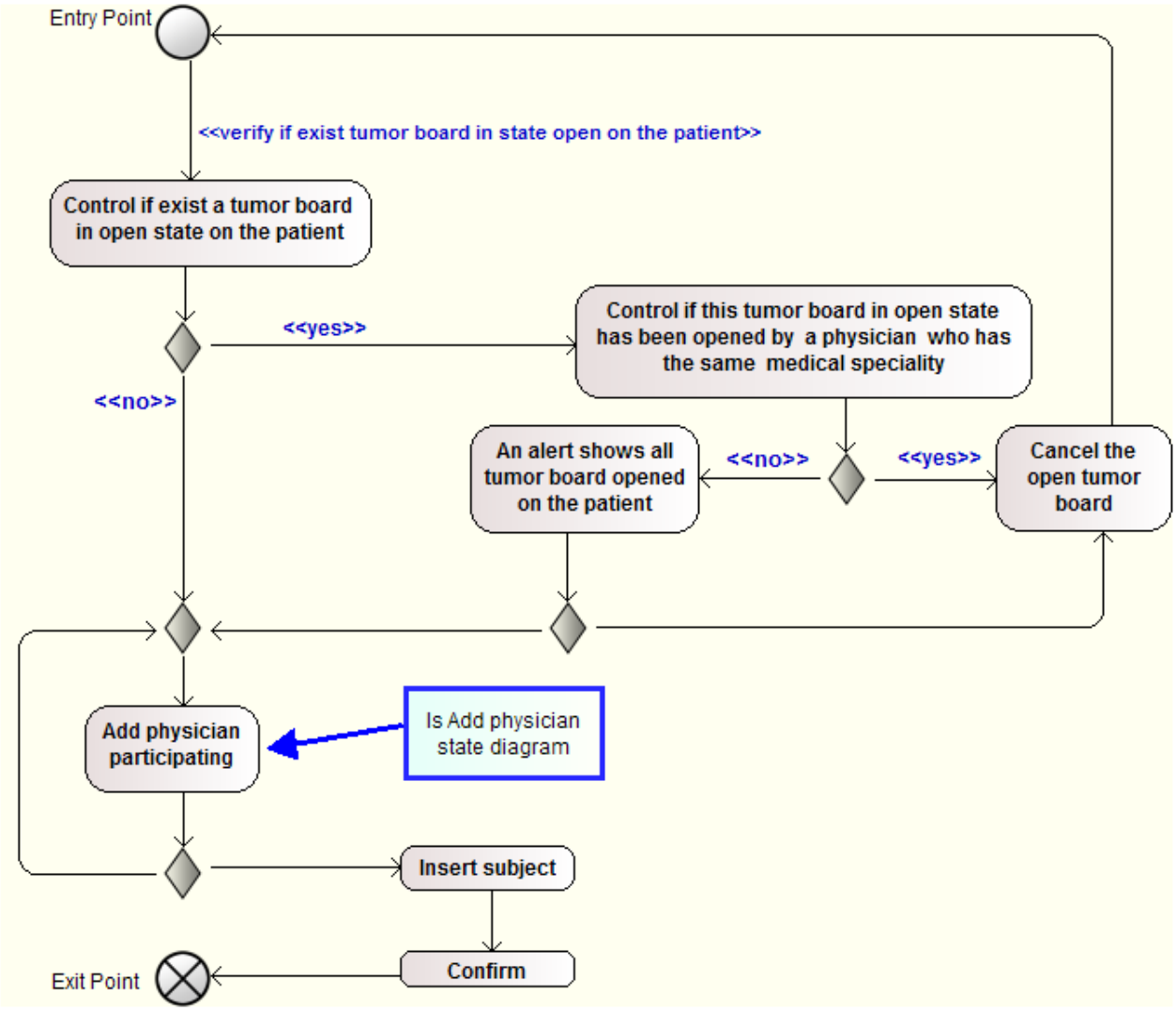

Fig. 25 - Open Board State Diagram

As we can see from the above use case diagram, the open board, can be only performed by the Physician organizer. The opening of the tumor board starts a sequence of controls and actions, which create the virtual tumor board environment, as follows:

1) Verifies if there's a still open tumor board on the same patient,

2) If NO, authorizes the opening of a new tumor board, if YES, the system checks if the open tumor board has been opened by a Physician of the same medical specialty (or same medical ward)

3) If NO, an alert shows all the boards open on the same patient and the physician can proceed and open a new Board or cancel the opening of the tumor board. If YES he can cancel the opening of the tumor board.

If all the controls let the Physician to open the board, it's mandatory to invite at least one **Physician Participating** (and have his acceptance) using the function **Add physician** and insert a text describing the subject/topic of the board going to be opened.

Below we present, using a sequence diagram, any operation provided by our system with the interaction with external agents that may be systems or other actors.

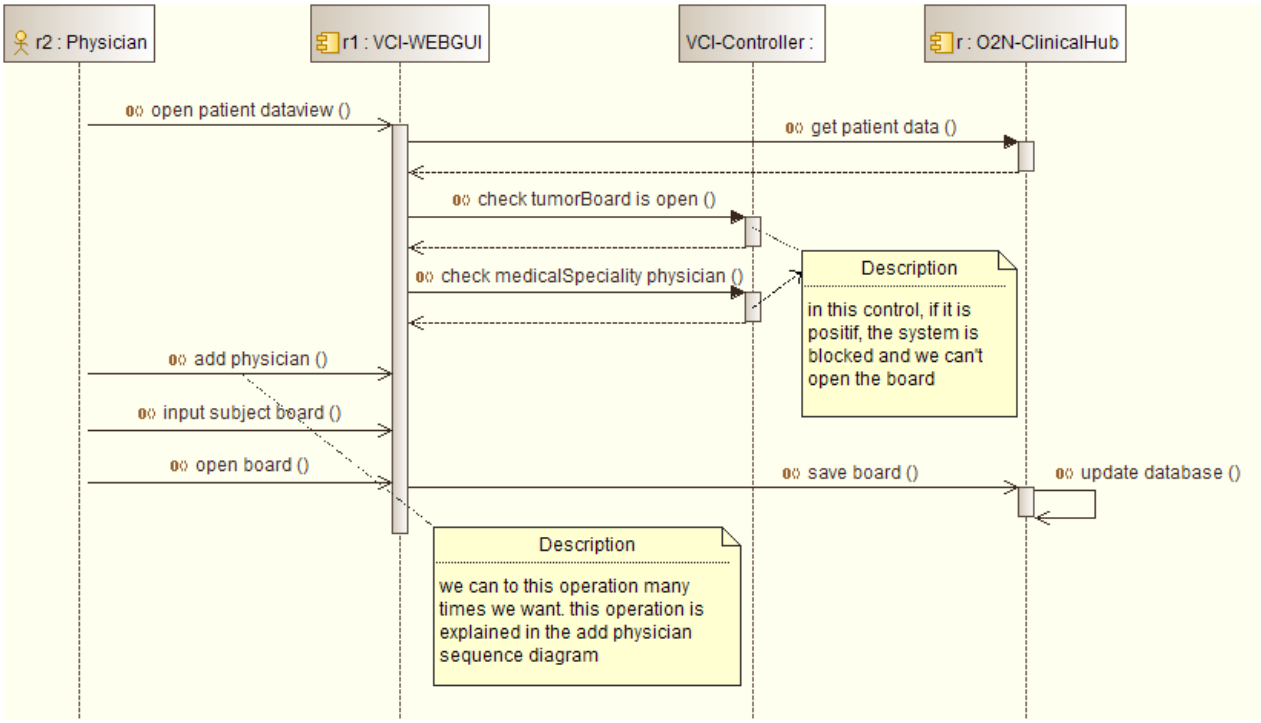

Fig. 26 - Open board sequence diagram

6.2.3.2 Add physician

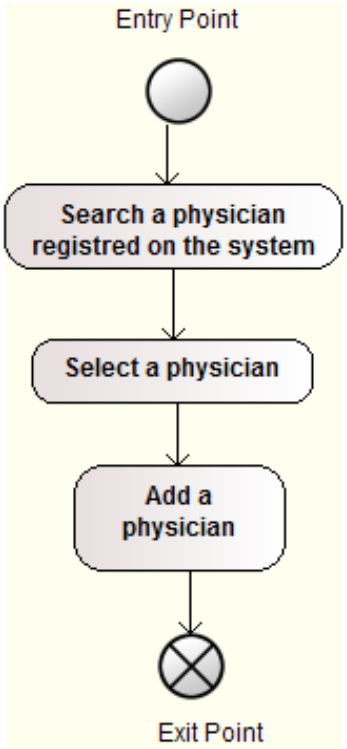

Fig. 27 - Add Physician State diagram

This function can be activated only by users with Physician Organizer roles and performed in two different phases only. First of all, this can be activated (at least once) while opening the tumor board. Lately, during the tumor board, this function can be activated following particular needs while the tumor board is ongoing.

The physician organizer reviews the physicians already registered in the system and adds those selected to participate to the tumor board (this action starts a notification message, that can be either an SMS, mail or smart-phone app, to the chosen physician/s). This action can be performed several times.

The following sequence diagram, presents any operation provided by our system with the interaction with external agents that may be systems or other actors.

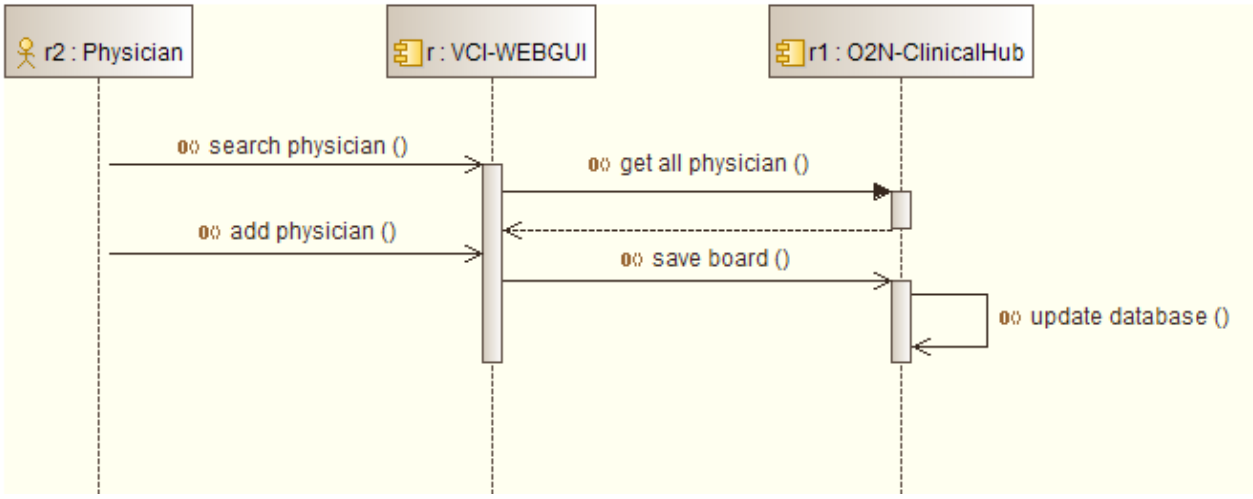

Fig. 28 - Add physician sequence diagram

6.2.3.3 Participate discussion

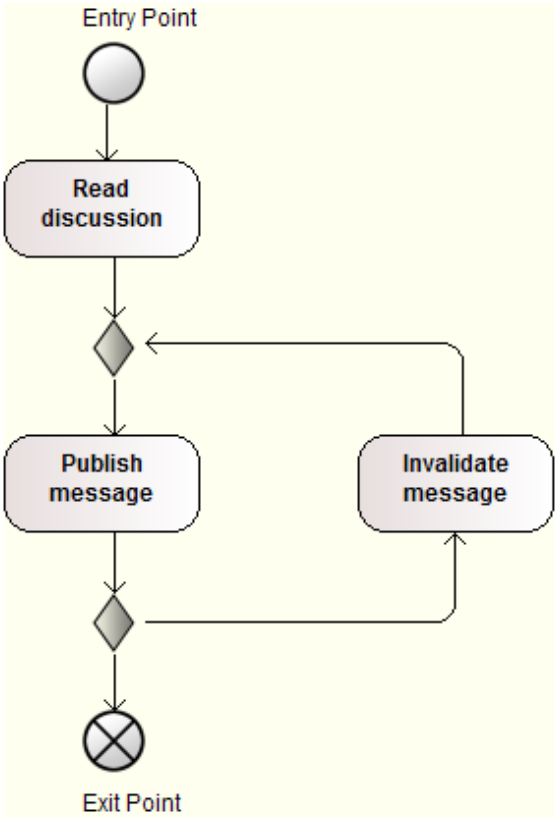

Fig. 29 - Participate discussion state diagram

When participating to a tumor board, the whole history of the discussion is shown. The single physician can insert his message/s that will be queued. A Physician can invalidate his message/s. A Physician participating must leave at least one message (even a simple ok to show his approval) to show his active participation at the board.

Below we present, using a sequence diagram, any operation provided by our system with the interaction with external agents that may be systems or other actors.

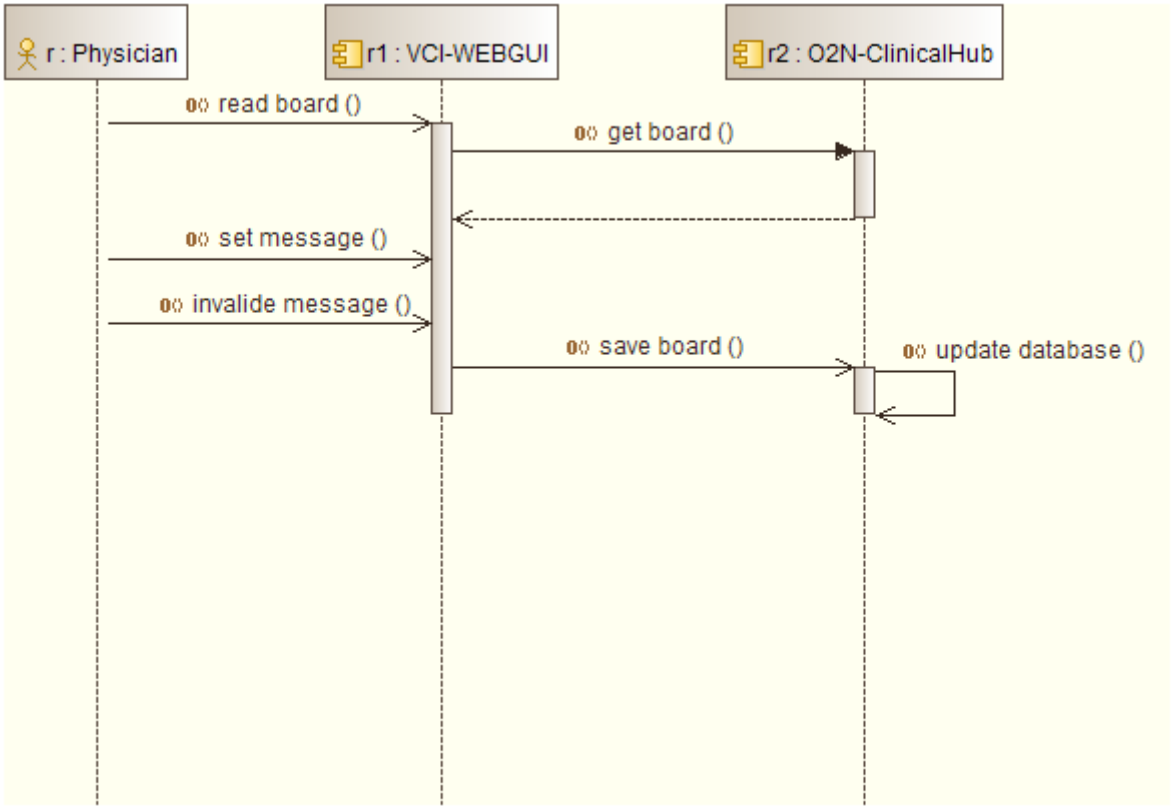

Fig. 30 - Participate discussion sequence diagram

6.2.3.4 Participate audio/video conference

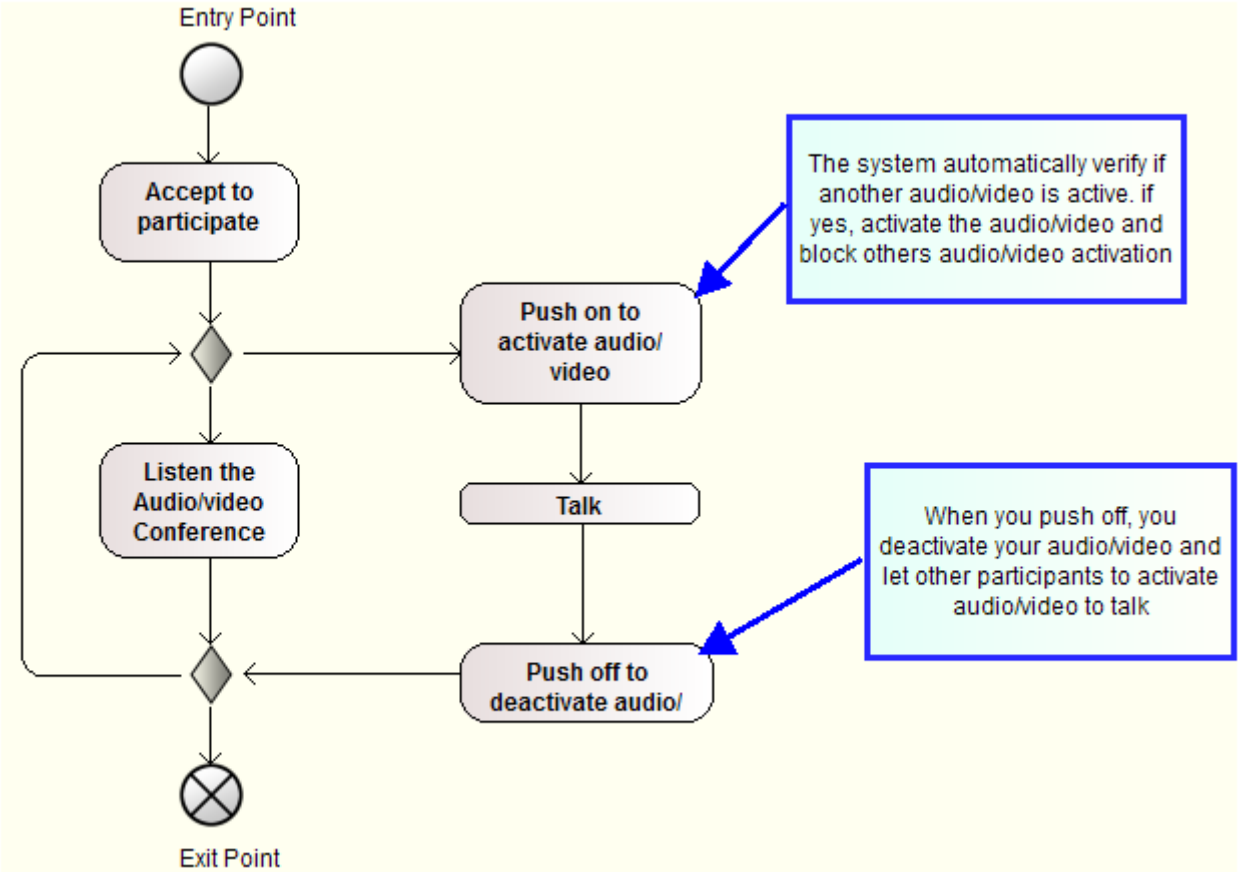

Fig. 31 - Participate Audio/video Conference state diagram

As you can see from the diagram, a Physician participating, after having accepted to participate to the synchronous audio/video conference, can simply choose to listen. During the whole conference the patient clinical data will be fully accessible. If a Physician wants to actively participate and intervene, he must follow the speaking protocol. The protocol requires that, in order to talk, the physician presses a keyboard button (push-to-talk) to activate the microphone. The system checks if there's already an open microphone in the conference group, if not the actor can freely activate the microphone and talk. This will prevent voice overlapping. When the actor has finished to talk he releases the microphone key and others can talk (only one microphone active at once).

The following sequence diagram, presents any operation provided by our system with the interaction with external agents that may be systems or other actors.

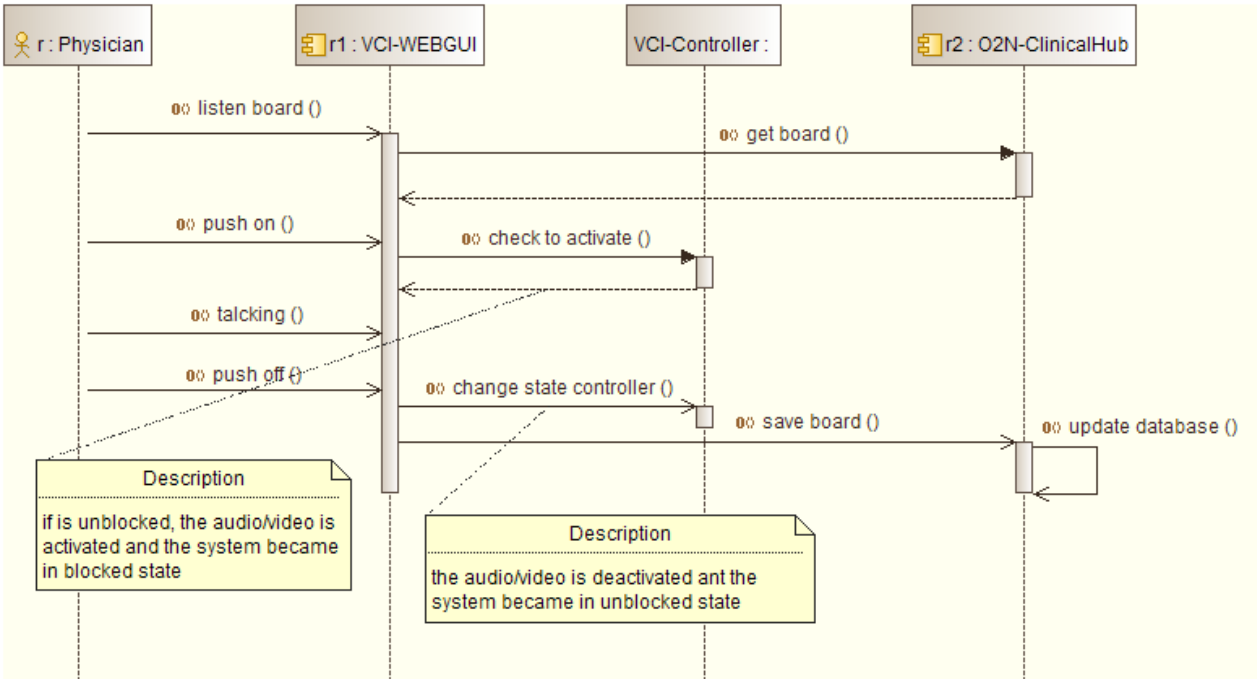

Fig. 32 - Participate audio/video conference sequence diagram

6.2.3.5 Close Board

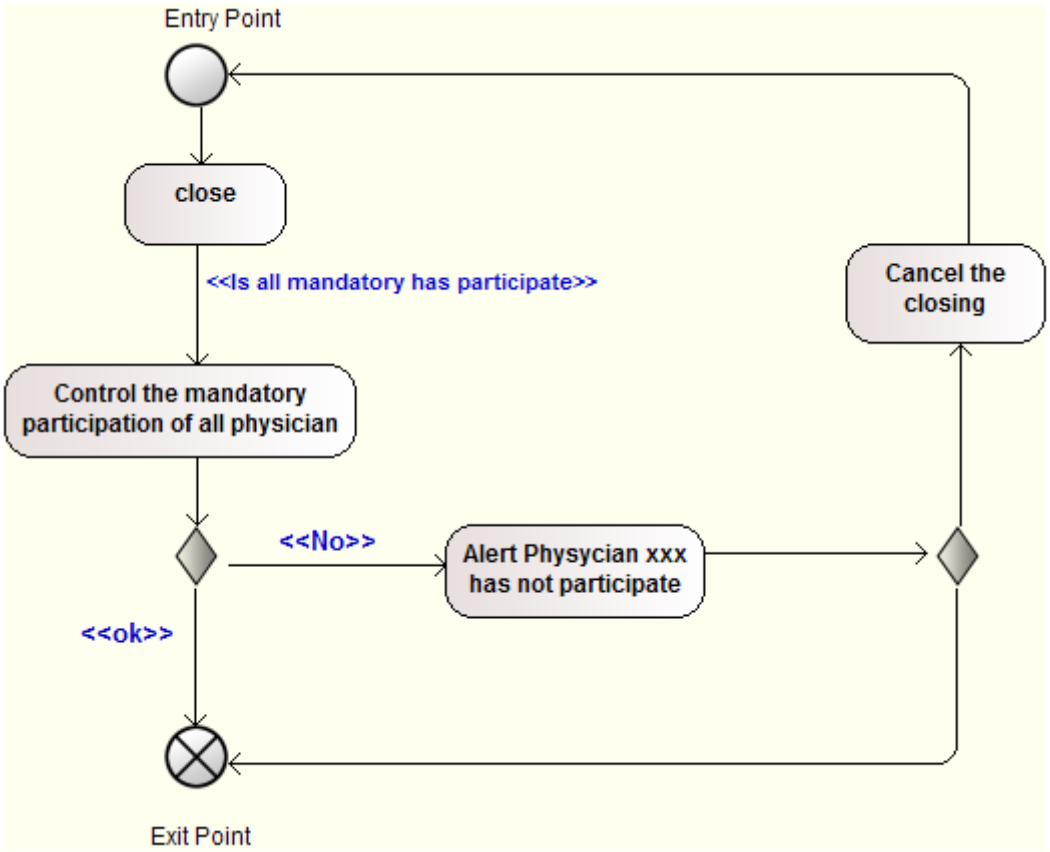

Fig. 33 - Close board state diagram

Only the Physician organizer can close the tumor board. Obviously he can decide to close the board only if he's fully satisfied by the contribution and information collected from every single Physician participating. While closing, the system controls if all the Physicians participating had at least 1 interaction with the system (at least 1 message or audio/video contribute) during the board of the single patient.

If YES the Board can be closed.

If NO an alert should state all the physicians not having left a contribution, at this point the Physician organizer can choose to close the tumor board or to wait for more contributions.

The following sequence diagram, presents any operation provided by our system with the interaction with external agents that may be systems or other actors.

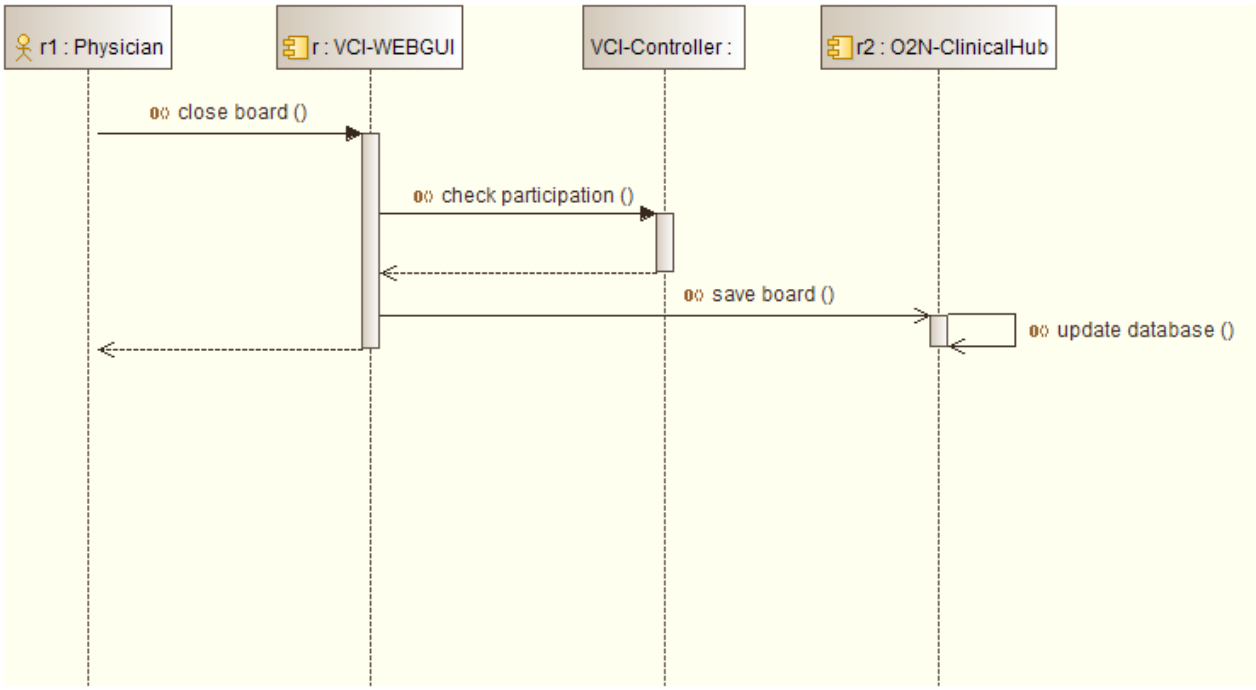

Fig. 34 - Close board sequence diagram

6.3 Multilayer Data Acquisition System

6.3.1 Manual data input system

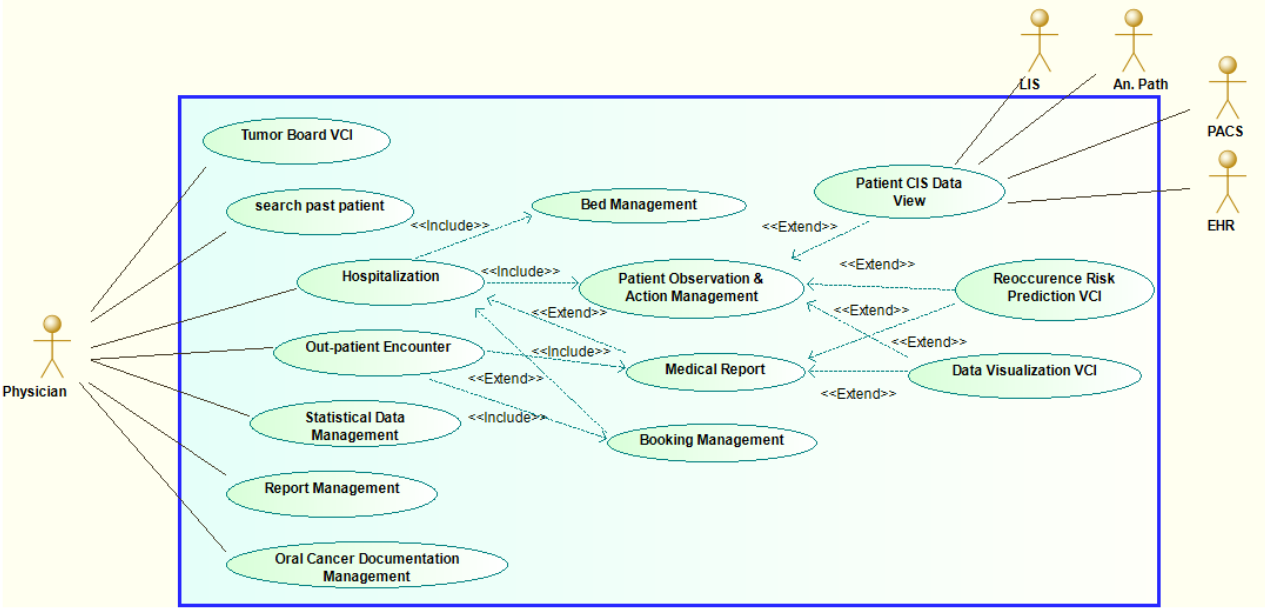

Fig. 35 - Manual data input use case diagram

As you can see from the picture above, our system (manual data input) represents the majority of the front-end layer of OraMod, namely GUI. All the services made available to the physician are listed, such as Tumor Board, Search Past patient, Hospitalization, Out-patient Encounter, Statistical data management, Report Management and Oral Cancer Documentation Management.

The Physician is the main actor of our system, but there are some other types of actors, belonging to other systems, interacting with Manual data input system (EHR, LIS, Anatomic Pathology, PACS).

As you can also see from the figure, our system provides other services, mostly to the main actor, in order to help him to achieve its many purposes.

6.3.2 Search past patient

The **Search Past Patient** Service allows us to manage all patient data already registered in our system. The service allow us through search fields to set the search parameters; in this way the system will return a list of patients that match the search parameters; the physician must select, from the list, the chosen patient in order to display all the clinical data from all the encounters performed by the patient in the past, but, also, all the encounters booked in the future.

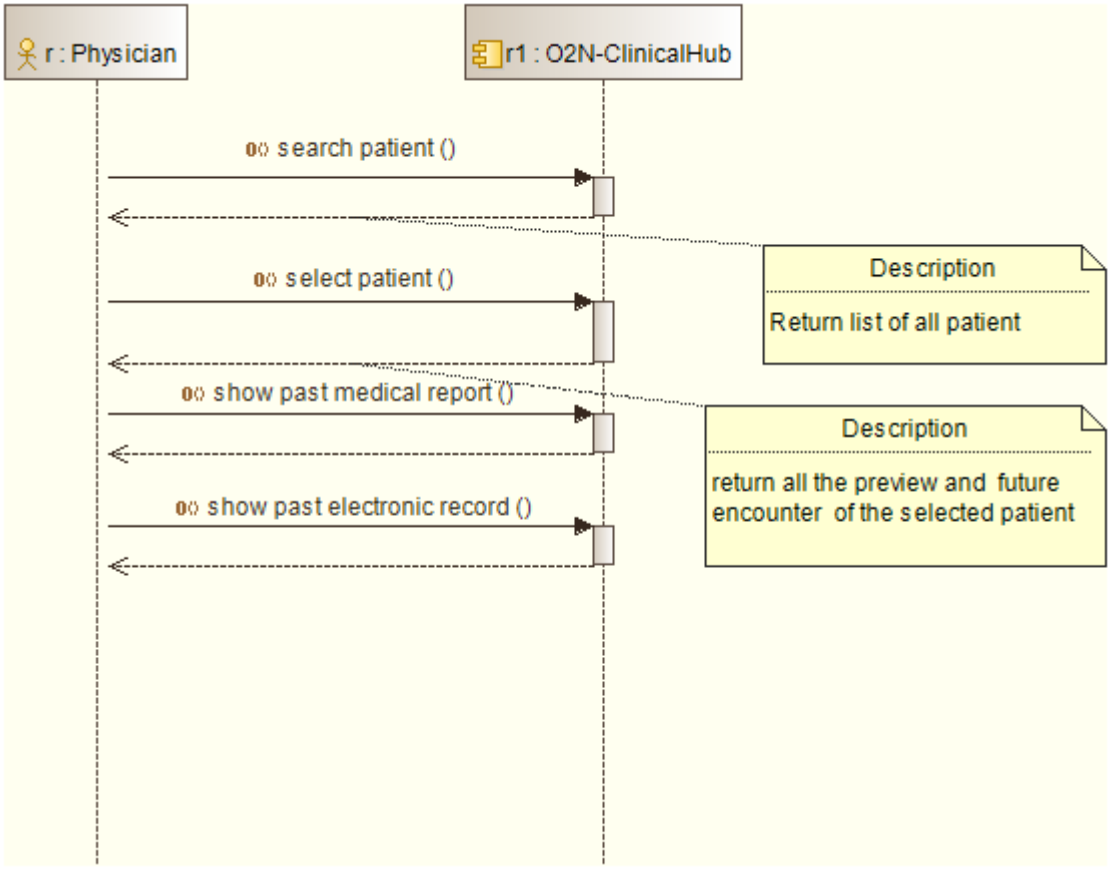

Fig. 36 - Search Past Patient State Diagram

6.3.3 Hospitalization

The Hospitalization service provides the management of a patient that needs to be hospitalized. From a practical point of view, it is necessary that the patient is already hospitalized (ADT system should have already communicated his admission) in order to activate the management of the beds and to allocate a patient to a bed; after that, by selecting the bed, the system will provide us the following options:

- view all clinical data registered in our system for this patient;
- book an encounter, for example: blood analysis, pathological anatomy, request of all the images related to that patient and EHR data.

The communication between our system and the systems that manage the encounters are made using HL7 messaging protocols. These different systems will communicate all the stored data stored for this patient, those data will be recorded in our system and made available to the user.

The user then can access to view add and modify any medical observation and action, such as therapeutic prescriptions, clinical data, display images (from PACS), make calculations by reoccurrence risk prediction, visually navigate that data. The system also allows to discharge a patient from the hospital.

Below we represent, using a sequence diagram, any operation provided by our system with the interaction with external agents that may be systems or other actors.

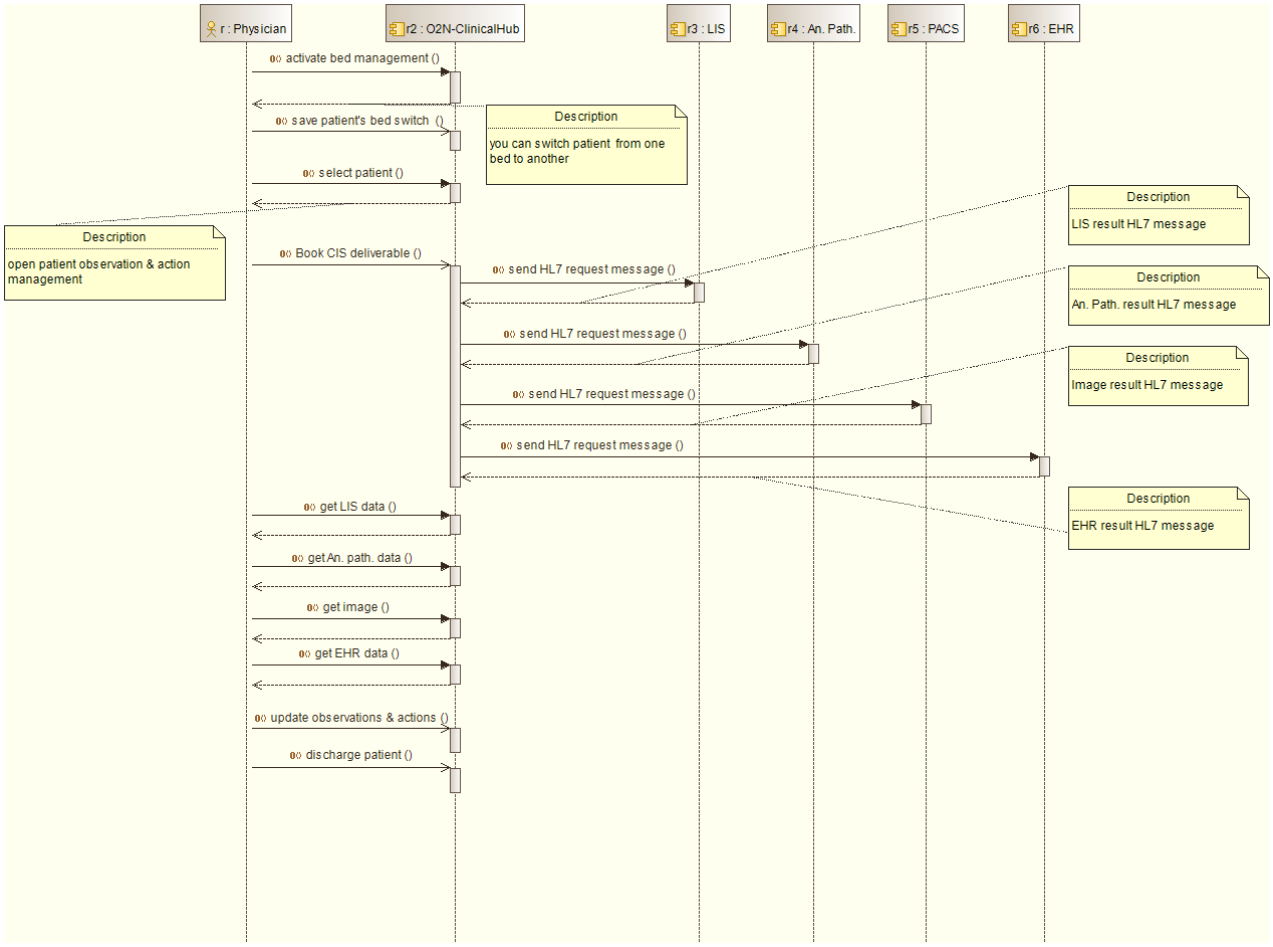

Fig. 37 - Hospitalization State Diagram

6.3.4 Out-patient Encounter

This service will provide to the users the management of the outpatient department for a single hospital.

The main functions are the Agenda Management, the booking of medical appointments for the patient, the registration of medical observations and actions during the patient visit and the final production and publication of the medical report.

The following diagram depicts this use case.

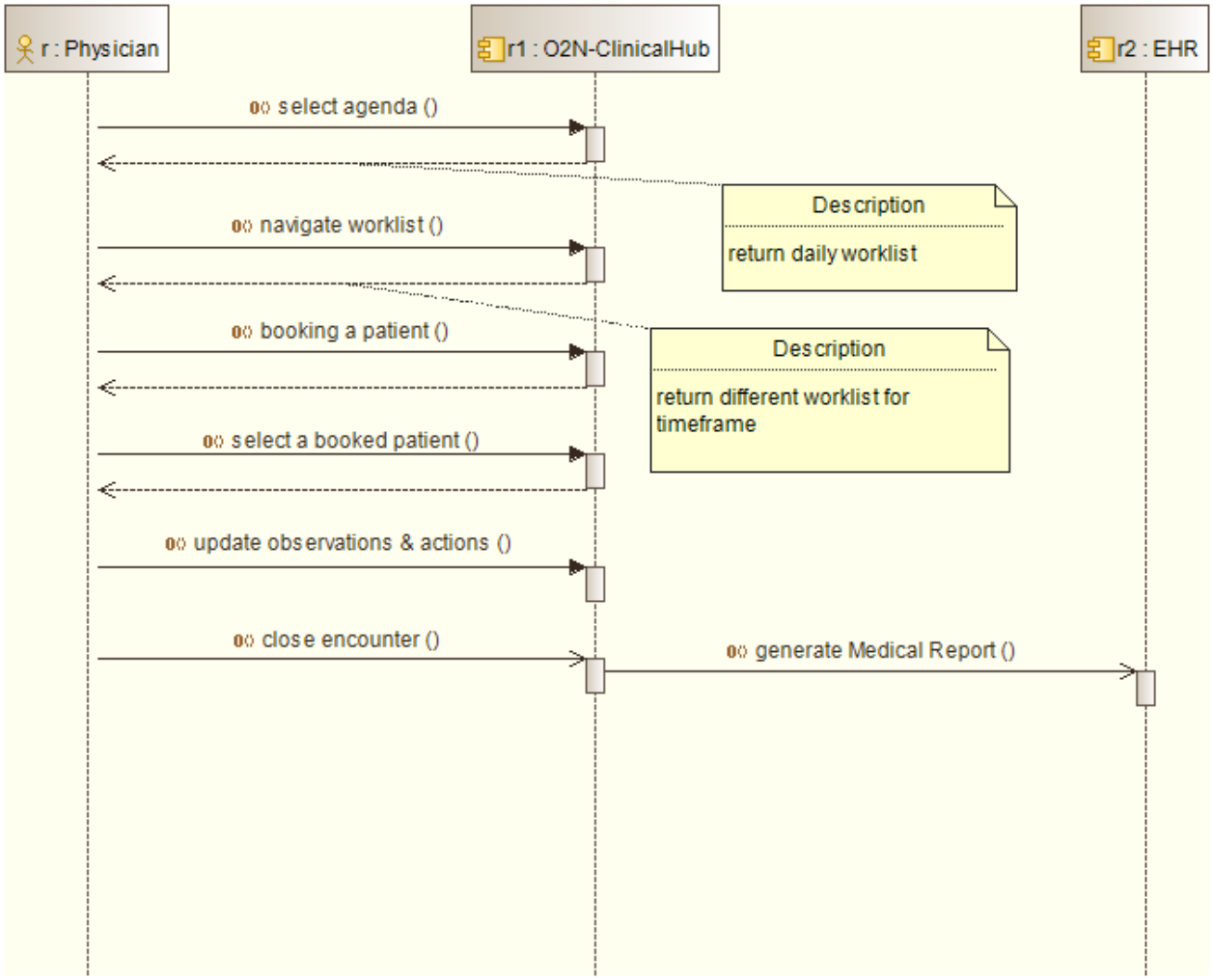

Fig. 38 - Our Patient Encounter State Diagram

6.3.5 Statistical data management

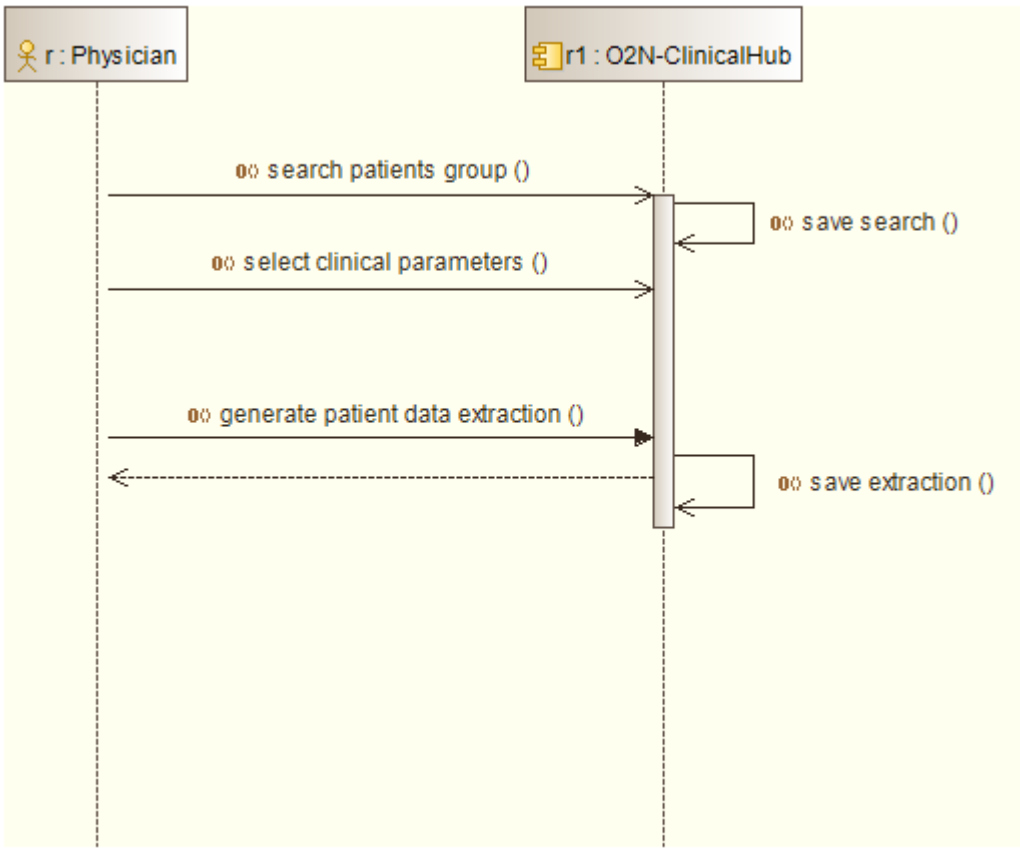

Fig. 39 - Statistical Data Management State Diagram

The service deals with the extraction of the clinical data of the patient for statistical purpose. Practically, this service provides to the user a function to select a group of patients depending on the search parameters. As a result the system shows a list of patients corresponding to the search criteria and provides an interface to select which specific clinical data will be shown. The data resulting from this query can be saved as a Comma Separated Value file for further data analysis (outside OraMod). In a similar way the search parameters (the query) can also be saved for future data search.

6.3.6 Report Management

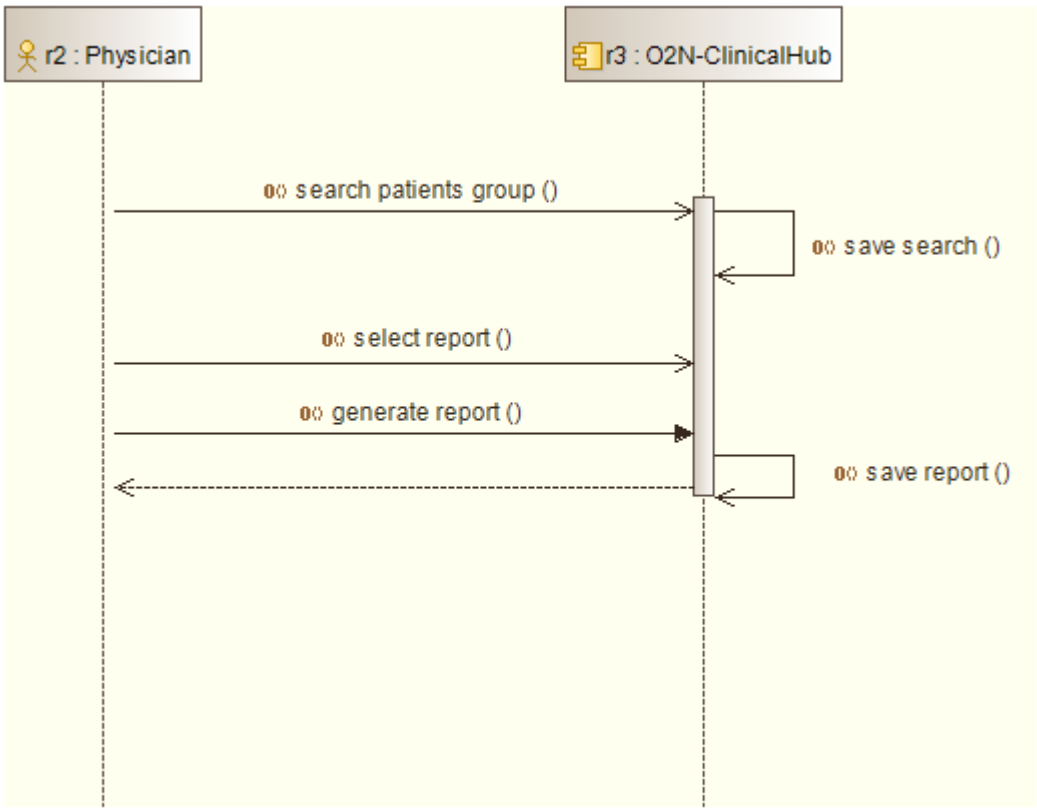

Fig. 40 - Report Management State Diagram

The **Report Management** service is responsible for processing reports for a single or a group of patients. The goal is to obtain a document showing patient's clinical data, patient's management data or system usage data. After choosing the type of the report required, as well as the patient selection parameters if applicable, the system will provide the type of report requested, populated with the group of selected patients if this case applies. Results can be saved on excel file or .pdf. As you can see from the chart, our system allows to save the search parameters for the report on a user basis.

6.3.7 Oral Cancer Documentation Management

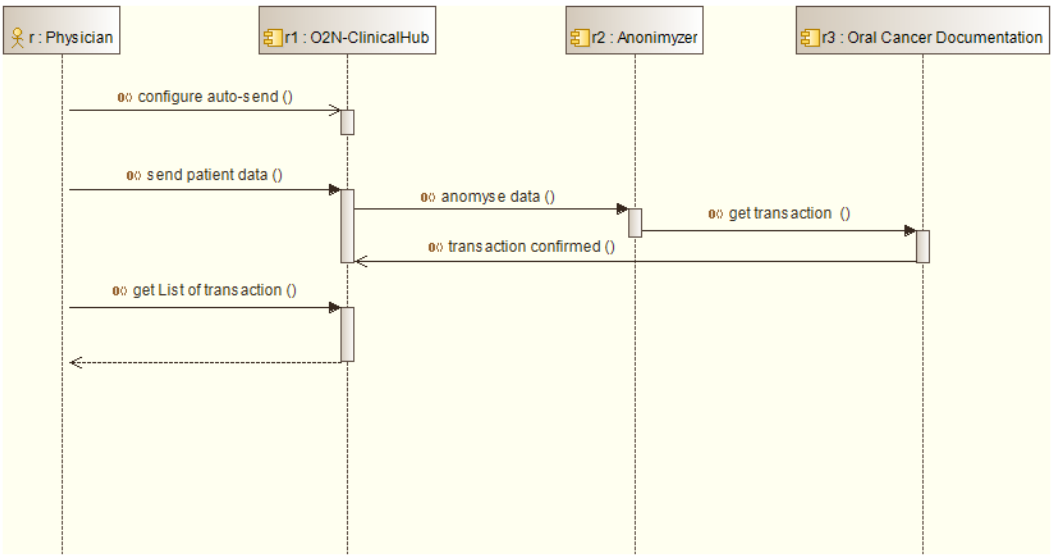

Fig. 41 - Oral Cancer documentation Management State Diagram

This service provides a function to transfer clinical data from the single hospital systems to the central database. It provides three operations as listed below:

- The ability to configure the auto transactions, namely configure our system so that it can send the data in an automatic way according to some parameters (time, which data and how to send data).
- The possibility to activate the transaction in manual mode, giving the opportunity to manually send new data to the central system.
- The system also will show all the transactions performed towards the central database, listing all the transaction made from the single hospital system to the central database.

Please note that our system will send the data to the anonymization system provided by every hospital IT services. This system will completely remove any patient related confidential data, before sending clinical parameters to the Oral Cancer Documentation database. The central database, after saving the data, will start an handshaking communication in order to confirm the correct reception of data and the correct acknowledgment to the hospital.

6.4 Image Processing Tool

Here we analyze how the images coming from RIS have to interact in OraMod.

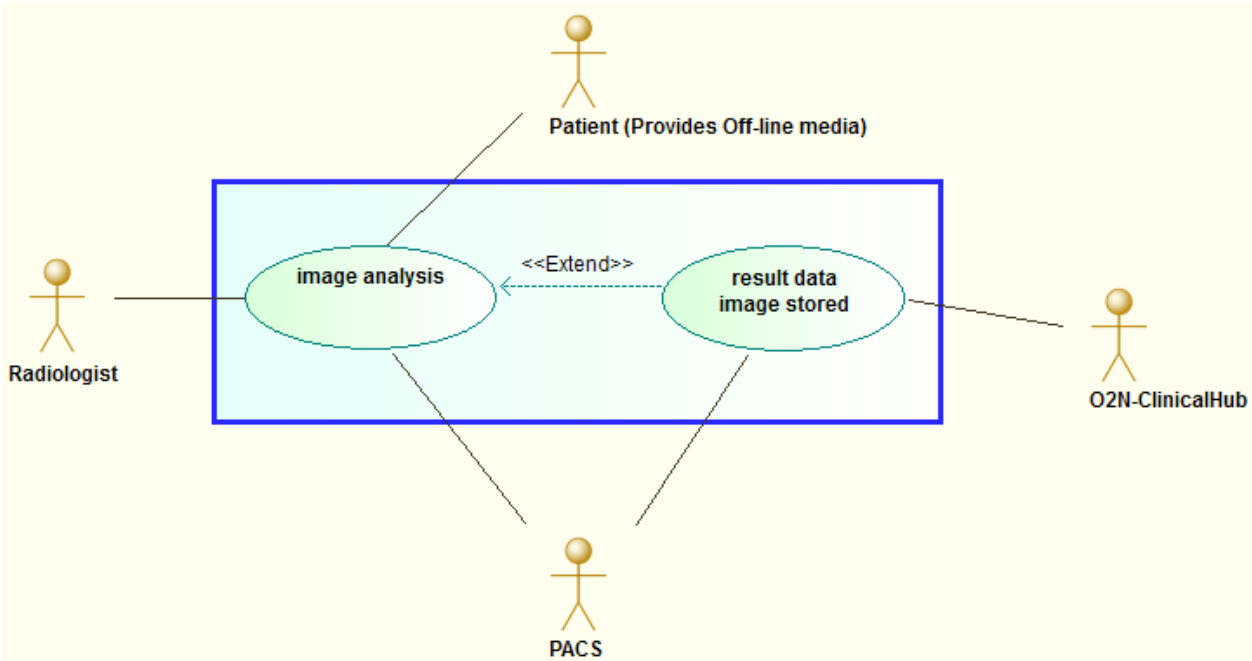

Fig. 42 - Image Processing Tool Use case diagram

6.4.1 Image analysis

As we can see from the above use case diagram, our systems interacts with one single specific actor (the Radiologist is a Physician type specialized in diagnosis using medical imaging techniques). This system analyzes patient imaging data coming from different systems and generates as a result a new image set and parametric patient clinical data related to the image set. Both the new image set and the parametric patient data will be saved. The original imaging data can be obtained from two different sources online data from PACS and/or Off-line Media.

6.4.1.1 Online data source option

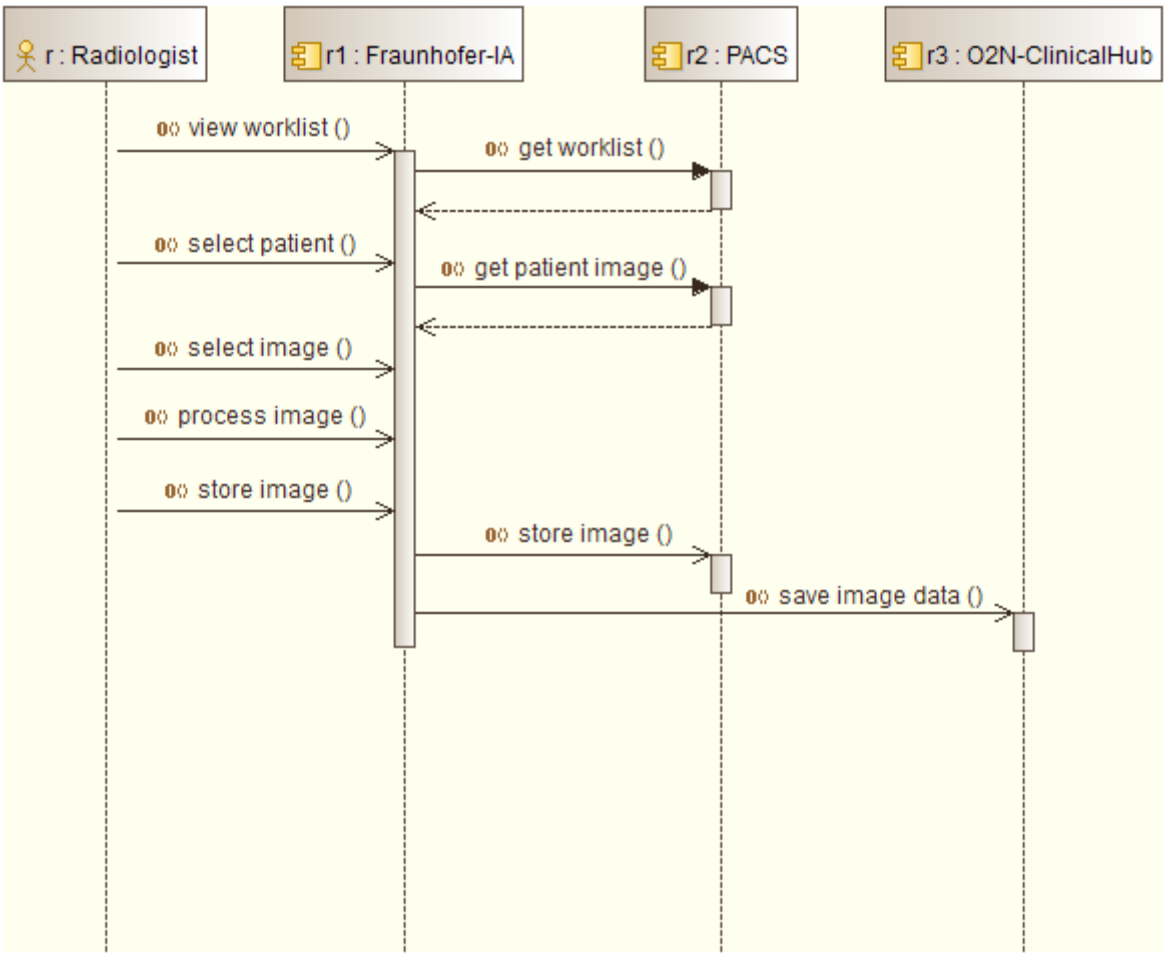

Fig. 43 - Image Analysis Online Modeling Sequence diagram

In this case, the Radiologist, using the Image Processing Tool, makes a request of the daily working list or the single patient data from the **PACS** (**modality worklist query**); the PACS then returns the detailed list of planned tasks/patients. When the Radiologist will select a patient from this list, the PACS will returns to the Image processing tool all the previously stored imaging procedures related to this patient. The Radiologist selects all the procedures or the single images needed for the processing and the Tool retrieves from the PACS the selected images (**Query/Retrieve**). The result of the processing is a set of images and a defined set of data: the set of images will be saved back to the PACS (**Storage**) the data will be saved in the Multilayer Data Acquisition System.

6.4.1.2 Off-line Media option

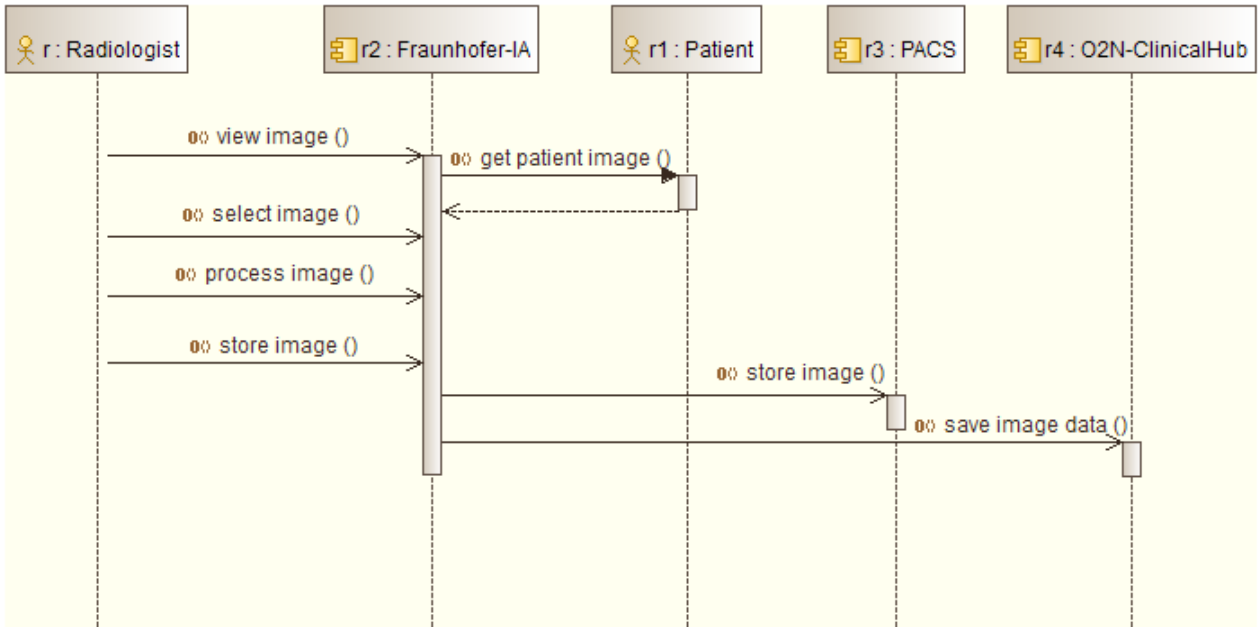

Fig. 44 - Image Analysis Off-line Modeling Sequence diagram

The Radiologist will select and retrieve the patient images from one or more media provided directly by the patient. Images are then elaborated in the Image Processing Tool and, again, the Tool will generate a set of images and a defined set of data: the set of images will be saved back to the PACS (**Storage**) the data will be saved in the Multilayer Data Acquisition System.

6.4.1.3 Result Image and Data Storage

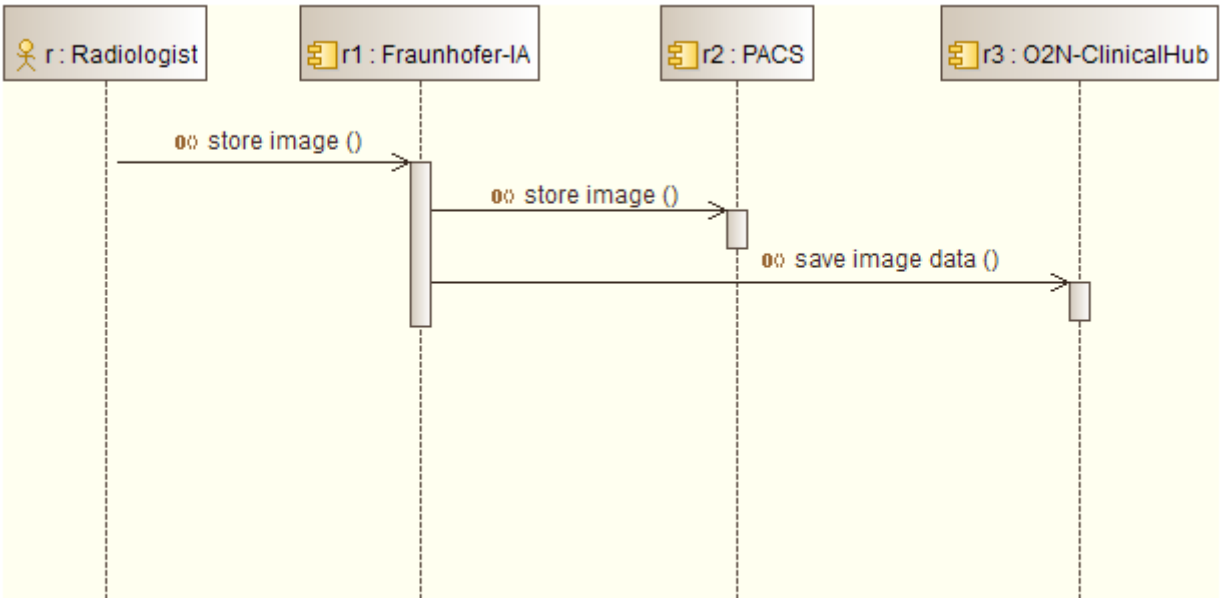

Fig. 45 - Result Image and Data Storage Sequence diagram

As we can see from the diagram as well as from previous paragraphs the Image Processing Tool will allow to save the results of the performed analysis. The results will be both a new set of images and a set of parametric clinical data. Both sets will be saved, as a single atomic operation, in two different storage systems. Images will be saved in the PACS (either the Hospital PACS or a specific OraMod PACS). The parametric clinical data will be saved in the Multilayer Data Acquisition System (ClinicalHub).

6.5 qRT-PCR Device

To obtain genomic data for OraMod environment we have identified the use case explained below.

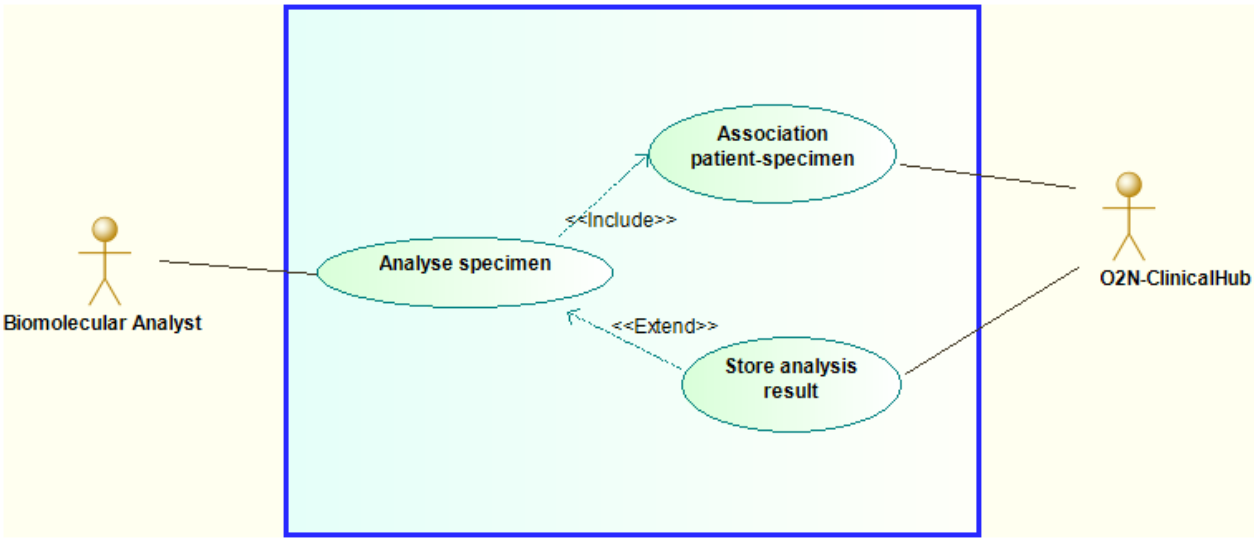

Fig. 46 - qRT-PCR Device system use case

As we can see from the above picture the system will provide one main function:

1. ***Analyze specimen*** – Analyze the test cartridge content and generates results.

Still from the above picture the function **Analyze specimen** additionally allows the user to save the result data but has, as a prerequisite, the association patient - test cartridge.

Note that we are referring to the qRT-PCR System as a whole system not considering the split between the qRT-PCR managing software AND the device itself (the device is considered a peripheral of the managing system)

6.5.1 The qRT-PCR state diagram

To better explain this procedure we designed the following state diagram.

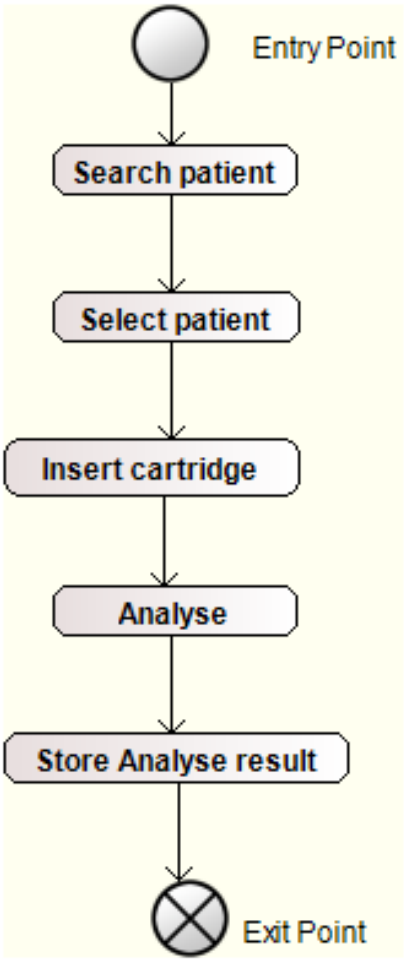

Fig. 47 - qRT-PCR Device system state diagram

The Biomolecular Analyst inserts the test cartridge (already filled with the purified specimen) in the qRT-PCR device. The Biomolecular Analyst, using the qRT-PCR interface, will research the patient from a list already obtained from the Multilayer Data Acquisition System, and links it to the test cartridge (obtaining the cartridge unique ID and the cartridge Lot ID). The Biomolecular Analyst executes the analysis and the relative results (already univocally linked to the patient) will be saved. Since many operations require interactions with different systems and actors we produced a general sequence diagram of the system showing all the links with other systems.

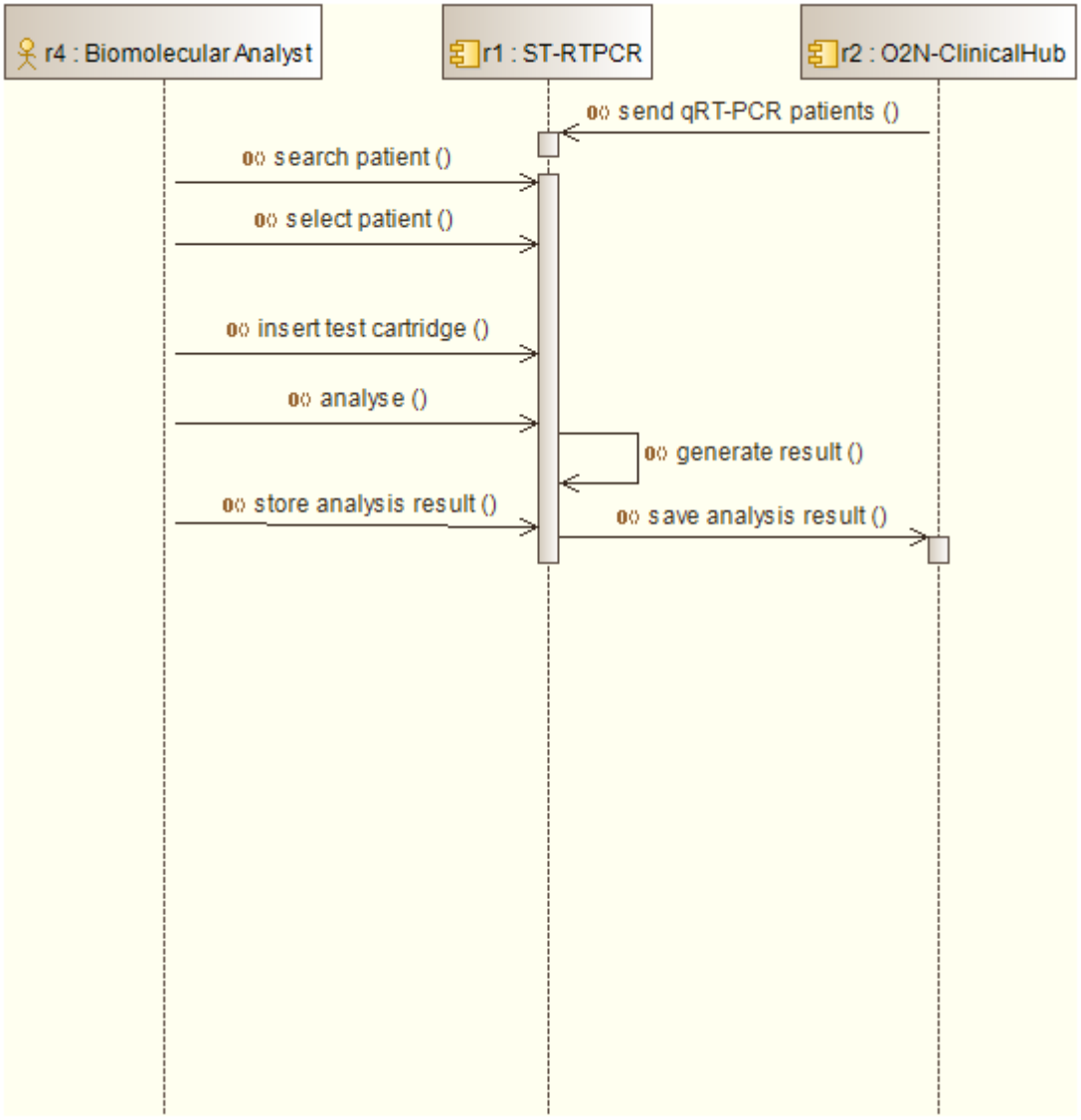

Fig. 48 - qRT-PCR Device system sequence diagram

The Multilayer Data Acquisition System will send a work-list and all their changes to the qRT-PCR system. The Biomolecular Analyst will search a patient within the work-list, and selects the patient, linking it to the test cartridge. Subsequently the cartridge will be inserted in the qRT-PCR System and specimen analysis will be started; once a result is be obtained it will be also saved on the Multilayer Data Acquisition System (ClinicalHUB).

6.5.1.1 Association Patient-Test cartridge

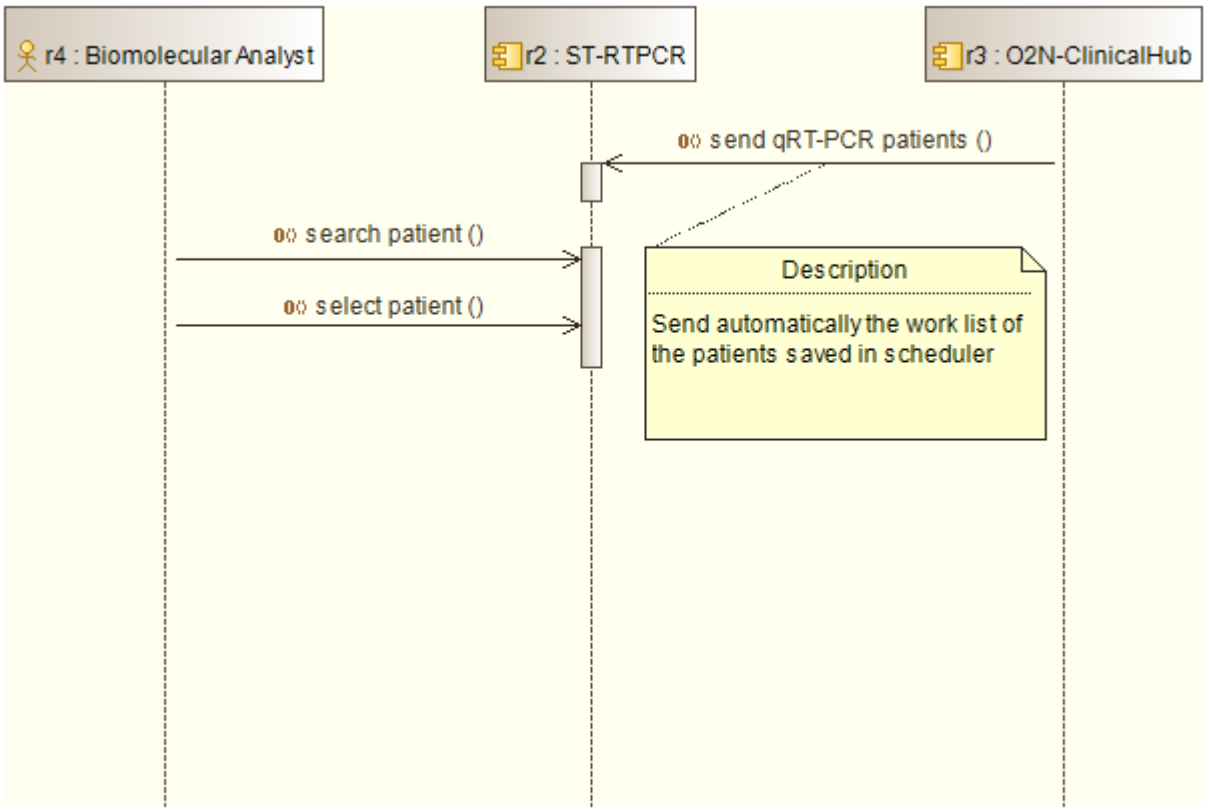

Fig. 49 - Association Patient-Test cartridge Sequence diagram

This service will allow the association between the patient and the test cartridge. From the qRT-PCR System the Biomolecular Analyst will search a patient within the work-list. The Biomolecular Analyst then selects the specific patient and associates it to the test cartridge.

6.5.1.2 Analyze specimen

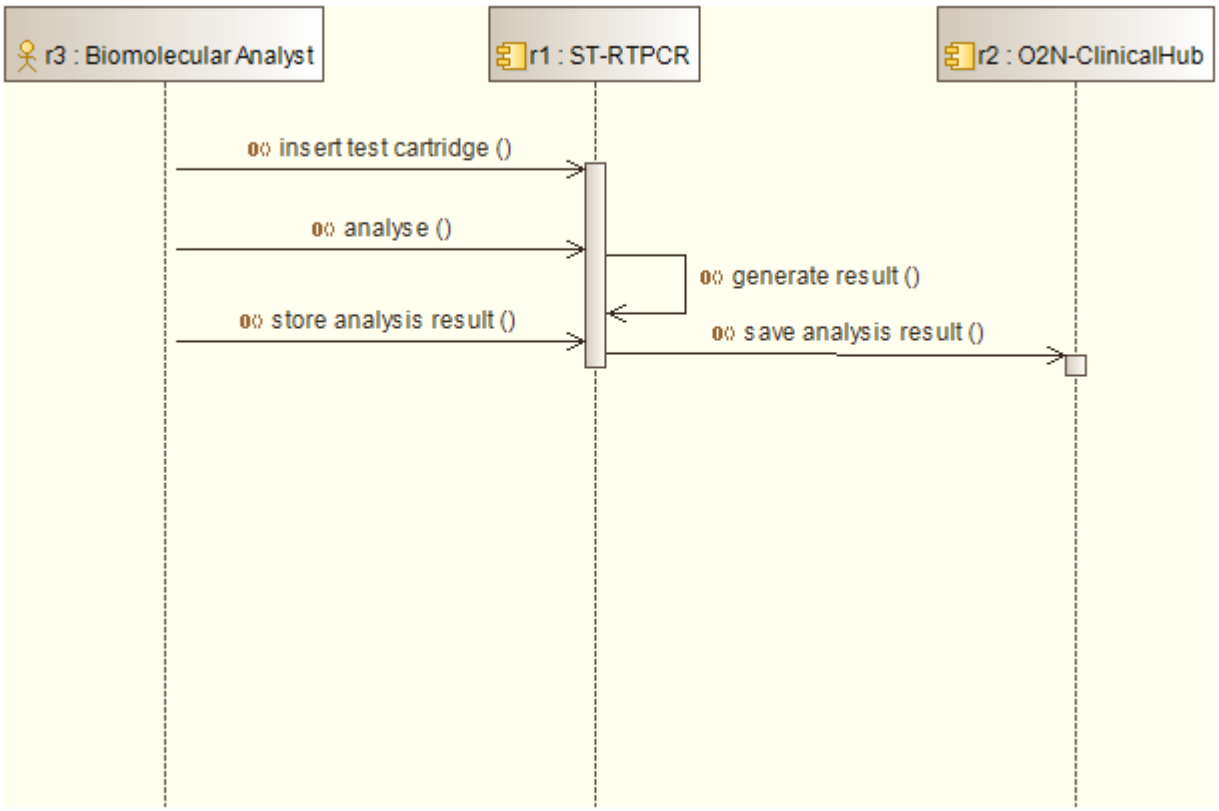

Fig. 50 - Analyze specimen sequence diagram

This Function or Service will analyze the specimen contained in a cartridge carrying a specific unique ID by inserting it in the system. Insertion starts the analysis operation and the obtained result will be sent to and saved in the Multilayer data Acquisition System (ClinicalHUB).

6.6 Oral Cancer Predictive Model Generator

This Section of the technical design, describing the prediction simulation tool, will be analyzed and designed in the Task 3.2, soon after the publication of the following deliverables:

D3.1) Data analysis algorithms: Document detailing the algorithms used and the final predictive model definition [month 12].

D3.2) Prediction simulation tool: Software prototype for the simulations of reoccurrence prediction based on users-defined parameters and biomarkers [month 18].

The integration of this tool will be implemented during the Task 3.4 "Model Validation" as described in the DOW, and will follow this steps:

D3.2 Software prototype for the simulation of reoccurrence prediction [Month 18]

D3.3 The OraMod final predictive model and its specifications for inclusion into the OraMod platform (T6.4) [Month 25]