



## Deliverable No. 11.3

### Report on the second evaluation workshop round

Grant Agreement No.: 600841  
Deliverable No.: D11.3  
Deliverable Name: Report on the second evaluation workshop round  
Contractual Submission Date: 31/03/2016  
Actual Submission Date: 15/04/2016

Dissemination Level		
PU	Public	
PP	Restricted to other programme participants (including the Commission Services)	
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (including the Commission Services)	X



<b>COVER AND CONTROL PAGE OF DOCUMENT</b>	
Project Acronym:	<b>CHIC</b>
Project Full Name:	Computational Horizons In Cancer (CHIC): Developing Meta- and Hyper-Multiscale Models and Repositories for In Silico Oncology
Deliverable No.:	D11.3
Document name:	Report on the second evaluation workshop round
Nature (R, P, D, O) <sup>1</sup>	R
Dissemination Level (PU, PP, RE, CO) <sup>2</sup>	CO
Version:	6.0
Actual Submission Date:	15/04/2016
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#### **ABSTRACT:**

This deliverable reports on 2 different evaluation workshops. The first was held in Söllereck, Oberallgäu in Germany from the 9<sup>th</sup> to the 13<sup>th</sup> of January 2016. The second took place during the 9<sup>th</sup> International Renal Tumor Biology Conference in Toronto, Canada from the 2<sup>nd</sup> to the 3<sup>rd</sup> of April 2016. During the first of these evaluation workshops the most important objective of this session was the question, if the nephroblastoma hypermodel, as a test of principle, can serve as a clinical decision support tool for paediatric oncologists in the future. Results are encouraging. We received 43 answers to our questionnaire out of 52 participants with an overall positive resonance. At the second of these evaluation workshops the Clinical Data Repository (CDR) and the two hypermodels (phenomenological and multimodeller) for nephroblastoma running under the Clinical Research Application Framework (CRAF) were evaluated. Out of 65 participants we received feedback from 28 regarding CDR and from 33 regarding the CRAF evaluation. Results of the evaluation for both tools are very promising. They will help to optimize them. To continue with evaluations of the CRAF a web-based CRAF is under development to allow the scientific community to test CRAF and the hypermodels in the future.

#### **KEYWORD LIST:**

Evaluation workshops, CDR, CRAF, hypermodelling, cancer, in silico oncology

<sup>1</sup> R=Report, P=Prototype, D=Demonstrator, O=Other

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

*The research leading to these results has received funding from the European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 600841.*

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<b>MODIFICATION CONTROL</b>			
<b>Version</b>	<b>Date</b>	<b>Status</b>	<b>Author</b>
1.0	15/10/2015	Draft	Norbert Graf
2.0	15/01/2016	Draft	Norbert Graf
3.0	11/02/2016	Draft	Norbert Graf
4.0	25/03/2016	Draft	Norbert Graf
5.0	29/03/2016	Draft	Norbert Graf
5.1	04/04/2016	Draft	Roman Niklaus
5.2	04/04/2016	Draft	Stelios Sfakianakis
5.3	09/04/2016	Draft	Norbert Graf
5.4	11/04/2016	Draft	Norbert Graf
6.0	14/04/2016	Final	Norbert Graf

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## 1 Executive Summary

According to the DoW a second evaluation workshop was planned as part of task 11.3. This deliverable reports on two different evaluation workshops. The first was held in Söllerneck, Oberallgäu in Germany from the 9<sup>th</sup> to the 13<sup>th</sup> of January 2016. The second took place during the 9<sup>th</sup> International Renal Tumor Biology Conference in Toronto, Canada from the 2<sup>nd</sup> to the 3<sup>rd</sup> of April 2016. During the first of these evaluation workshops the most important objective of this session was the question, if the nephroblastoma hypermodel, as a test of principle, can serve as a clinical decision support tool for paediatric oncologists in the future. Results are encouraging and presented in detail in this deliverable. We received 43 answers to our questionnaire out of 52 participants with an overall positive resonance. At the second evaluation workshop the Clinical Data Repository (CDR) and the two hypermodels (phenomenological and multimodeller) for nephroblastoma running under the Clinical Research Application Framework (CRAF) were evaluated. Out of 65 participants we received feedback from 28 regarding CDR and from 33 regarding the CRAF evaluation. Results of the evaluation for both tools are very promising and shown in detail in this deliverable. The results of both evaluation workshops will help to optimize CDR and CRAF.

To continue with testing and evaluations of the CRAF a web-based CRAF is under development to allow the scientific community to get access to CRAF and the hypermodels in the future.

As the results of the evaluations are very promising the CHIC consortium decided to set this deliverable on confidential to protect IP issues.

## 2 Introduction

### ***2.1 Purpose of the second evaluation workshop***

The purpose of the second evaluation workshop, as proposed by the DoW, was to test integrated hypermodels of CHIC to demonstrate that end-users will be able to run such tools. For that purpose we also evaluated the Clinical Data Repository (CDR) as data management is of utmost importance for end-users.

During the preparation of the second CHIC evaluation workshop, that should have taken place in Schloss Dagstuhl in Wadern/Germany from the 7<sup>th</sup> to the 9<sup>th</sup> of September in 2015, we received less than 10 applications for this workshop. As a result of this low number we decided to skip this workshop and instead to go to clinical meetings or conferences to do evaluations with the participants of such meetings. We identified two excellent occasions:

1. The second ‘Winter School’ held by the Society of Paediatric Oncology in Söllereck, Oberallgäu in Germany from the 9<sup>th</sup> to the 13<sup>th</sup> of January 2016, and
2. The 9<sup>th</sup> International Renal Tumor Biology Conference in Toronto, Canada from the 2<sup>nd</sup> to the 3<sup>rd</sup> of April 2016

Clinicians and basic scientists attend these meetings and were regarded as an excellent audience for the evaluation. The organizers of the Summer School as well as of the Biology Conference in Toronto accepted our proposal to evaluate integrated tools of CHIC.

The following sections describe the two evaluation workshops and give the obtained results. The corresponding questionnaires are found in the Appendices of this document.

### 3 Evaluation at the German School of Paediatric Oncology and Haematology

#### 3.1 Introduction

The **German-School-of-POH** was held in Söllerneck, Oberallgäu in Germany from the 9<sup>th</sup> to the 13<sup>th</sup> of January 2016. This was the second ‘Winter School’ held by the Society of Paediatric Oncology in Germany. The school was organized by Prof. Dr. Dominik Schneider, from Children’s Hospital in Dortmund, Germany. The topic of this year’s school was solid tumours in childhood including nephroblastoma. 52 physicians from Germany participated. Most of them were paediatricians and trainees for Paediatric Oncology. For the different topics altogether 20 teachers presented different topics mainly as lectures. A nephroblastoma-only evaluation workshop was held where the CHIC project and the nephroblastoma hypermodel were presented. The ‘Deutsche Kinderkrebsstiftung’ sponsored the event. The event itself was evaluated and achieved the following marks on a scale from 1 (excellent) to 6 (very bad):

For the organization: 1.19  
 For the concept: 1.30  
 For the workshop: 1.64  
 For the lectures: 1.47

The overall evaluation of the school for the 5 days was 1.04 and it was concluded that the **German-School-of-POH** will run further such events on a yearly basis.

The scientific program of the school included renal tumours of childhood. The teacher in this session was Norbert Graf, who divided his session in two parts. First he gave an overview of kidney cancers in childhood and explained problems in the diagnosis and treatment of these children based on individual case reports and discussed solutions to overcome these problems. In the second part the CHIC project was explained in detail and the nephroblastoma hypermodel was demonstrated and intensively discussed in a workshop with 52 participants. The main objective of this session were the questions, if the nephroblastoma hypermodel, as a test of principle, can serve as a clinical decision support tool for paediatric oncologists in the future to solve some of the problems identified during the first part of the kidney tumour session, and if the participants want to use such hypermodels in their daily clinical care of children with cancer. For that purpose a questionnaire was developed and all participants were asked to answer these questions at the end of the session. The questionnaire is added as appendix 1 to this document. The results of the questionnaire as well as the interactive discussion during the demonstration are summarized in the following chapters.

#### 3.2 Presentation of the CHIC project and interactive discussion of the nephroblastoma hypermodel

The scientific and clinical background of the CHIC project was explained in detail. Data protection and security were intensively discussed and the solution of the CHIC project presented. ObTiMA as the data management tool, the tool for data upload, pre- and post-processing of imaging data using DrEye and the description of molecular data, mainly miRNA data were demonstrated including the clinical data repository. The different hypomodels, as presented in deliverable D2.5 of the CHIC project, were intensively described including their composition to build the nephroblastoma hypermodel. The whole presentation was based on Powerpoint slides without direct usage of the different tools. Two of the main slides for the hypermodel are given in figures 3.2.1 and 3.2.2.



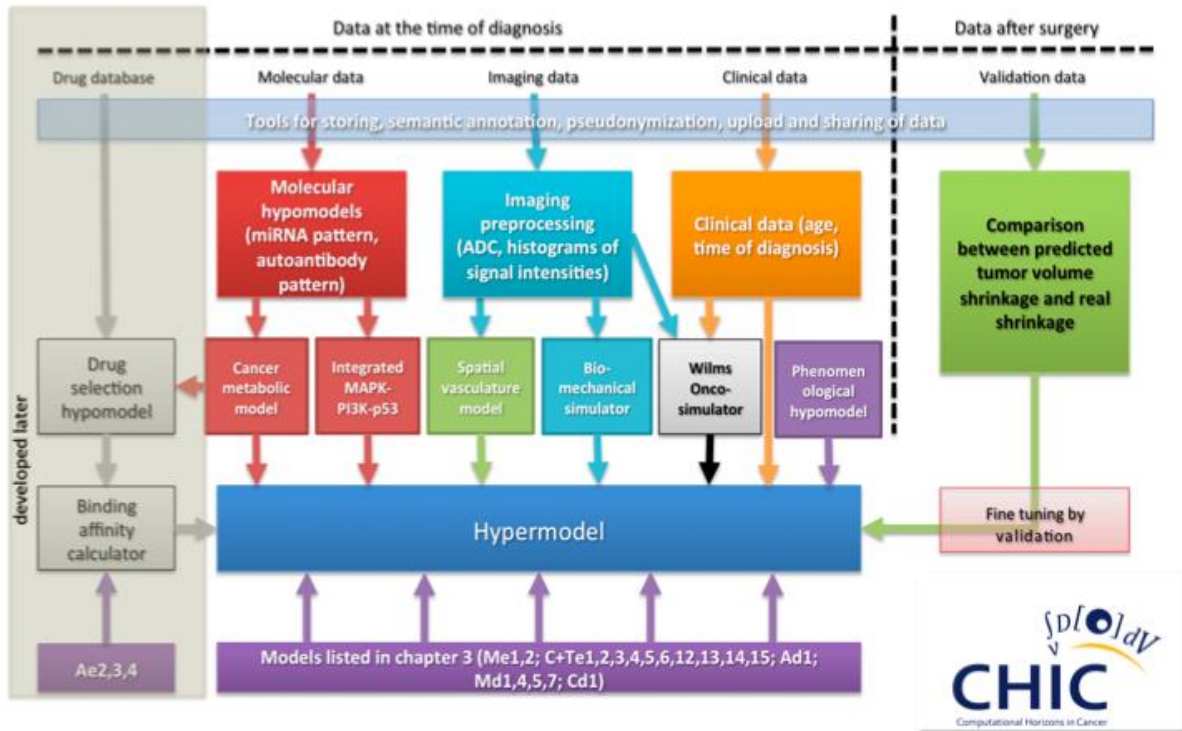


Fig. 3.2.1: Schema of the nephroblastoma hypermodel showing the different hypomodels

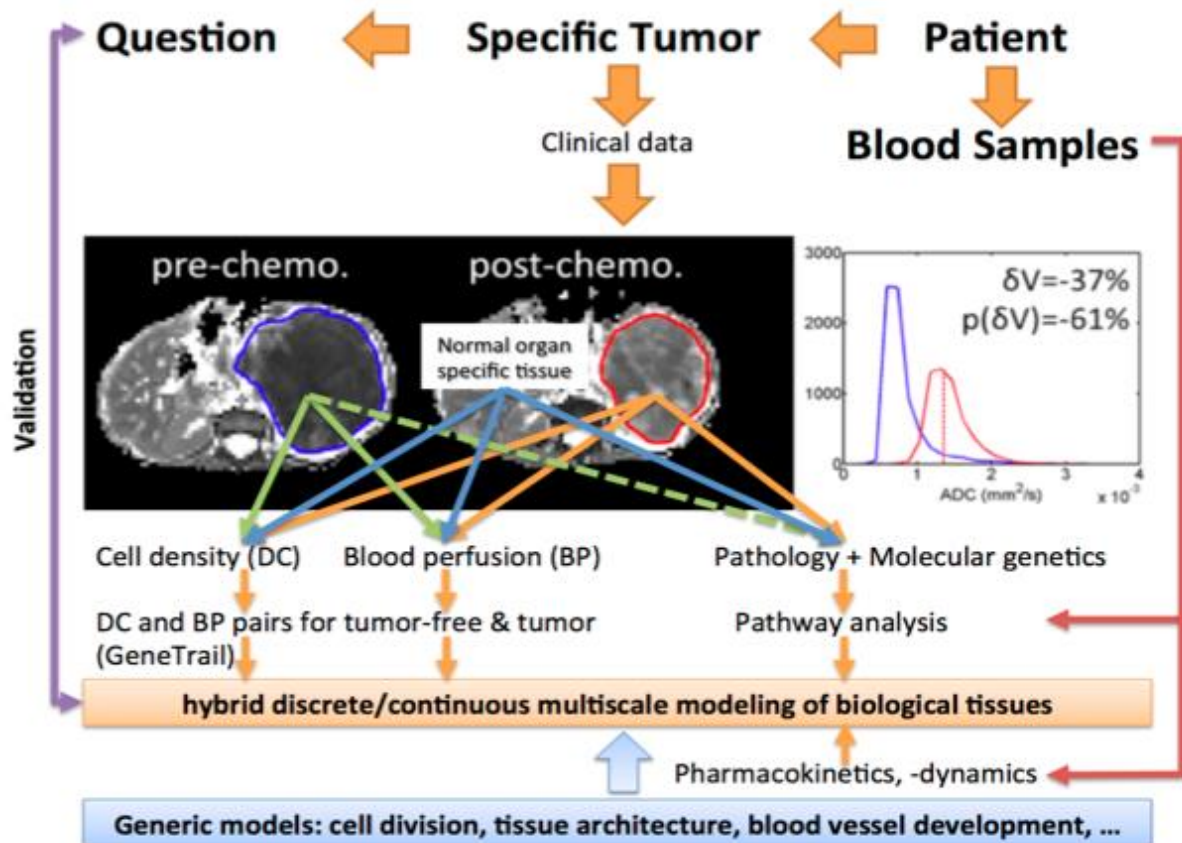


Fig.: 3.2.2: Data acquisition for the nephroblastoma hypermodel

### 3.3 Direct feedback during the workshop

The whole workshop can be characterized as a lively discussion of the hypermodel. The Feedback from the participants during the interactive discussions can be summarized as follow:

1. CHIC is an ambitious project
2. Not all participants are convinced that such hypermodels will play a role in the clinical care in the future
3. Most of the participants want to use the nephroblastoma hypermodel to ‘play’ with it, from data upload to running the model
4. Such hypermodels need to be integrated in prospective clinical trials for evaluation and validation
5. Decisions for an individual patient can only be done, if the hypermodel is validated and will give a correct answer to the corresponding clinical question
6. A hypermodel must be easy to use by clinicians without a lot of interventions
7. The background of the hypermodel needs to be understandable
8. Sustainability and maintenance needs to be guaranteed, if physicians use the hypermodels and the CHIC infrastructure

### 3.4 Results of the questionnaire

Of the 52 participants of the [German-School-of-POH](#) 43 (82.7%) did give feedback via the questionnaire. All of them were physicians, only one had an MD and PhD degree, 7 were paediatricians and 5 in addition paediatric oncologists. Their age ranged from 28 to 54 years with a mean age of 35 and a median age of 36.9 years. Their experience with hypermodels was very low; on a scale of 1 (not at all) up to 10 (very experienced) 34 participants specified such experience as 1, 4 as 2, 3 as 3 and only 1 as 7. One participant did not answer this question. The histogram is shown in figure 3.4.1a. For all further questions, dealing with the evaluation of the ‘in silico’ hypermodels and the CHIC infrastructure, participants could answer the different questions on a scale from 1 (not at all) to 10 (highest degree).

The participants showed a wide range of answers for the following questions:

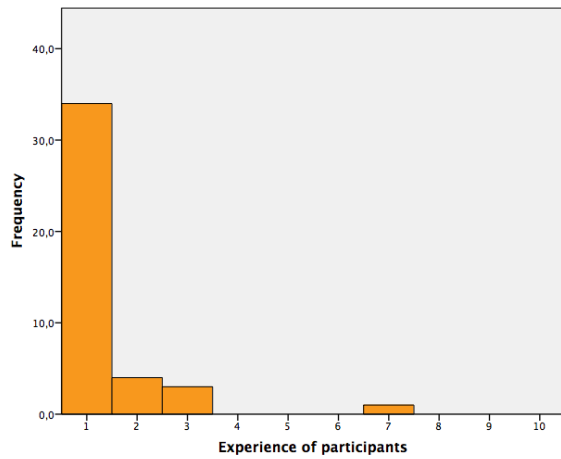
- ‘in silico’ models will be an important technology in health care in the future
- ‘in silico’ models will be useful for decision support in the future
- Physicians need to use ‘in silico’ models for decision support in the future
- ‘in silico’ models must be intuitive to work with (like an App)
- ‘in silico’ models need to be understandable in all details by physicians
- ‘in silico’ models need to run without further interaction by physicians besides the selection of the model and the patient

The median values were mainly between 4 and 6. All other questions show a high median value of at least 8. Three of these questions have a median value even of 10. These questions are:

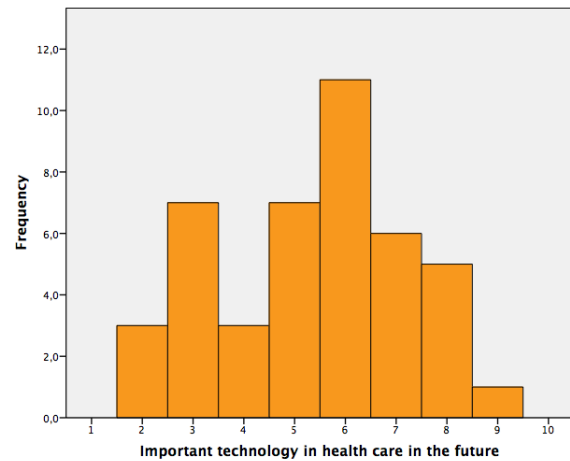
- ‘in silico’ models need to guarantee data safety and security
- The result of the ‘in silico’ model should be reproducible and precise
- The result of the ‘in silico’ model must be better than the weather forecast of today to use it in clinical care as a decision support service
- The result of the ‘in silico’ model must be given clearly and be easy to understand (e.g. visualization of tumour shrinkage)
- The ‘in silico’ model application should also be able to demonstrate to the patient how treatment affects his tumour

Results can be seen in figure 1xb – I below.

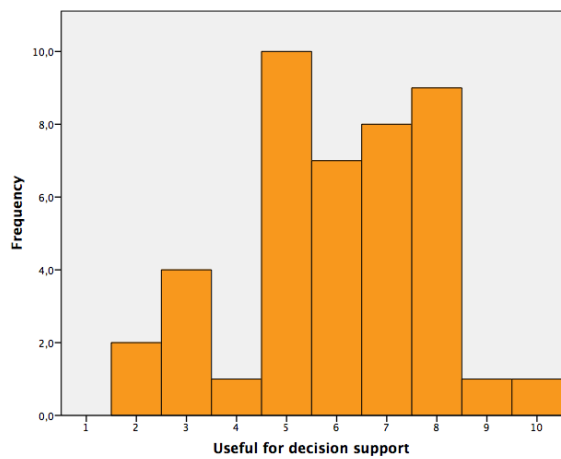
**a) median: 1; mean: 1.38**



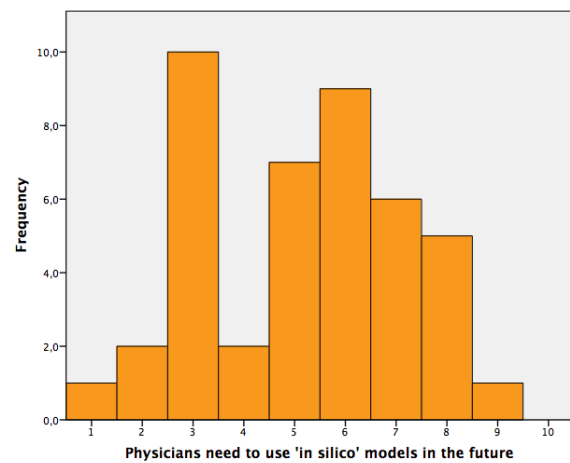
**b) median: 6; mean: 5.37**



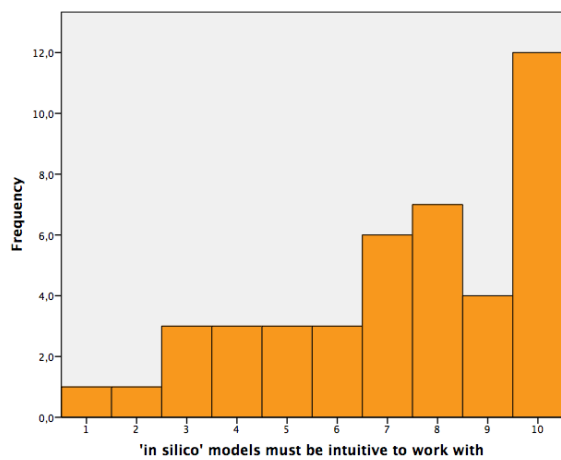
**c) median: 6; mean: 6.02**



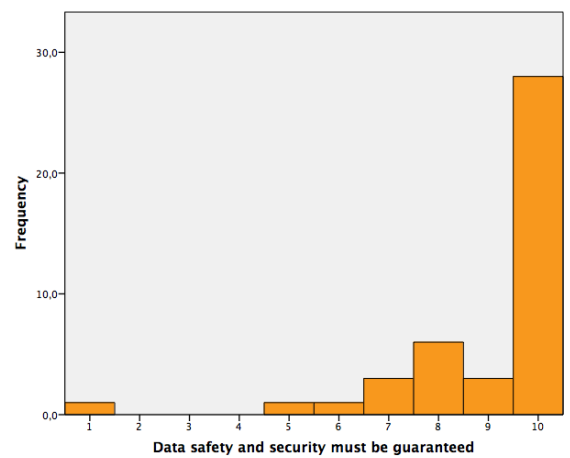
**d) median: 5; mean: 5.19**



**e) median: 8; mean: 7.23**



**f) median: 10; mean: 9.02**



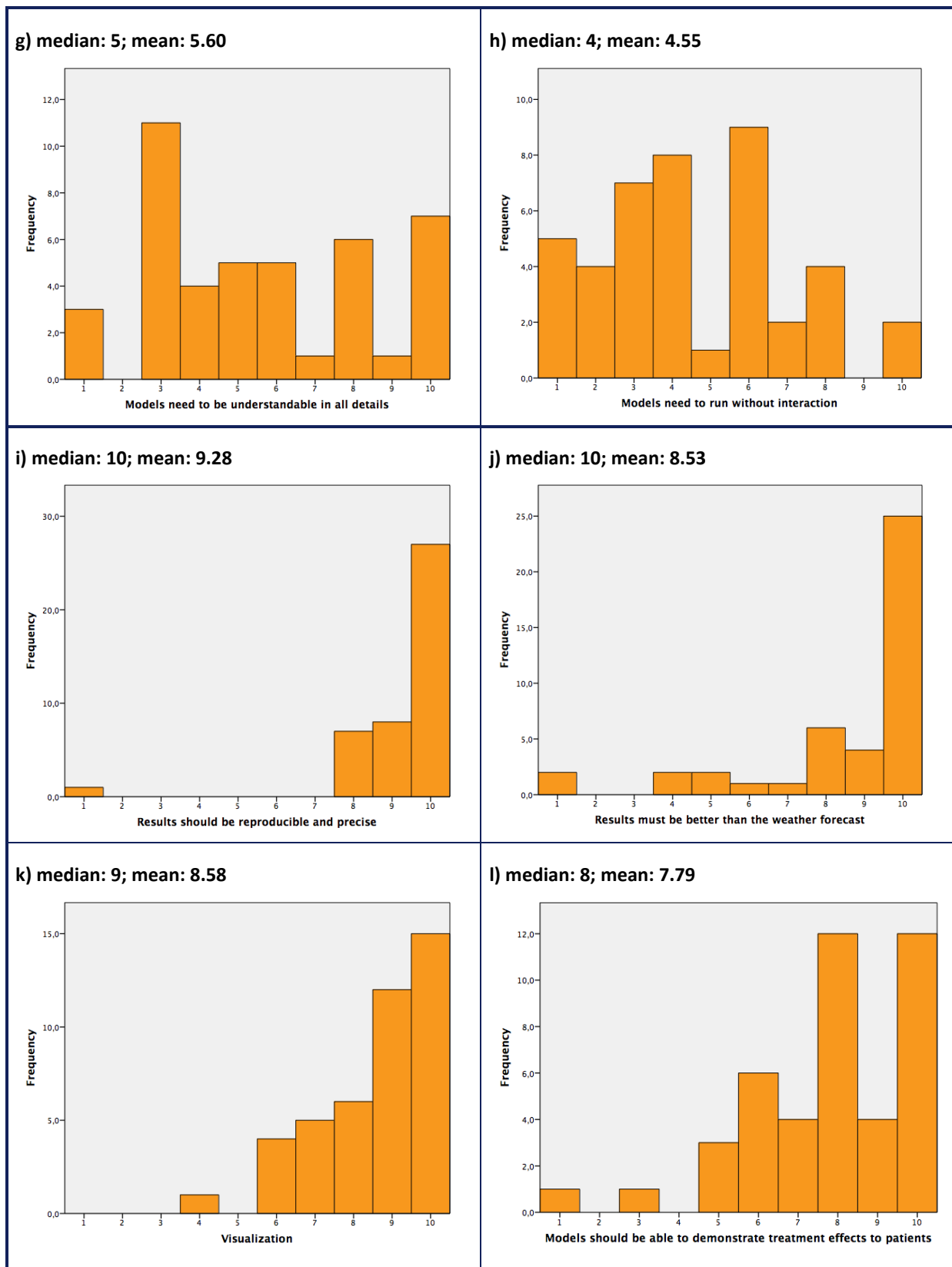


Fig. 3.4.1: Histograms of the answers of the different items of the questionnaire. Grading of the x-axis: 1 (not at all) up to 10 (highest degree). Figure 3.4.1a shows the experience with hypermodels

and not their experience in Paediatric Oncology, which was high. Figure 3.4.1k shows the answer for the need for clear visualization. The complete text of the questionnaire is reported in Appendix I

A comparison of the different questions is given in the following figure (fig. 3.4.2).

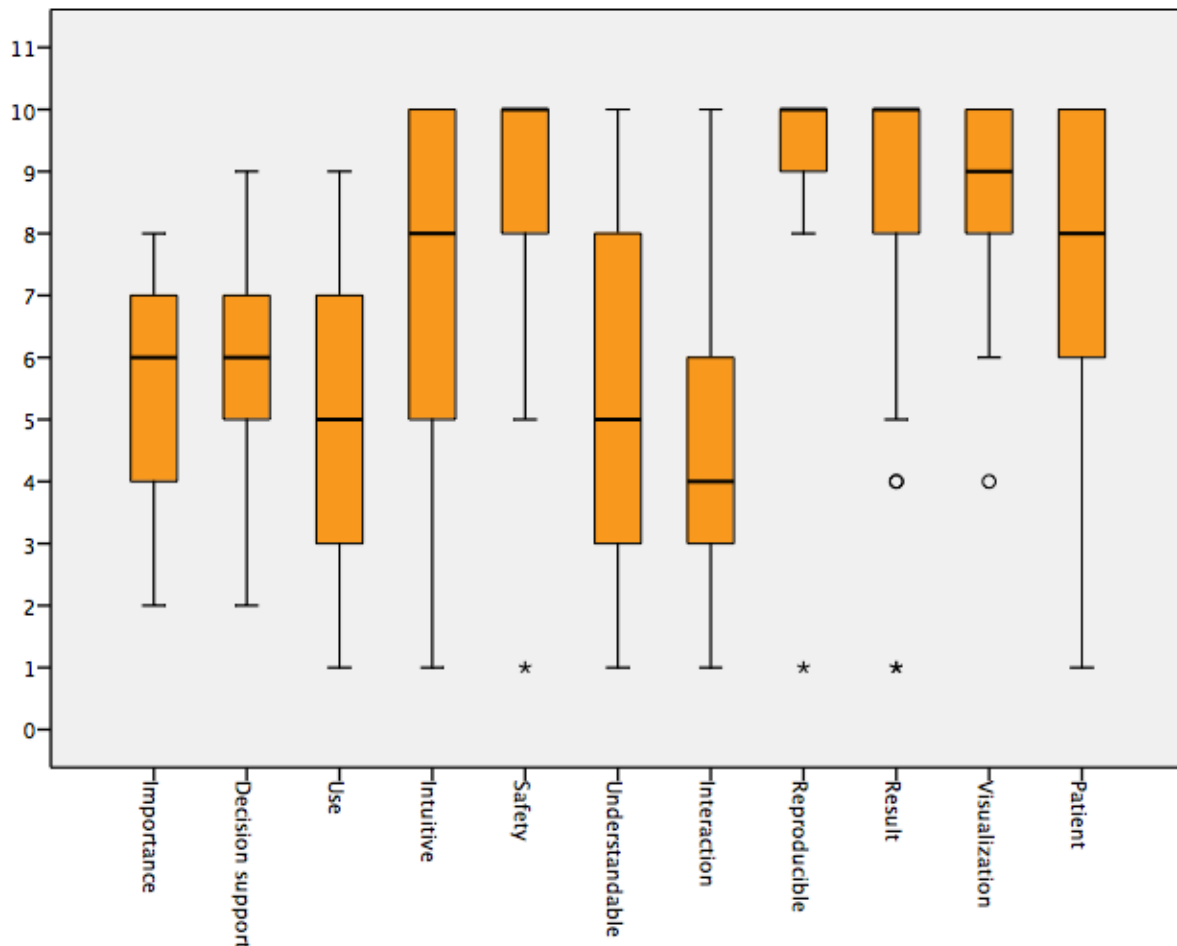


Fig. 3.4.2: Comparison of the distribution of the answers to the different questions as a boxplot.

The following free text was given for features that need to be integrated in 'in silico' models to make them useful for clinicians:

- Safety
- Clinical decision criteria
- Reliability; wide spectrum of possibilities included in model to ensure realistic representation and produce reliable data

The following general comments were given:

- 'in silico' models need careful prospective validation
- I just read *Robocalypse* from DH Wilson and have a lot of thoughts
- Tumour biology is difficult to simulate
- Needs to include the probability of correct forecast
- Good luck

### ***3.5 Summary of the Evaluation workshop and consequences for the CHIC project***

The evaluation workshop at the **German-School-of-POH** was very successful. We got 43 answers to our questionnaire from physicians, who evaluated the CHIC platform and the nephroblastoma hypermodel in a workshop.

Most of the participants want to ‘play’ with the hypermodel and test it. For usage in daily clinical care data safety and security needs to be guaranteed. In addition the prediction needs to be better than the weather forecast of today. The hypermodel needs to be validated within in prospective clinical trials to demonstrate the benefit of the hypermodel. Otherwise clinicians will not trust the prediction. The results need to be reliable and reproducible all the time. Most of the physicians want to understand the basics of the models on one hand and on the other hand they want to run these models without a lot of interactions. The visualization of the results is the best way for the end-user to display the results of a model. Another very important issue for the participants is the maintenance and sustainability of the CHIC platform in order to be able to use the hypermodels for clinical decision support in routine clinical care, if they can trust the results. If this is not guaranteed the hypermodels are not more than a ‘nice tool to play with’.

## 4 Evaluation workshop at the 9<sup>th</sup> International Renal Tumor Biology Conference

### 4.1 Introduction

The 9<sup>th</sup> International Renal Tumor Biology Conference was held in Toronto, Canada from the 2<sup>nd</sup> to the 3<sup>rd</sup> of April 2016. In total 65 clinicians, biologists and basic scientists with huge experience in the field of nephroblastoma attended the conference. All participants work in the area of nephroblastoma, including representatives of the two major clinical trial groups for nephroblastoma. These are members of the Children's Oncology Group from Northern America (COG) and from The SIOP Renal Tumour Study Group (SIOP-RTSG). The participants came from 10 different countries around the world (Brazil, Canada, France, Germany, Ireland, Italy, Sweden, The Netherlands, UK, USA).

During the workshop two different Evaluations took place. The first was dedicated to the CHIC Clinical Data Repository (CDR) and the second to the Nephroblastoma Hypermodels.

### 4.2 Evaluation of the CHIC Clinical Data Repository

For the participants of the workshop a test account for the CDR with fake data was created, so that participants were able to test and evaluate the CDR without breaching data protection and privacy issues. The link for the web based CDR is: <https://cdr-dev-chic.ics.forth.gr>. A demo account was created with the following credentials: username: demo and password: Dem0U\$er! The evaluation questionnaire was available through the following link: [https://docs.google.com/forms/d/1yJJ-DsMqlisQsE0prheFZMRb0hMCgicfCzN\\_cMwtK3E/viewform](https://docs.google.com/forms/d/1yJJ-DsMqlisQsE0prheFZMRb0hMCgicfCzN_cMwtK3E/viewform). A short video showing a possible workflow demonstrating the most relevant aspects of the system can be found at: [https://dl.dropboxusercontent.com/u/8118171/2016-03-21\\_23-43-40.mp4](https://dl.dropboxusercontent.com/u/8118171/2016-03-21_23-43-40.mp4). Test data for uploading were provided.

The following figure shows the CDR after login into the system.

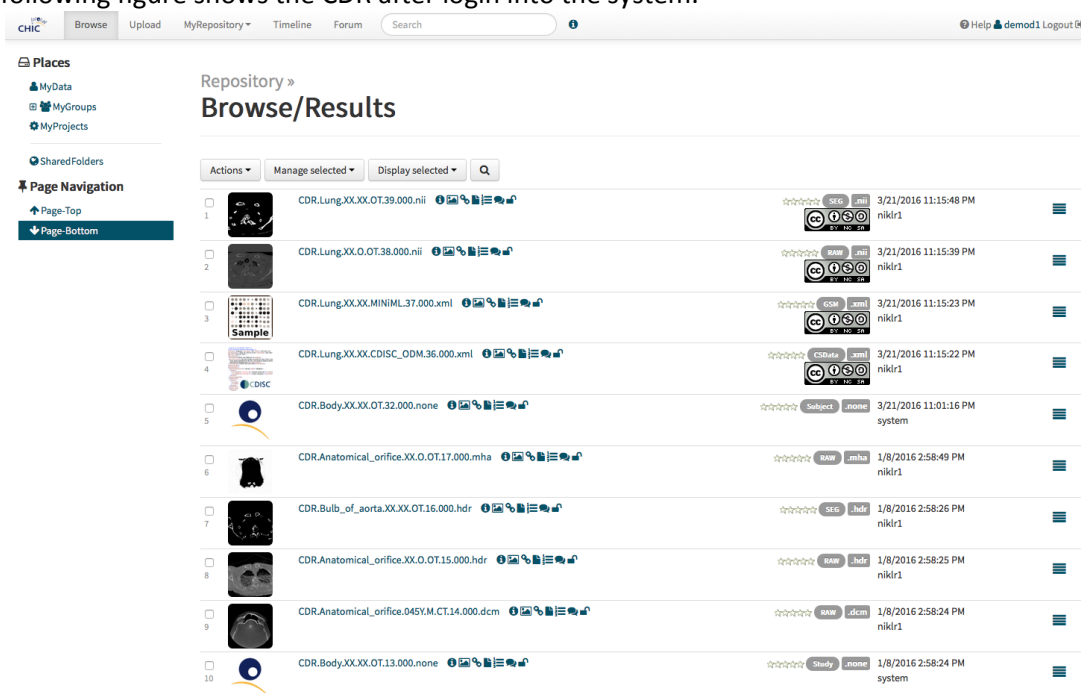


Fig. 3.5.1: The CDR after log-in.

## 4.2.1 Evaluation questionnaire for the CDR

The evaluation questionnaire for the CDR is listed in Appendix 2.

## 4.2.2 Direct feedback during the workshop

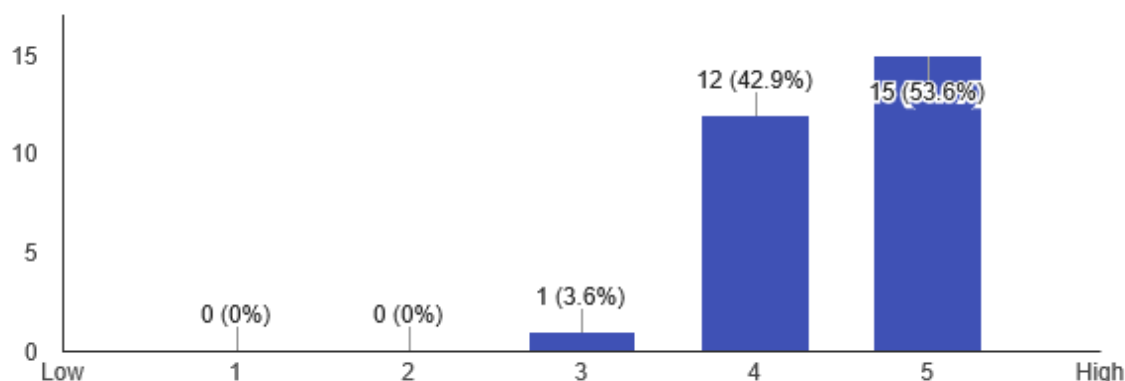
Most important for the participants was the fact that heterogeneous data can be uploaded to the CDR and then further used in their research. It was appreciated that a legal framework exists, albeit they could not test this functionality by starting with personal data up to the upload to the CDR with the steps of double pseudonymization. Most of the participants giving feedback were interested in using the CDR and asked about sustainability issues. The organization of the data including the timeline was positively recognized.

## 4.2.3 Results of the evaluation of the CDR

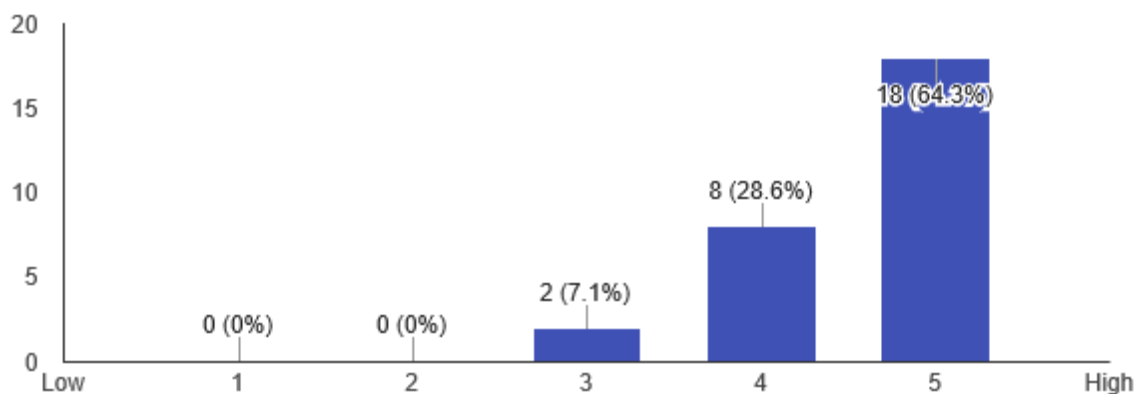
Overall, 28 participants took part during this evaluation round. For security reason, the development system of the clinical data repository deployed to the CHIC private cloud infrastructure located in Athens has been used.

### 4.2.3.1 Purpose and Content

Is the purpose of the web application clear?



Is the content provided by the web application understandable?



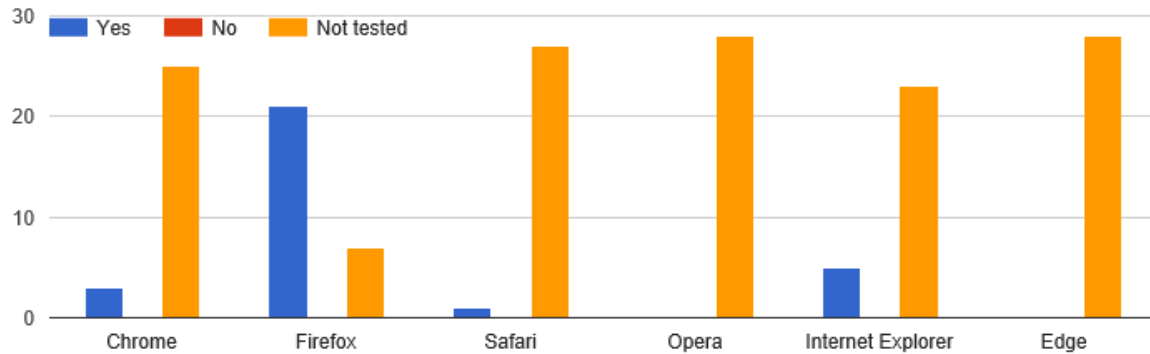


Comments related to "Purpose and Content". (optional)

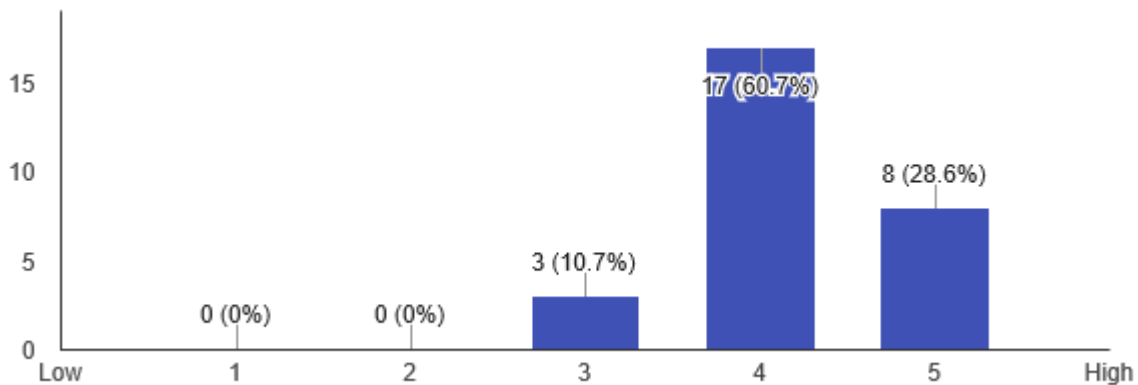
- Highly relevant tool!

#### 4.2.3.2 Accessibility

Is it displayed correctly in different browsers?

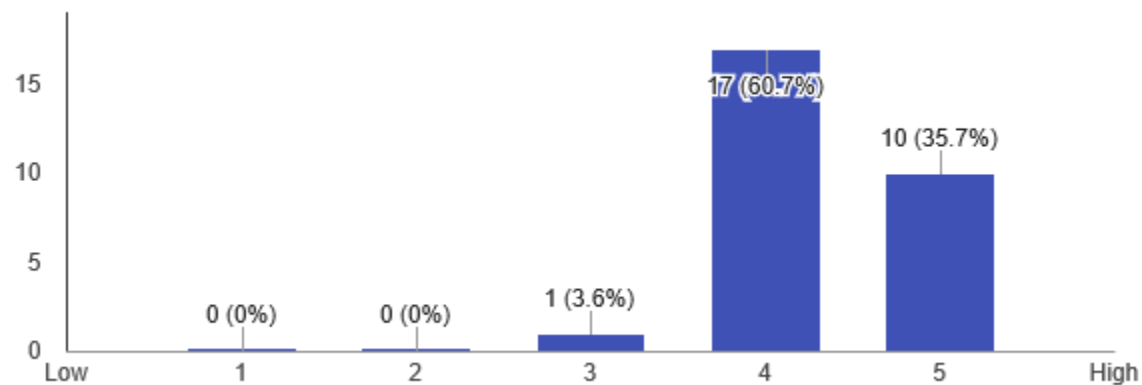


Does it load quickly?

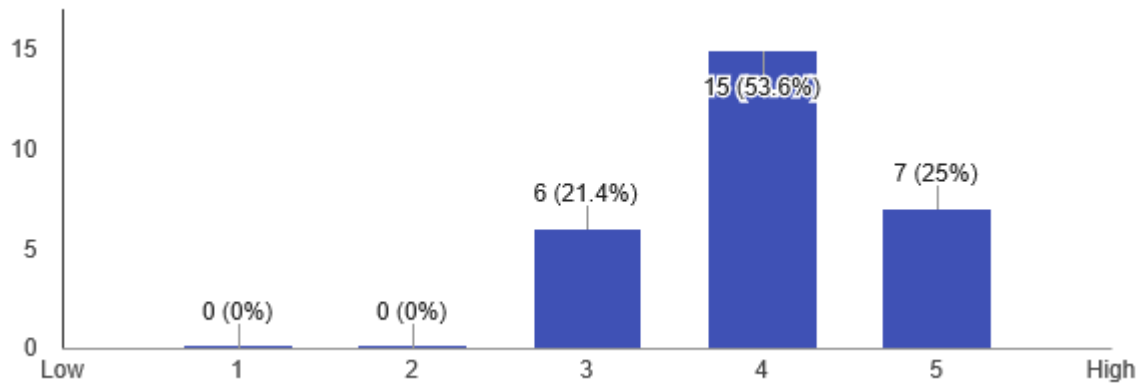


#### 4.2.3.3 User Experience

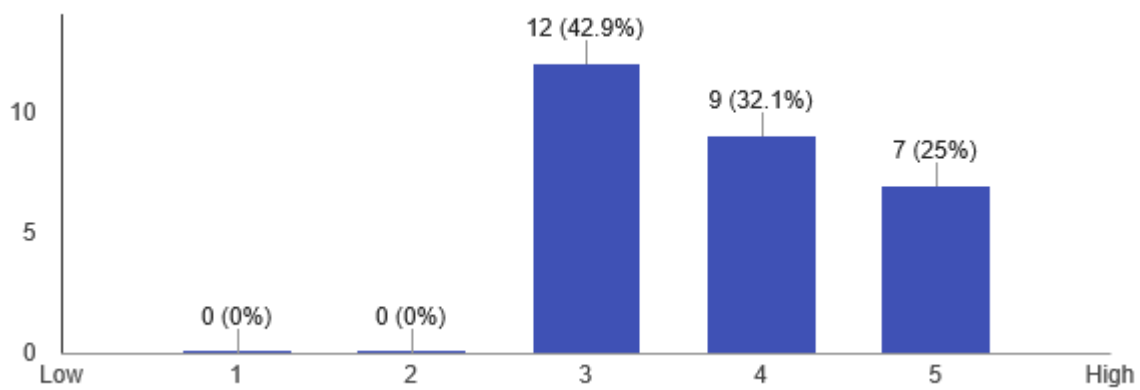
Is the design consistent across the web application?



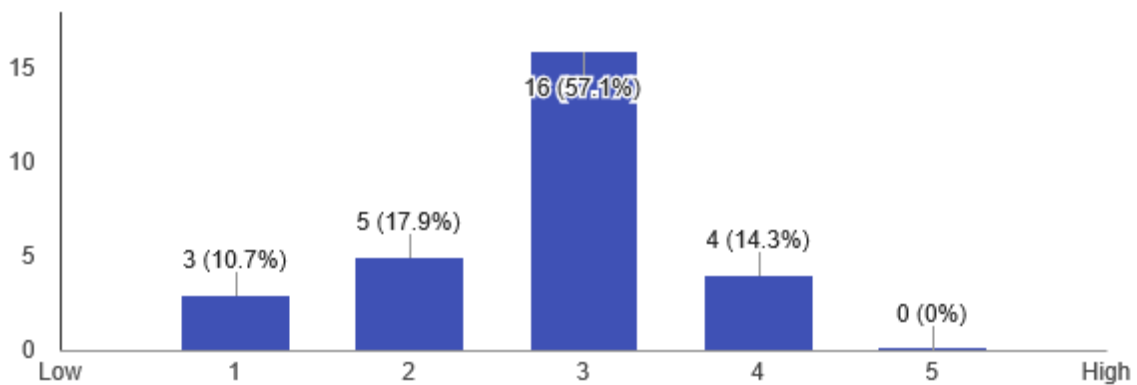
Does the design allow for easy navigation?



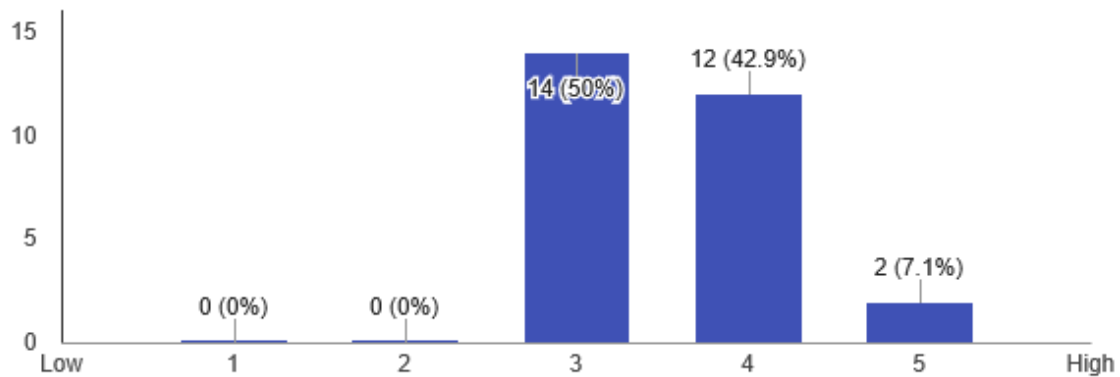
Is it visually appealing?



Is the page design overwhelming or confusing?



Is the font readable?

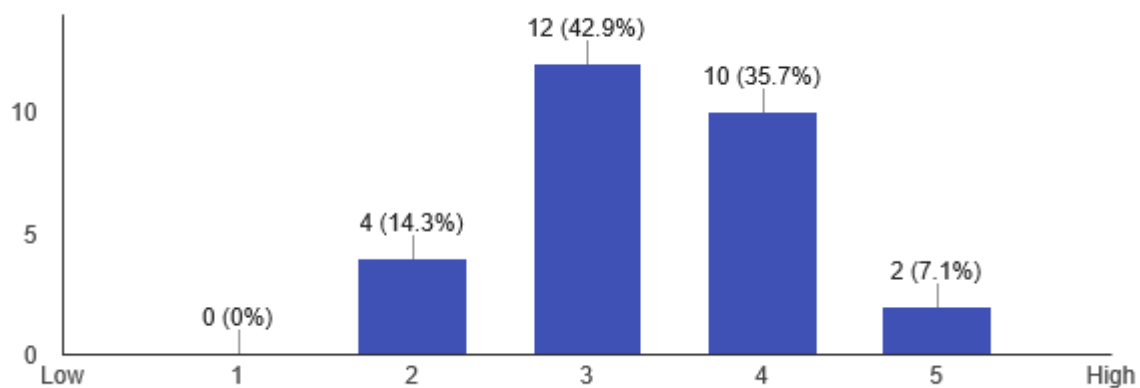


Comments related to "User Experience" (optional)

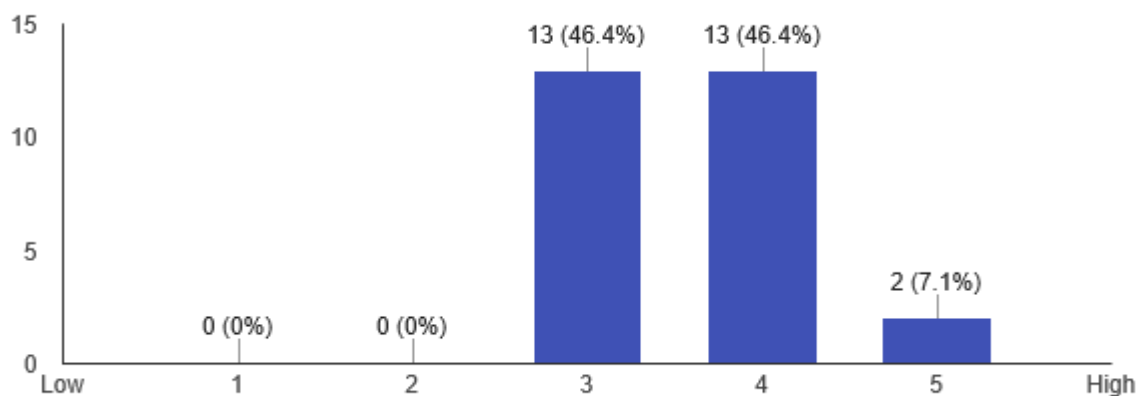
- I do not know the web application
- Too much information given to understand quickly

#### 4.2.3.4 Creativity and Innovation

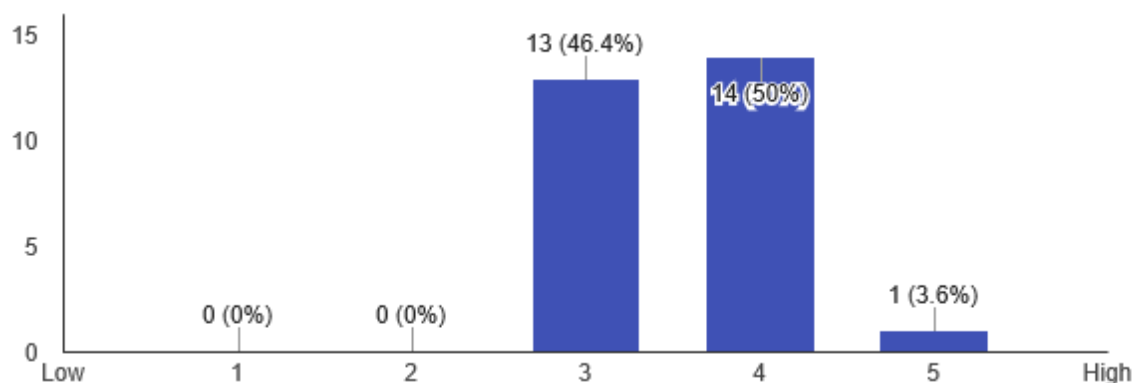
How unique is the clinical data repository?



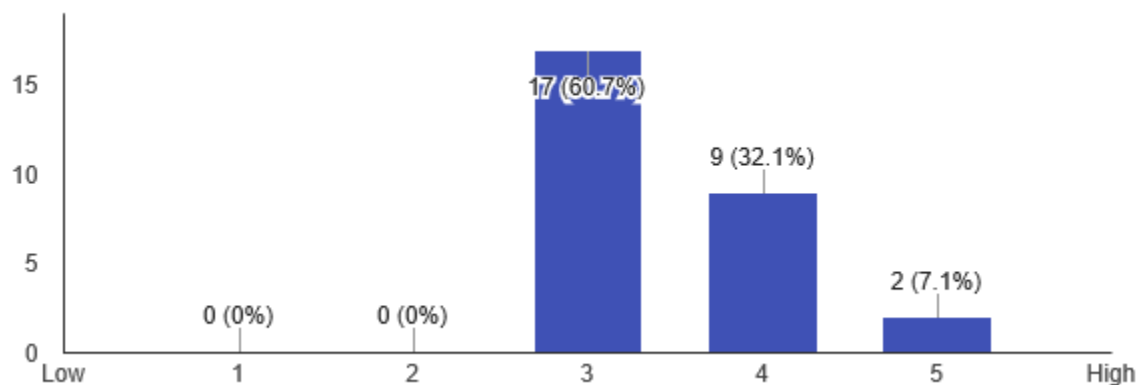
Is it distinguishable from other similar web applications?



Is the repository distinct and memorable?



Does the repository offer features not found elsewhere?

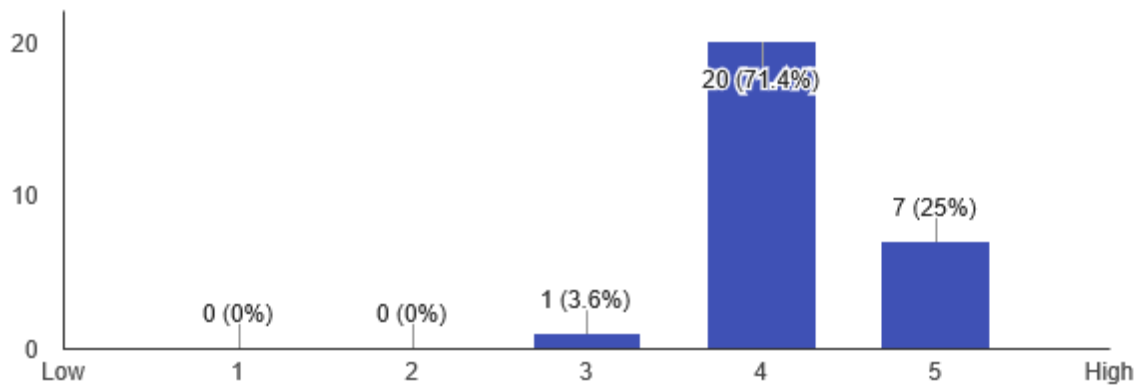


Comments related to "Creativity and Innovation" (optional)

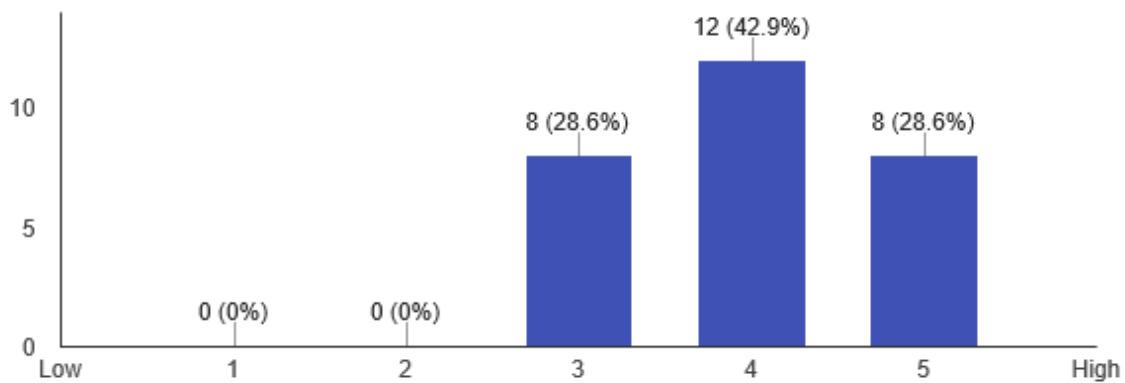
- Have not seen any other data warehouse, so can not answer some questions, therefore neutral answers
- Do not know others
- It looks for me as standard
- Other systems are unknown by me
- Other repositories are not known by me

#### 4.2.3.5 User Task Analysis

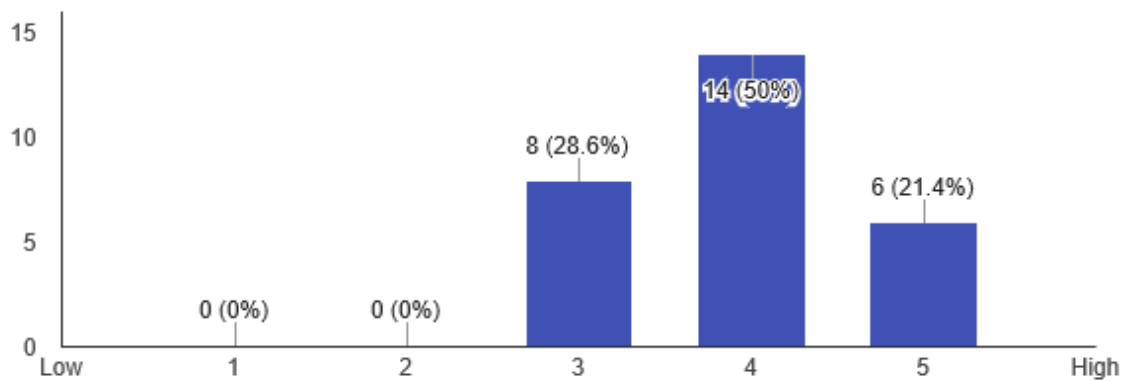
How obvious and easy is for the user to view and browse the content of the clinical data repository?



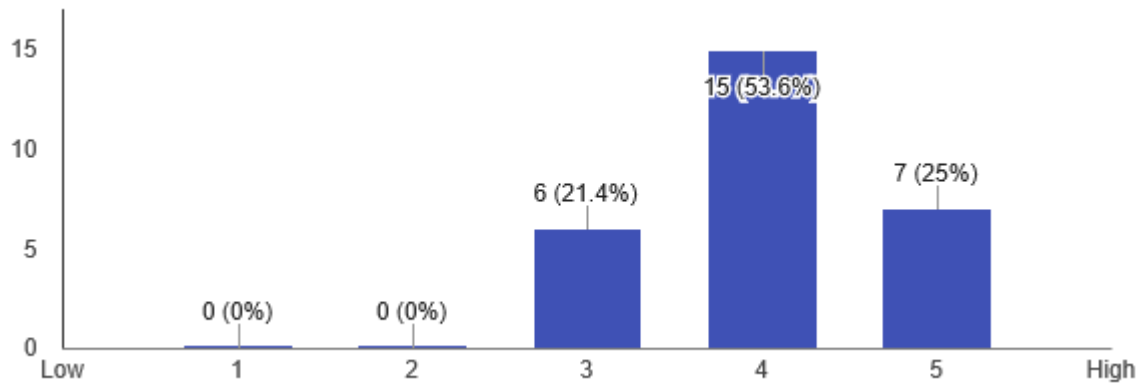
How obvious and easy is for the user to download data?



How obvious and easy is for the user to enter information about the data (descriptive information, permissions, comments, etc.)?



How obvious and easy is for the user to delete part of the content of the clinical data repository?

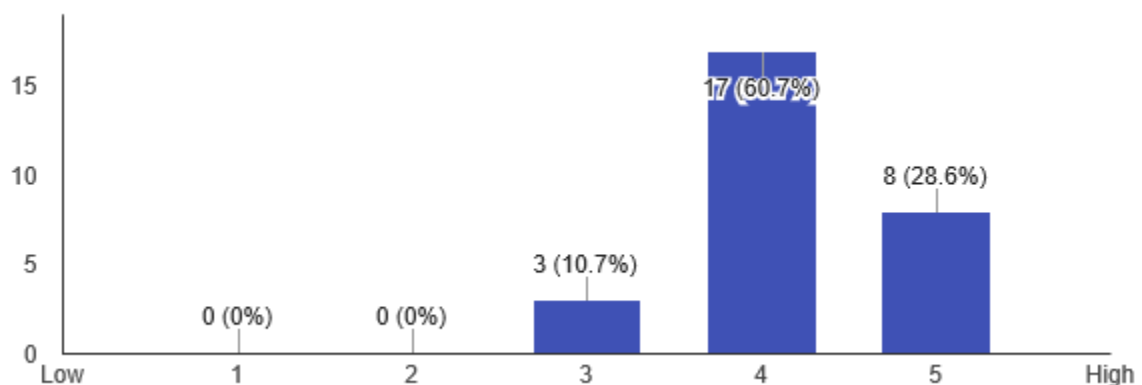


What feature do you like, miss or want to be improved (optional)

- A single instance of each dataset can be uploaded.. Good concept, but could be confusing for the user.
- Did not do this
- Did not upload or download data
- Want to test longer
- Need to test longer
- More time for testing is needed

#### 4.2.3.6 Overall

How would you rate your overall impression of the clinical data repository?



Any final comment is very welcome. (optional)

- Excellent tool!
- Great tool, would like to use for my research.
- Would like to work with the tool and test more intensively

### 4.3 Evaluation of the Nephroblastoma Hypermodels and CRAF

The nephroblastoma hypermodel and CRAF (Clinical Research Application Framework) were demonstrated on a local computer and were tested by the participants of the workshop on this computer. The participants had to interact with CRAF (Fig. 4.3.1.1) after logging in.

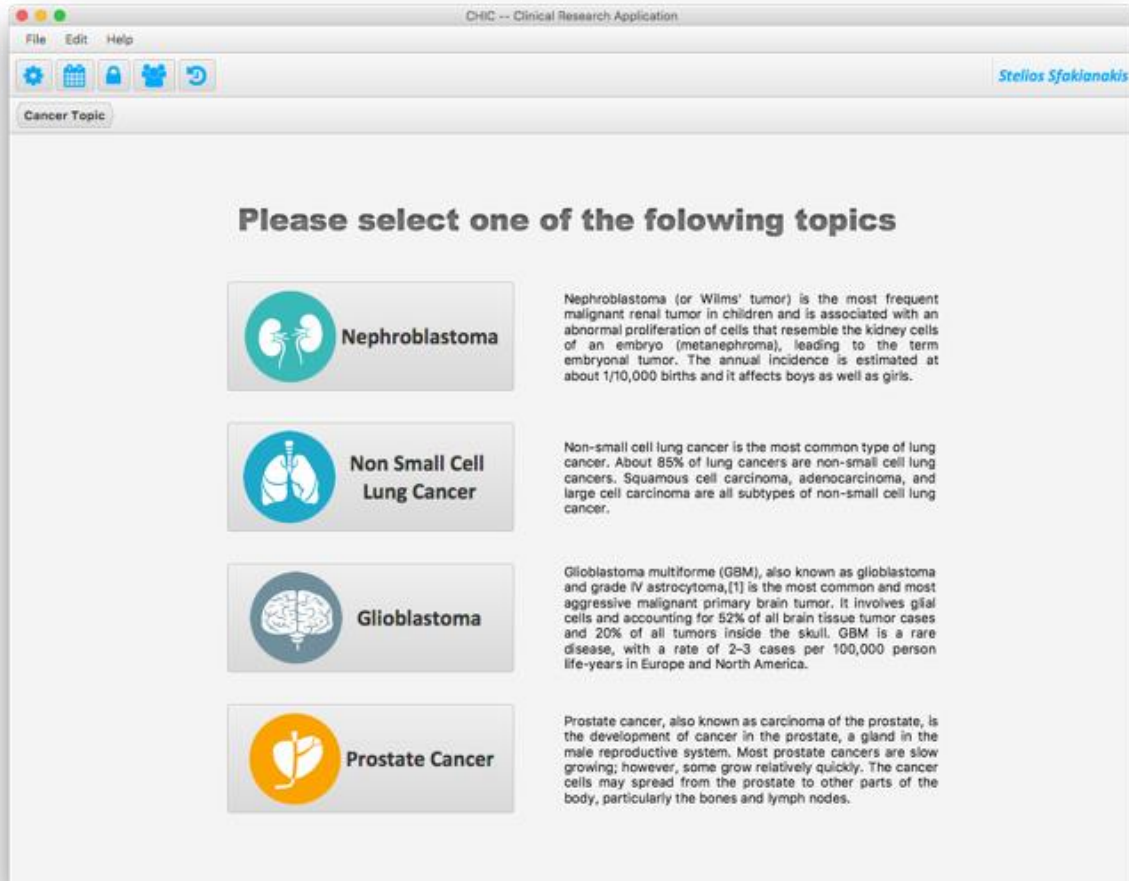


Fig. 4.3.1.1: The Clinical Research Application Framework (CRAF) as the starting point after login.

After selection of the nephroblastoma topic, possible research questions are shown. During this evaluation workshop only the question: 'Will a given nephroblastoma in a patient respond to pre-operative chemotherapy by tumour shrinkage, yes or no?' was possible to select (Fig. 4.3.1.2). Thereafter the participants could choose a patient and the available data of this patient were shown (fig. 4.3.1.3). To be compliant with the regulations of data protection and privacy only fake names are used. For a selected patient two hypermodel versions, the phenomenological and the multimodeller hypermodel, can be chosen (fig. 4.3.1.4) and executed (fig. 4.3.1.5). After the execution a report can be created and shown on the screen (Fig. 4.3.1.6). In case of the multimodeller hypermodel a 3D image of the tumour over time can be selected (Fig. 4.3.1.7) and images at different time points can be selected for input in the report. For that purpose CCGvis is connected with the CRAF. The first and second pages of the report are shown in figures 4.3.1.8 and 4.3.1.9.

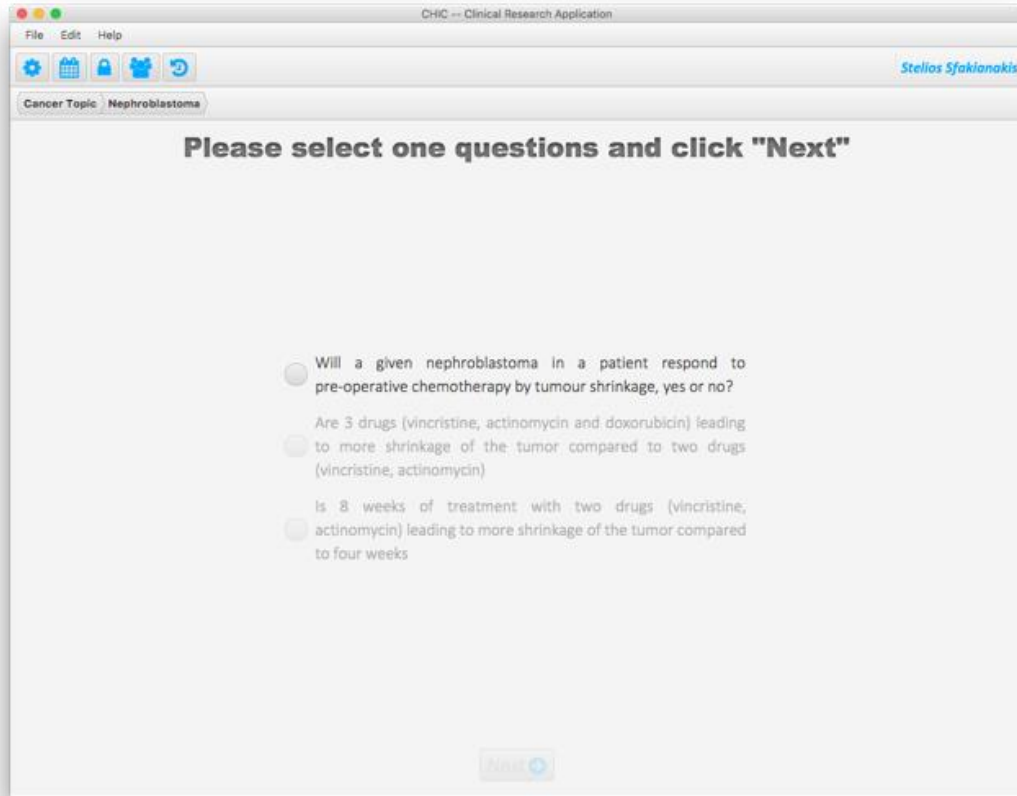


Fig. 4.3.1.2: Possible research question are show, of which only the first question could be selected.

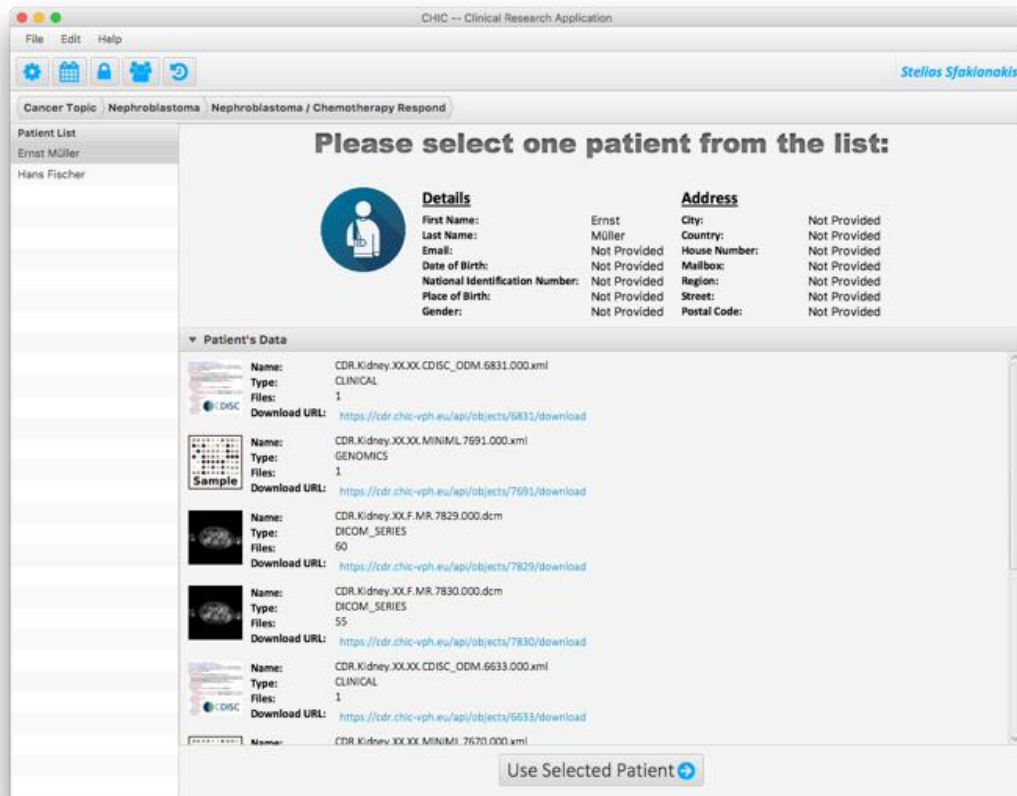


Fig. 4.3.1.3: The available data of a patient are shown.



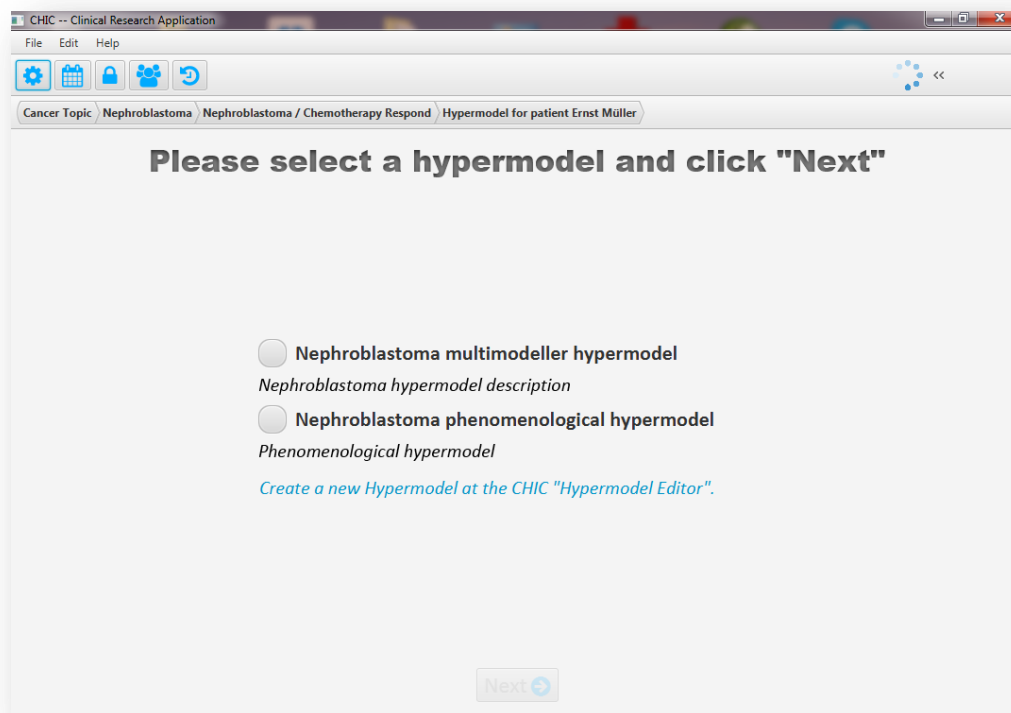


Fig. 4.3.1.4: The possibility of choosing one out of two hypermodels.

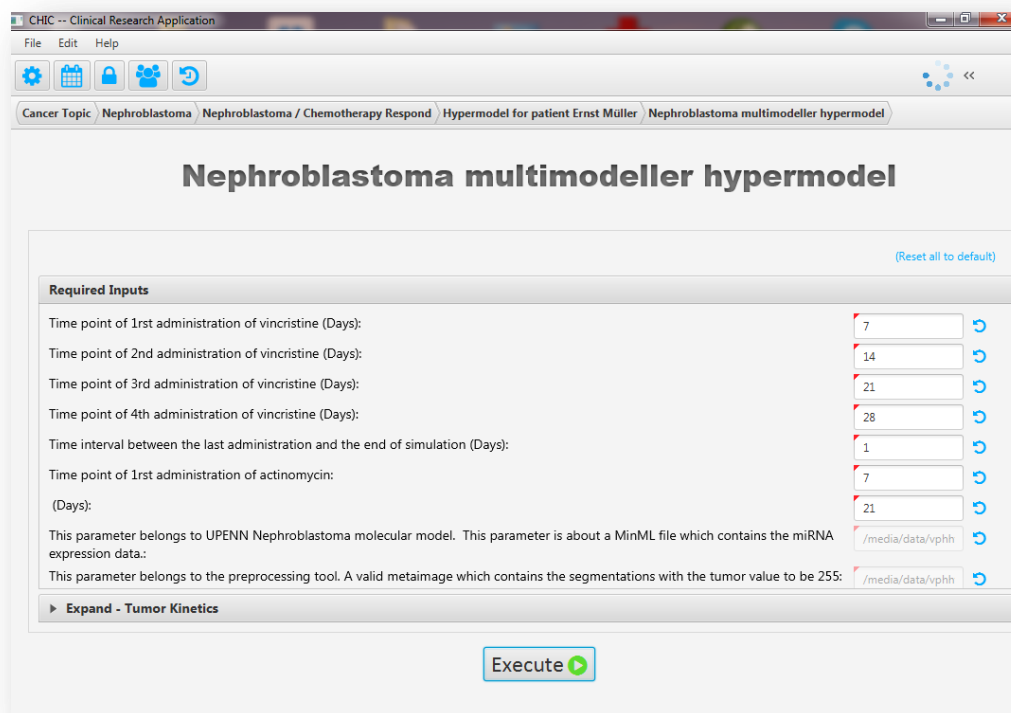


Fig. 4.3.1.5: The possibility of changing input data and execution of the hypermodel.

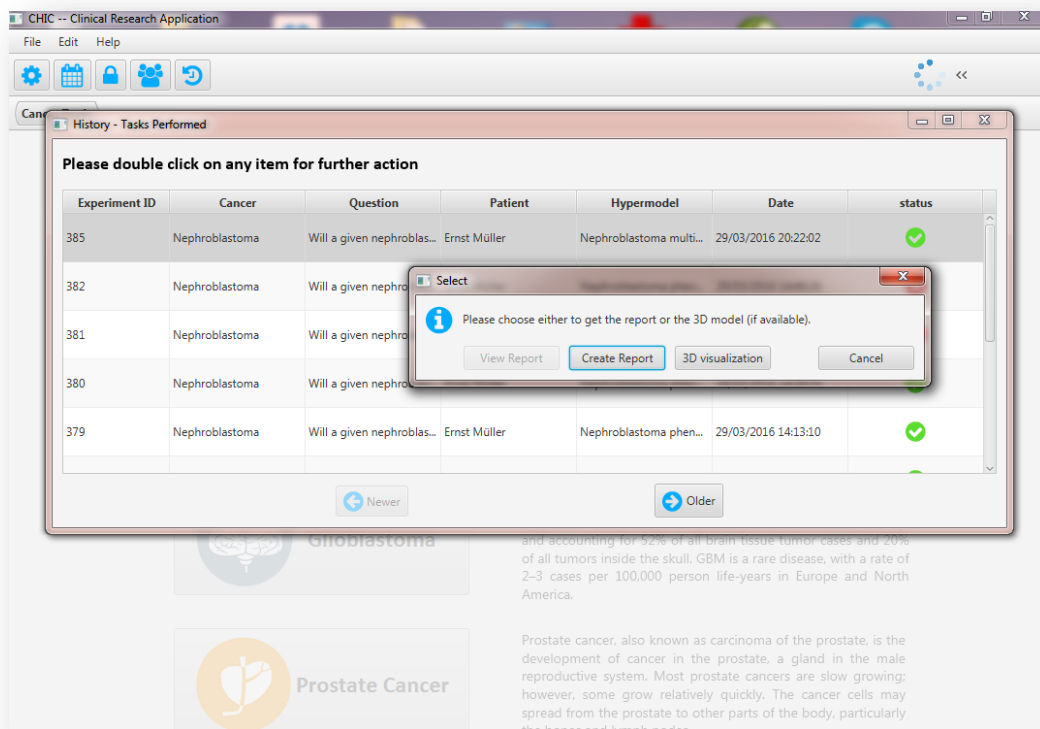


Fig. 4.3.1.6: A report can be created.

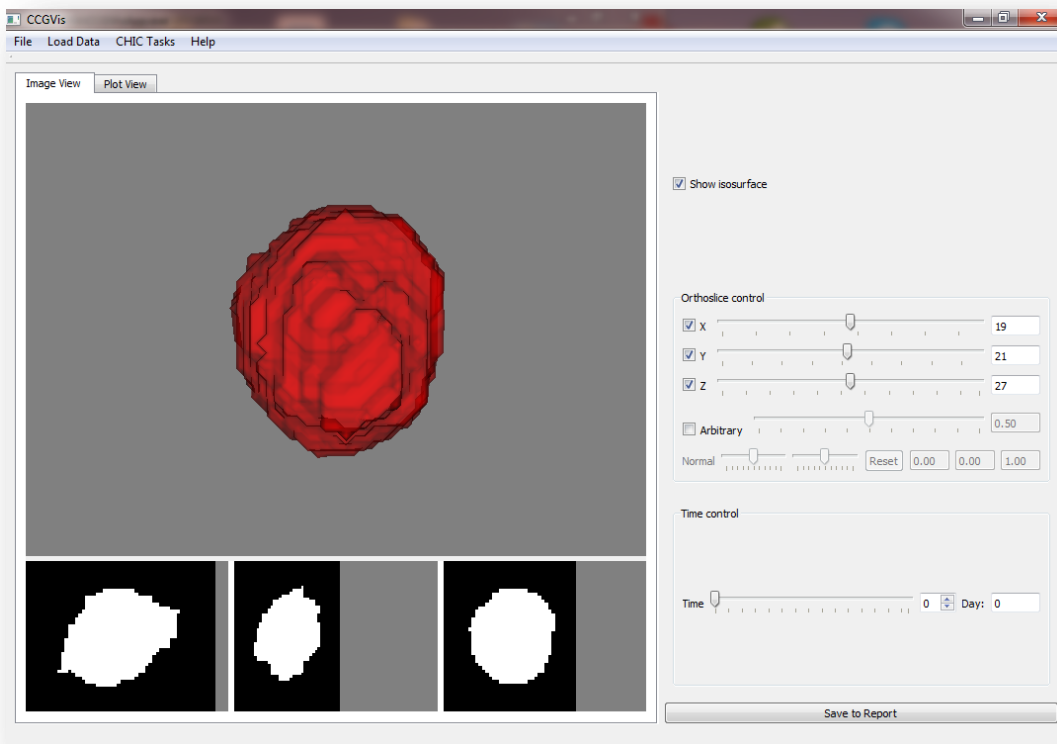


Fig. 4.3.1.7: In case of the multimodeller hypermodel a 3D image of the tumour over time is displayed and can be selected for integration into the report.

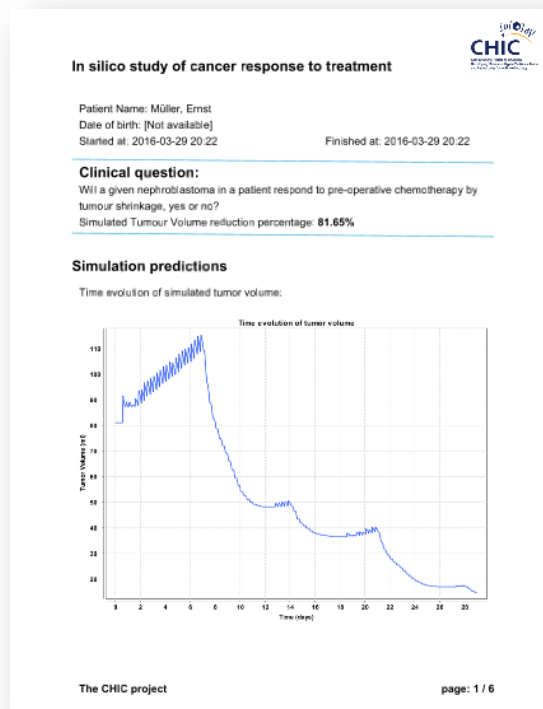


Fig. 4.3.1.8: Page 1 of the report showing the tumour shrinkage over time.

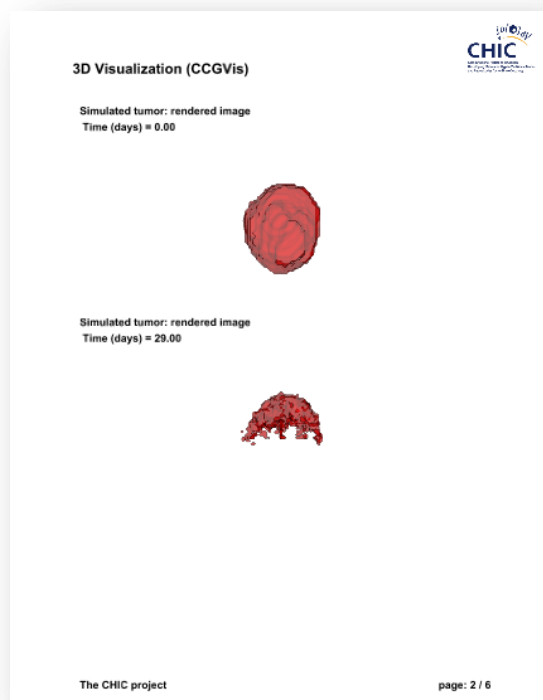


Fig. 4.3.1.9: Page 2 of the report with 3D images of the tumour at specific time points during pre-operative chemotherapy. This is only possible in case of the multimodeller hypermodel.

### **4.3.1 Evaluation questionnaire for the Nephroblastoma Hypermodels and CRAF**

The evaluation questionnaire was available through the following link: [https://docs.google.com/forms/d/10G61rcR4QlelV1tQSBNGBwCmpScgbcRc1s4wqWqR\\_-Y/viewform?fbzx=13495267652557300](https://docs.google.com/forms/d/10G61rcR4QlelV1tQSBNGBwCmpScgbcRc1s4wqWqR_-Y/viewform?fbzx=13495267652557300).

The evaluation questionnaires for the Nephroblastoma hypermodels and CRAF are listed in Appendix 3. Questionnaire B is based on a standardized questionnaire for evaluation.

### **4.3.2 Direct feedback during the workshop**

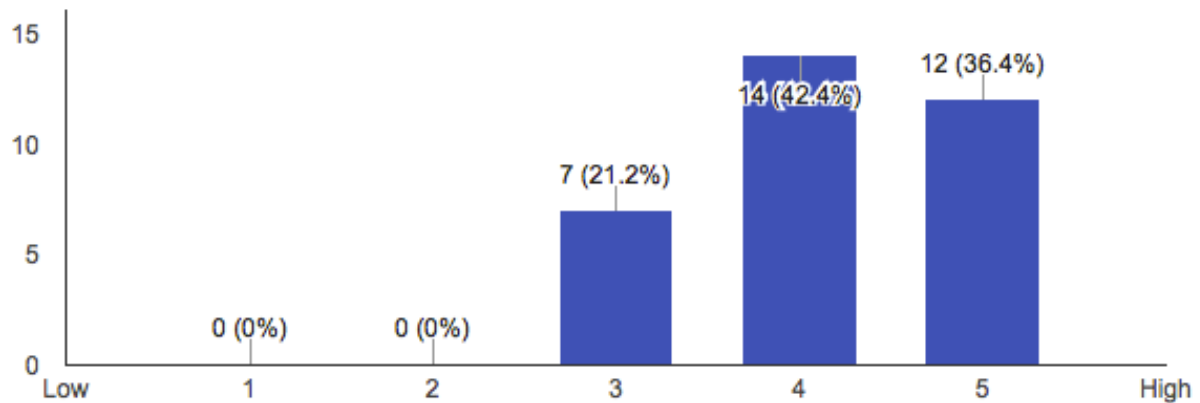
There were a number of sceptical remarks after first demonstrating the tool. But in addition, considerable interest and surprise was expressed that, out of heterogeneous data and the interaction of different hypomodels, such a tool is able to predict responses to preoperative chemotherapy. Most of the evaluators want to have the tool on their computer for playing with it and testing the outcome with different parameters. All of them were very much interested in comparing the prediction and the real response at least in 100 patients with nephroblastoma. They agreed that such a comparison needs to be done to see if such a tool will be usable in daily clinical care. They addressed the need for sustainability after the lifetime of CHIC and also the need for (medical device) certification, if it will be used for clinical decision support. If the tool will be validated/certified, logistics need to be solved, as many heterogeneous data including miRNA data in single patients are needed shortly after diagnosis to have the ability to start treatment according to the prediction soon after diagnosis. Otherwise the hypermodel will have no value for clinical care of patients. These logistics would include the need to make results of miRNAs, the rendering data of the tumour and the necessary clinical data available in the CDR in time. In summary the multimodeller hypermodel was regarded as a very innovative piece of research.

### **4.3.3 Results of the evaluation of the CRAF**

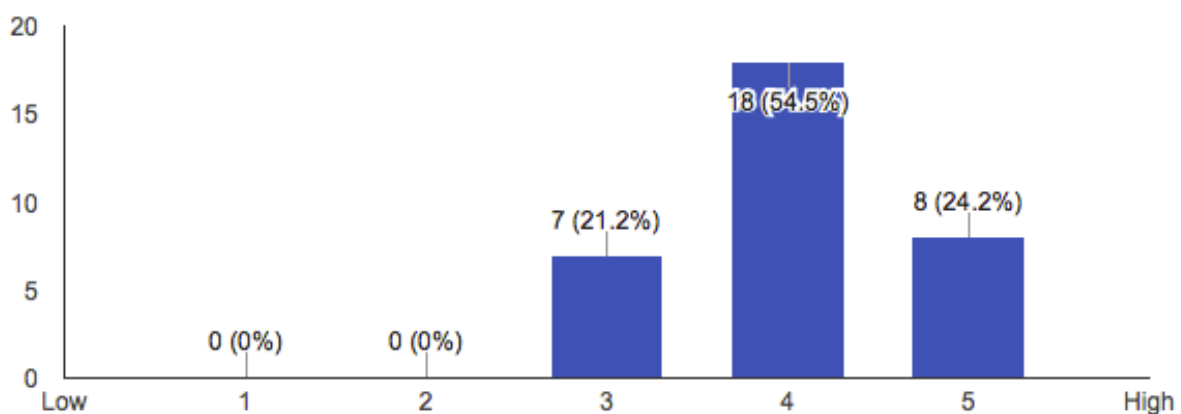
Overall, 33 participants took part during this evaluation round. The Clinic Research Application Framework (CRAF) which integrates almost all the back-end components of the CHIC platform (the Clinical Data Repository CDR, the Model repository MR, etc.) was evaluated through the simulation of Nephroblastoma patients under a clinical question addressed by two hypermodels (the Nephroblastoma multimodeller hypermodel and the Nephroblastoma phenomenological hypermodel).

#### 4.3.3.1 Purpose and Content

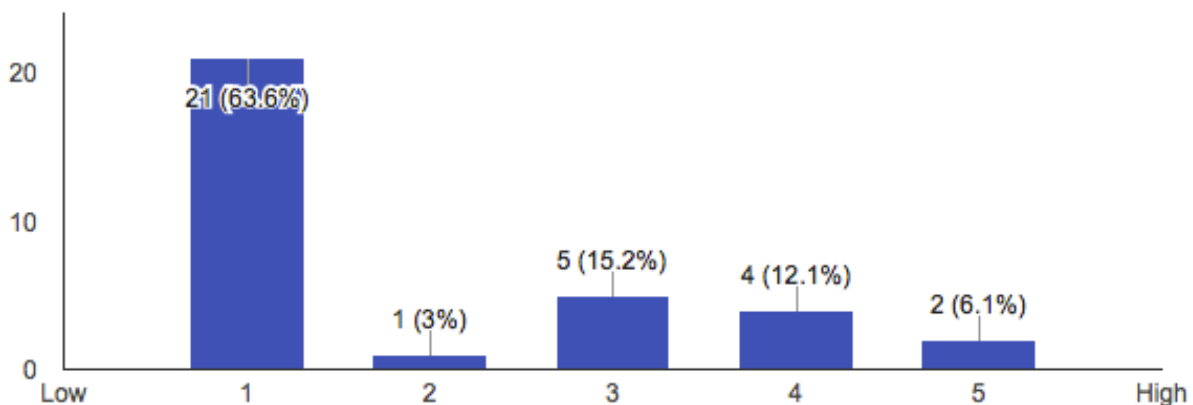
Can the application perform the required tasks?



How satisfied are you with the performance of the application?

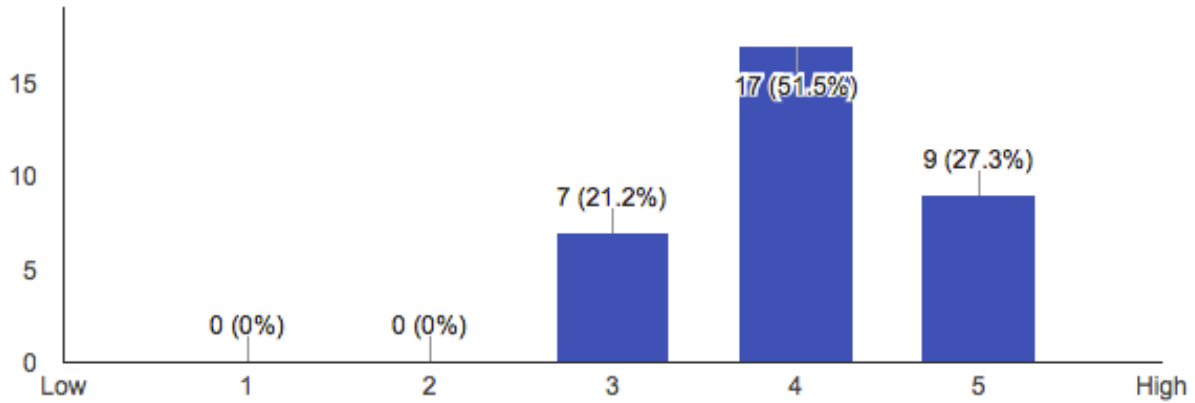


Do you know other similar tools? If yes, is this tool better than the other you know?

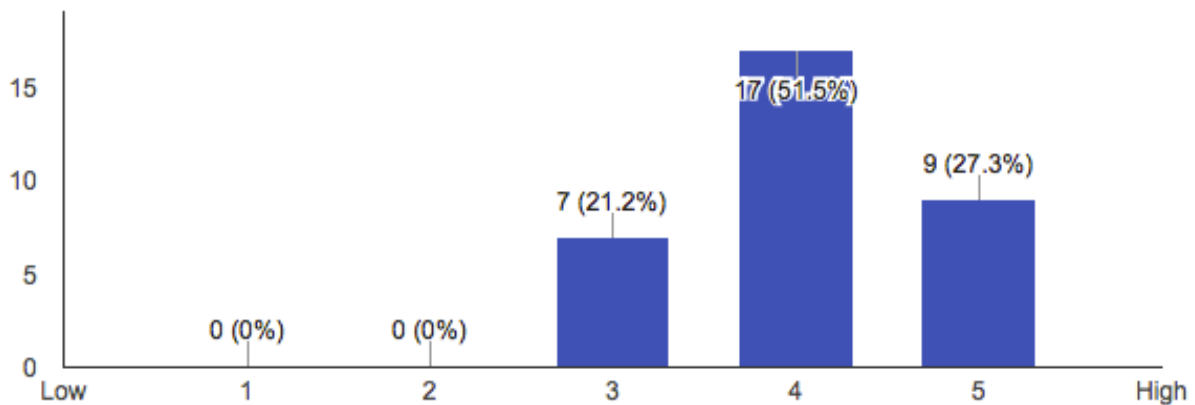


Those answering with 1 did not know other similar tools.

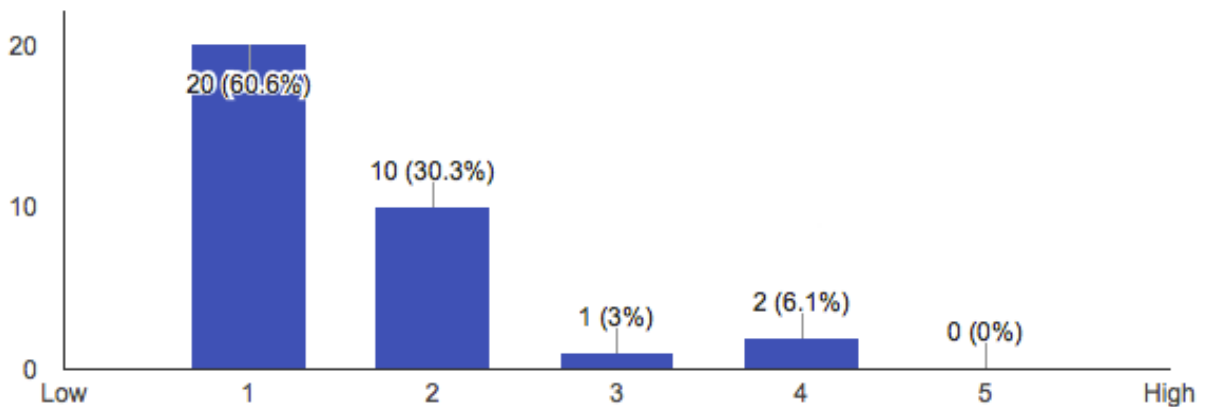
Is it easy to understand the functionality of the application?



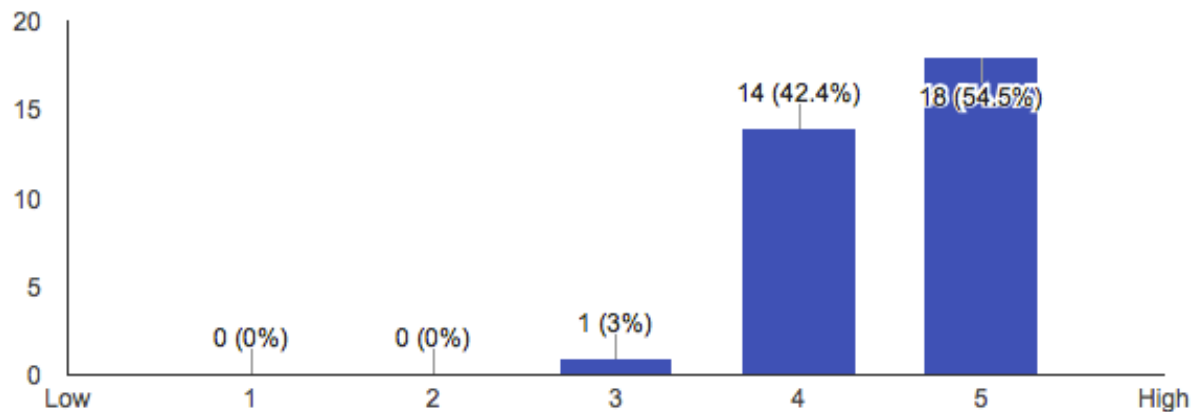
Have you managed to familiarize yourself with ease in the handling of the application?



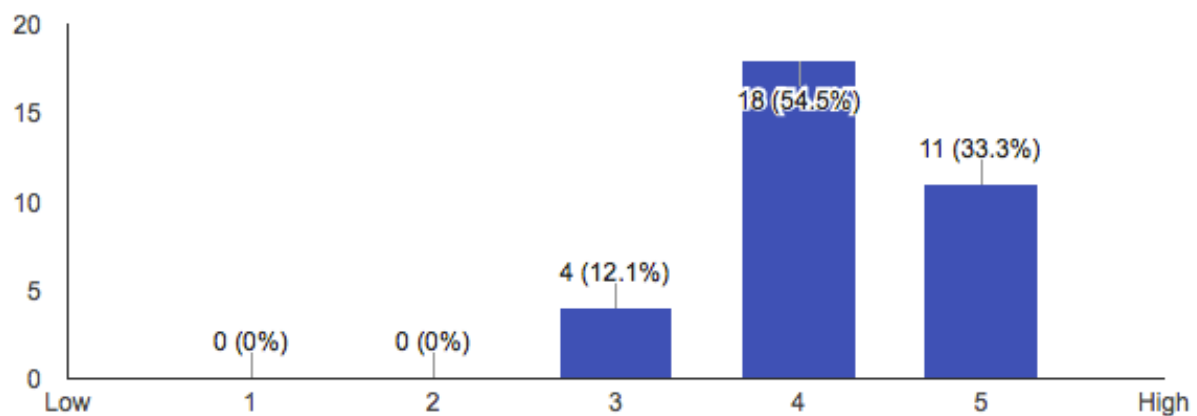
How long did it take you to learn the handling of the application?



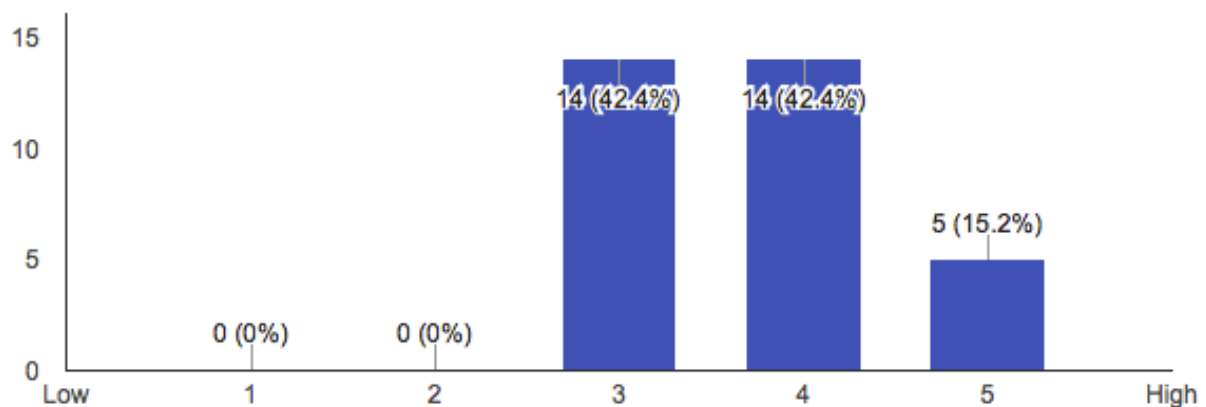
Can you use the application without much effort?



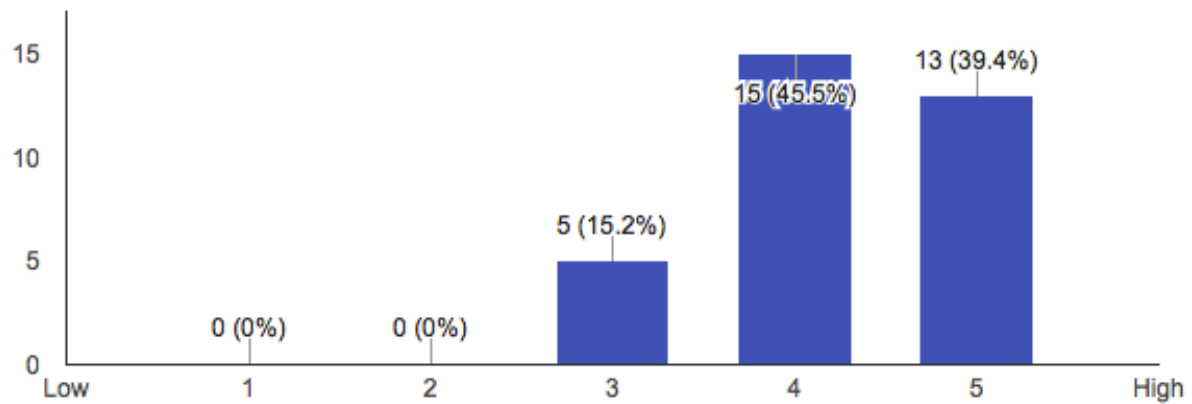
Does the interface look good?



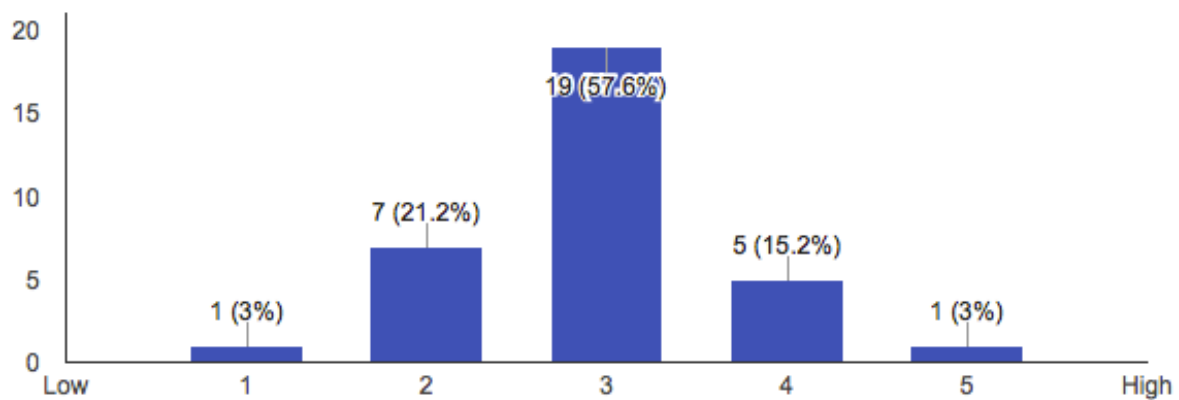
Does the interface provide all required information?



Is the usage of the application intuitive?

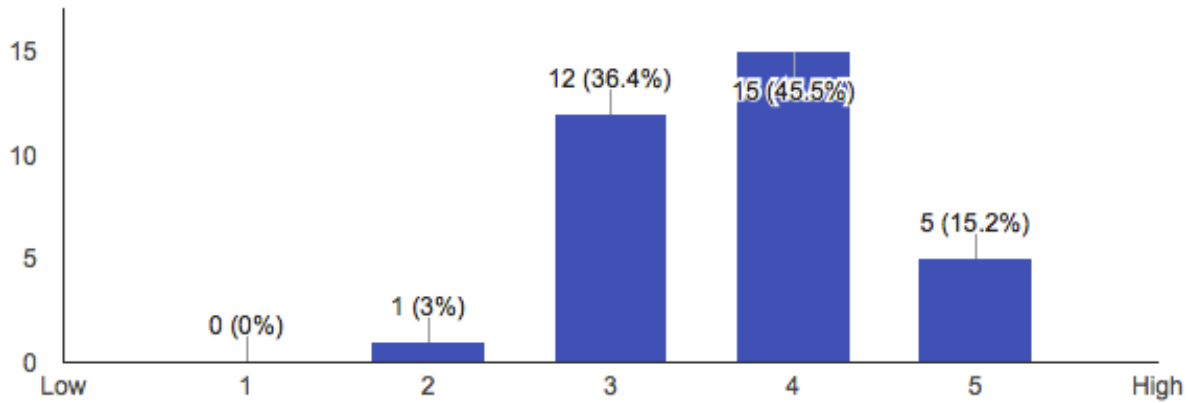


Do you think your data are secure?

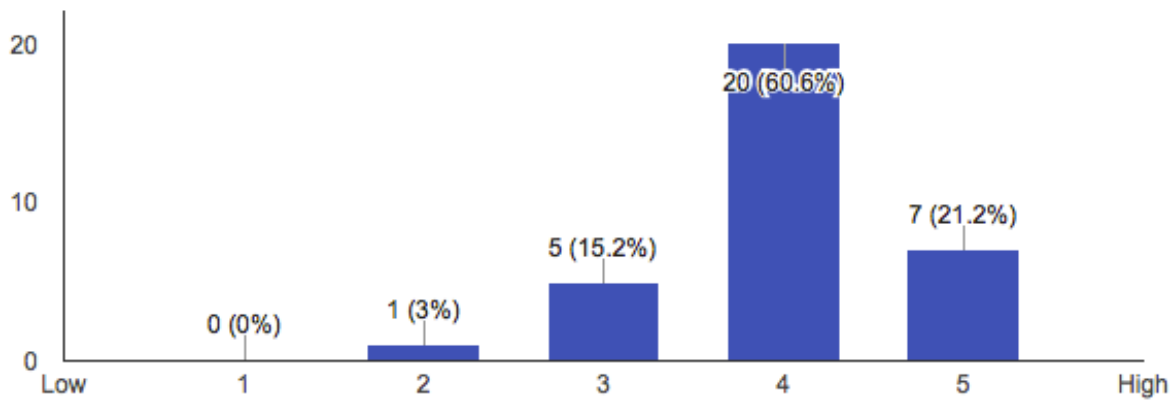


How complete is the application for the intended use?

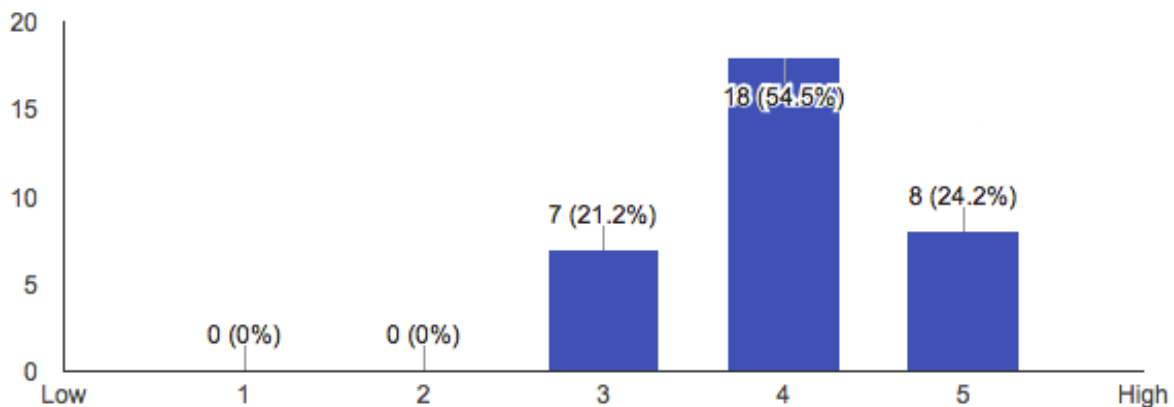




Does the application satisfy the perceived achievement of pragmatic goals?

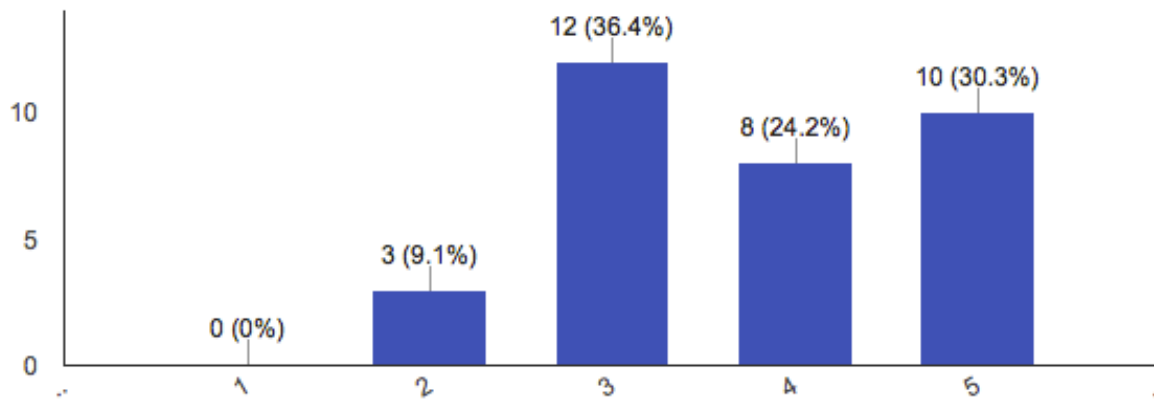


How satisfied are you of the application?

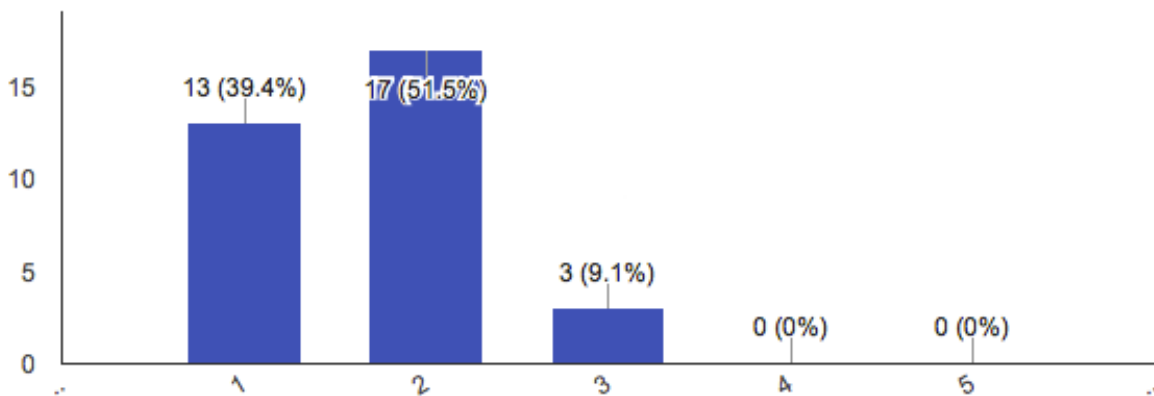


#### 4.3.3.2 Standardized Usability Questionnaire

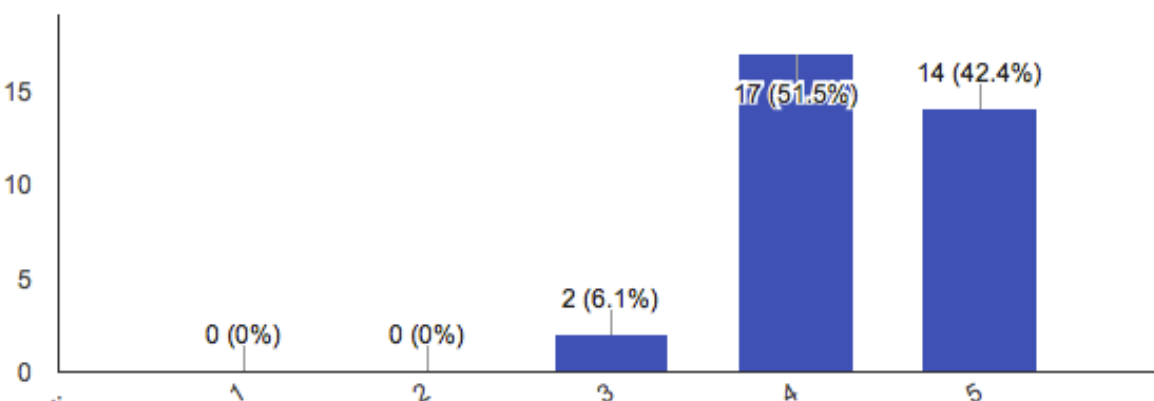
I think that I would like to use this system frequently



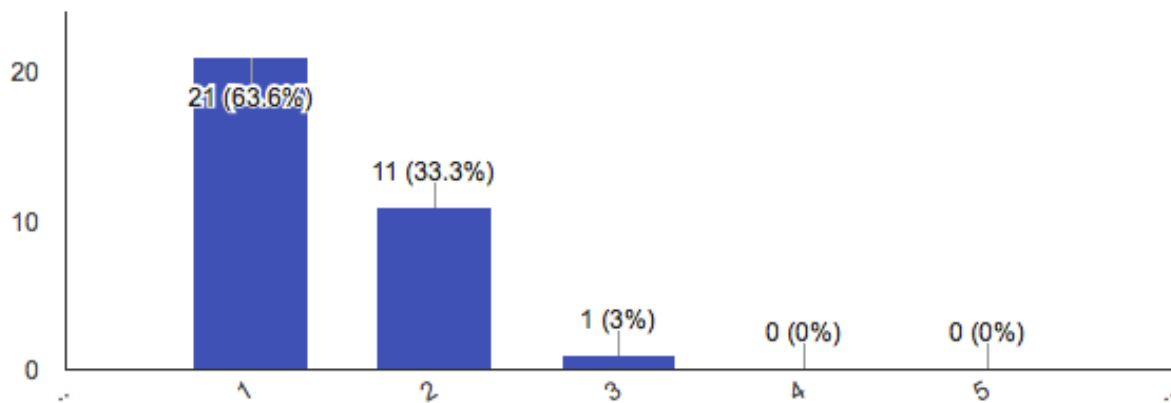
I found the system unnecessarily complex



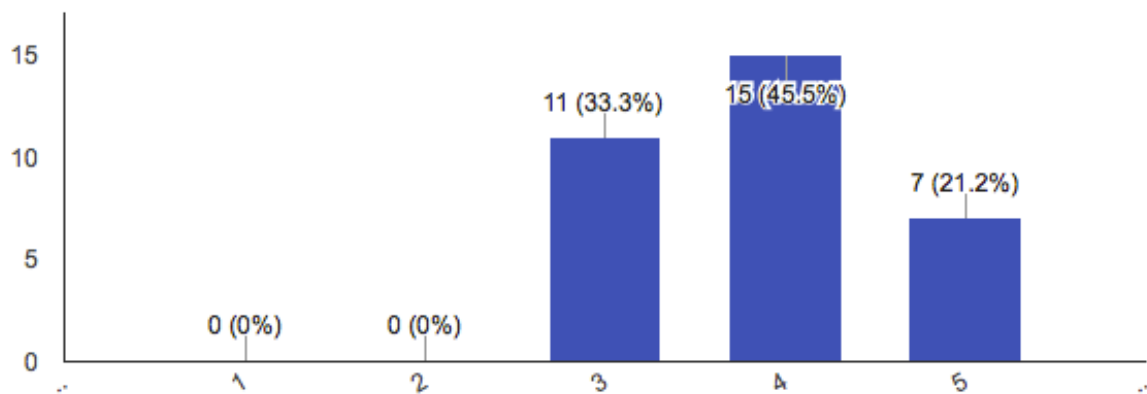
I thought the system was easy to use



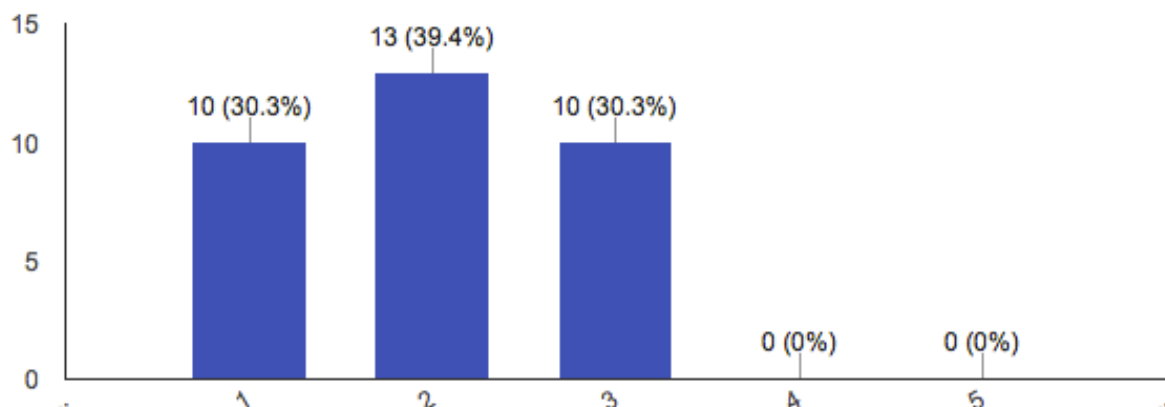
I think that I would need the support of a technical person to be able to use this system



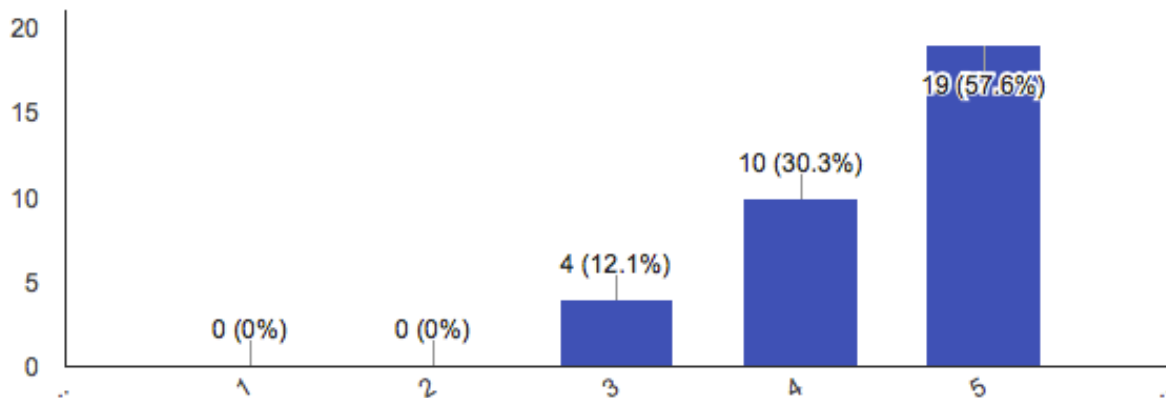
I found the various functions in this system were well integrated



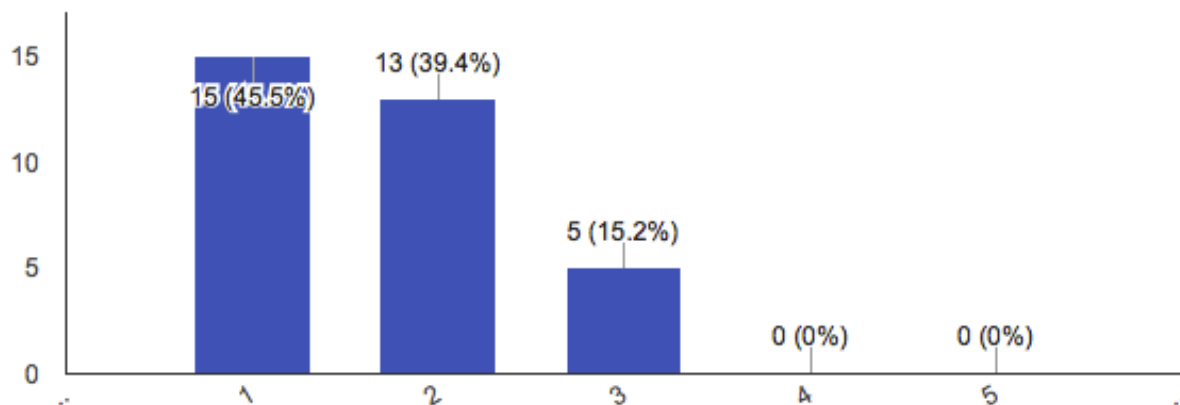
I thought there was too much inconsistency in this system



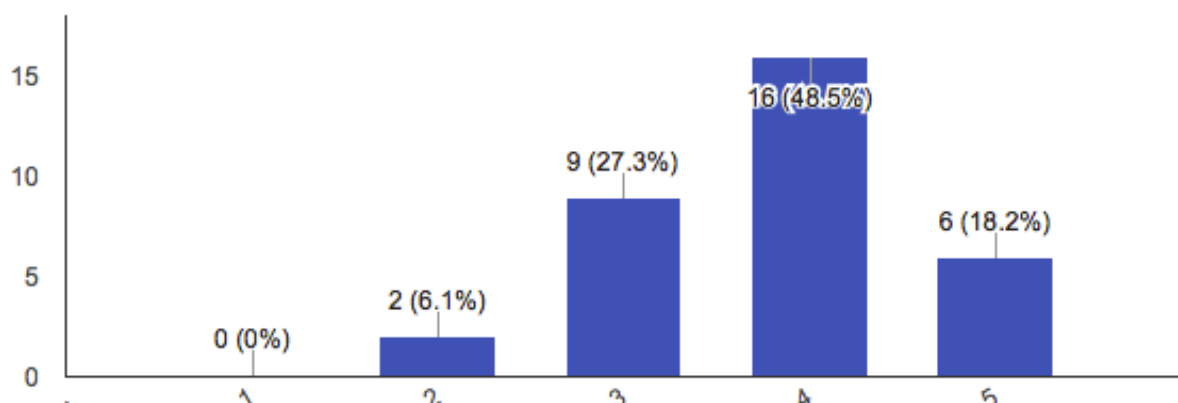
I would imagine that most people would learn to use this system very quickly



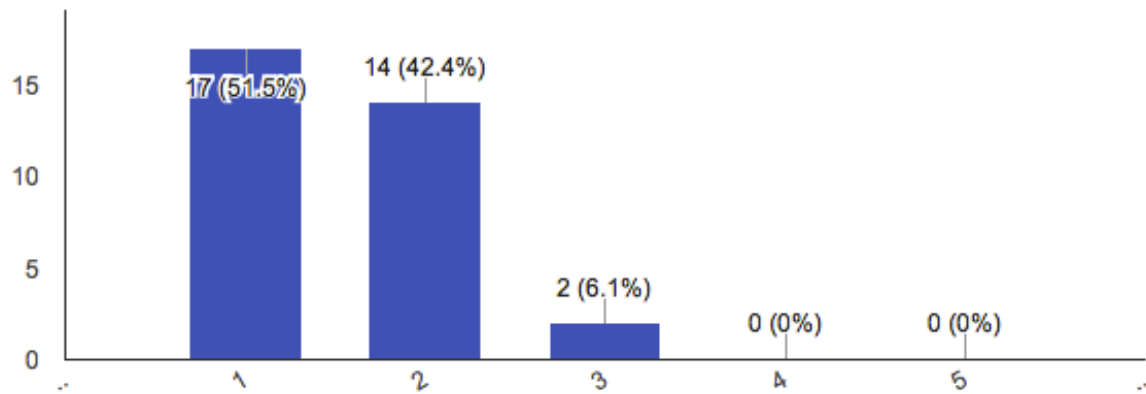
I found the system very cumbersome to use



I felt very confident using the system



I needed to learn a lot of things before I could get going with this system



#### 4.4 Summary of the Evaluation of the CDR and the CRAF

First of all it needs to be mentioned that the participants of the 9<sup>th</sup> International Renal Tumor Biology Conference were all experienced clinicians or basic scientists. Most of them are working in the field of nephroblastoma for more than 10 years. Many of them are in leading positions at their Universities.

Altogether the evaluations of the CDR and the CRAF were very successful. 28 out of 65 participants gave feedback for the CDR and 33 for the CRAF via the questionnaires. Detailed results are provided in chapter 4.2.3 and 4.3.3. Averages of all answers are provided in tables 4.4.1 and 4.4.2 and in Figures 4.2.1 and in 4.2.2.

Both applications were regarded as easy to use and were highly intuitive to use. Independent of the item low values were given only rarely. The overall impression was for both tools positive. A summary of the average values per item is provided in the following two tables.

STD	Average	
0,58	4,50	Is the purpose of the web application clear
0,63	4,57	Is the content provided by the web application understandable
0,61	4,18	Does it load quickly
0,55	4,32	Is the design consistent across the web application
0,69	4,04	Does the design allow for easy navigation
0,82	3,82	Is it visually appealing
0,84	2,75	Is the page design overwhelming or confusing
0,63	3,57	Is the font readable
0,83	3,36	How unique is the clinical data repository
0,63	3,61	Is it distinguishable from other similar web applications
0,57	3,57	Is the repository distinct and memorable
0,64	3,46	Does the repository offer features not found elsewhere
0,50	4,21	How obvious and easy is it for the user to view and browse the content
0,77	4,00	How obvious and easy is it for the user to download data
0,72	3,93	How obvious and easy is it for the user to enter in formation
0,69	4,04	How obvious and easy is it for the user to delete part of the content
0,61	4,18	How would you rate your overall impression of the clinical data repository

*Table 4.4.1: Average values of the items of the evaluation questionnaire for the CDR. All values above 4 are excellent.*

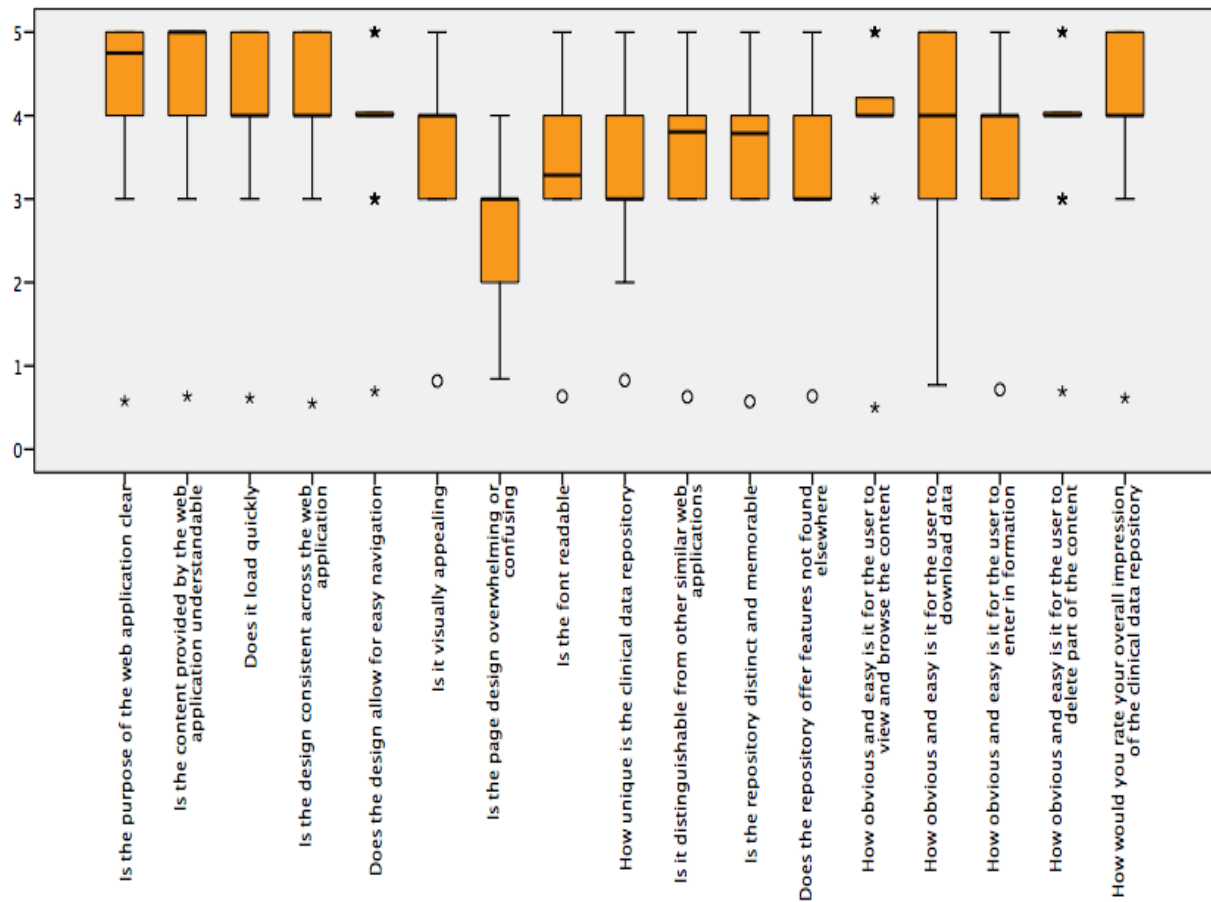


Fig. 4.4.1: Comparison of the distribution of the answers for the CDR to the different questions as a boxplot.

STD	Average	
0,74	4,15	Can the application perform the required tasks?
0,67	4,03	How satisfied are you with the performance of the application?
1,35	1,94	Do you know other similar tools? If yes is this tool better than the other you know?
0,69	4,06	It is easy to understand the functionality of the application?
0,69	4,06	Have you managed to familiarize yourself with ease in the handling of the application?
0,82	1,55	How long did it take you to learn the handling of the application?
0,56	4,52	Can you use the application without much effort?
0,64	4,21	Does the interface look good?
0,71	3,73	Does the interface provide all required information?
0,70	4,24	Is the usage of the application intuitive?
0,78	2,94	Do you think your data are secure?
0,75	3,73	How complete is the application for the intended use?
0,70	4,00	Does the application satisfy the perceived achievement of pragmatic goals?
0,67	4,03	How satisfied are you of the application?
0,99	3,76	I think that I would like to use this system frequently
0,63	1,70	I found the system unnecessarily complex
0,59	4,36	I thought the system was easy to use
0,55	1,39	I think that I would need the support of a technical person to be able to use this system
0,73	3,88	I found the various functions in this system were well integrated
0,78	2,00	I thought there was too much inconsistency in this system
0,70	4,45	I would imagine that most people would learn to use this system very quickly
0,72	1,70	I found the system very cumbersome to use
0,81	3,79	I felt very confident using the system
0,61	1,55	I needed to learn a lot of things before I could get going with this system

Table 4.4.2: Average values of the items of the evaluation questionnaire for the CRAF. All values above 4 are excellent and marked in green. In addition values below 2 are marked in green if a low value is excellent as e.g. short time to line the application.



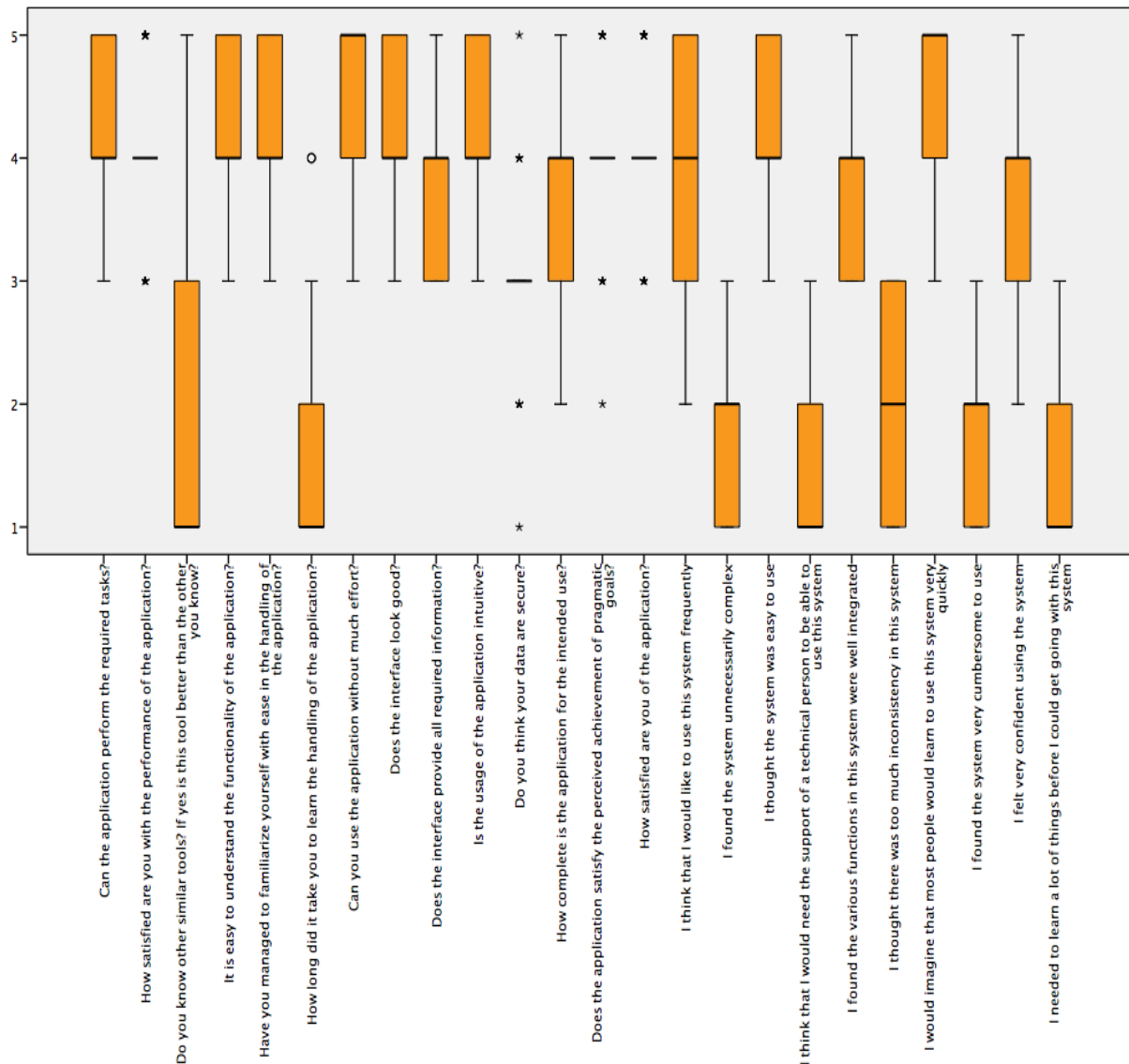


Fig. 4.4.2: Comparison of the distribution of the answers for the CRAF and hypermodels to the different questions as a boxplot.

Altogether the evaluation of the CDR and the CRAF suggests that the tools are easy to use and that clinicians as well as basic scientists are very much interested in using them for their research. For that purpose IPR issues are getting more relevant for the project. The evaluation also shows us that there is potential for usage after the lifetime of CHIC. Therefore a sustainability plan is becoming of utmost importance for the project. Researcher, dealing with nephroblastoma, want to see results of the prediction of the two hypermodels from at least 100 patients. The comparison with the real tumour reduction plays an important role to see if one can rely on the prediction. In other words validation of the applications are urgently needed.

In addition a further evaluation workshop is foreseen to take place during the international Conference on Pediatric Oncology and Clinical Pediatrics in Toronto, 11<sup>th</sup> – 13<sup>th</sup> August 2016<sup>3</sup>.

<sup>3</sup> <http://pediatriconcology.conferenceseries.com/>

## Virtual evaluation of CRAF and the hypermodels

### 4.5 Introduction

To get more end-users enrolled in the evaluation of CRAF and the hypermodels, the CHIC consortium decided to build a virtual platform where end-users can evaluate the CHIC platform as well as the nephroblastoma hypermodel with all its components. When the hypermodels for lung cancer, prostate cancer and glioblastoma are ready they will also be connected to the web-based CRAF to evaluate them as well. A web-based CRAF is (tentatively) available at <http://biomodeling.ics.forth.gr/app/craf/>. The application will be announced via our website and contacts to potential researchers. An interested user needs to get in contact with the CHIC consortium to receive credentials for the evaluation of the application. Some screen shots of this web application are shown below:

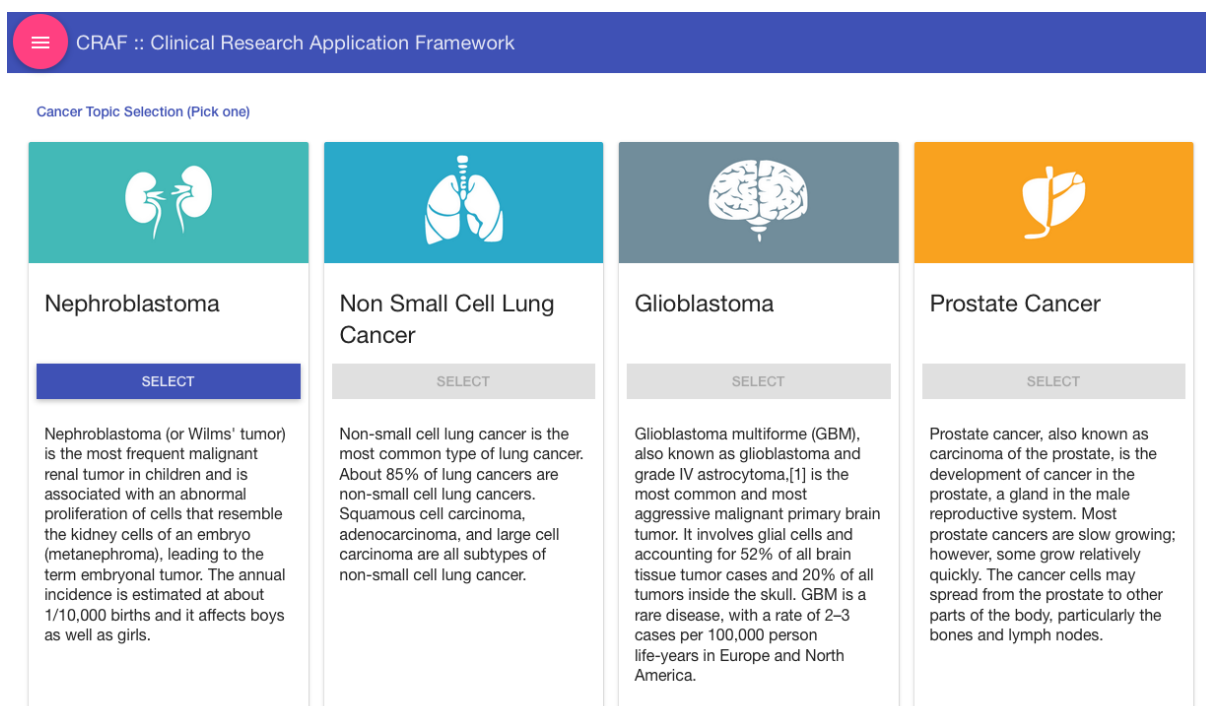


Fig. 5.1.1: The initial webpage of the CRAF application after login.

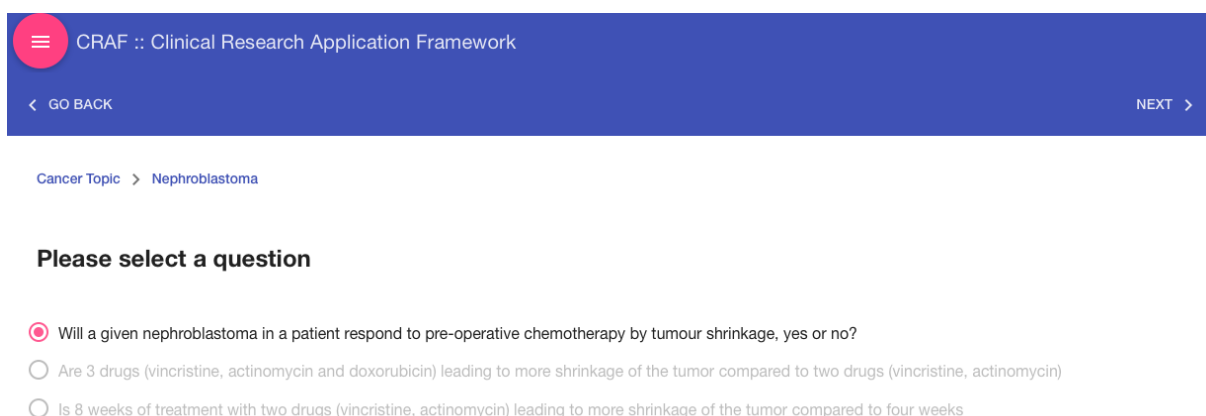


Fig. 5.1.2: After selection of nephroblastoma one can select a question that will be answered by the hypermodel

CRAF :: Clinical Research Application Framework

GO BACK
NEXT >

Cancer Topic > Nephroblastoma > Patient Selection

Please select a patient

☒ Ernst Müller  
☐ Hans Fischer

Patient Card

### Patient's Information

Demographics

First Name	Last Name	Gender	Date Of Birth	E-mail
Ernst	Müller	Not Provided	Not Provided	Not Provided

### Clinical Data

CDR.Kidney.XX.XX.CDISC\_ODM.6633.000.xml  
Type: CLINICAL, # Files: 1  
<https://cdr.chic-vph.eu/api/objects/6633/download>

CDR.Kidney.XX.XX.MINIML.7670.000.xml  
Type: GENOMICS, # Files: 1  
<https://cdr.chic-vph.eu/api/objects/7670/download>

CDR.Kidney.XX.F.MR.7833.000.dcm  
Type: DICOM\_SERIES, # Files: 40  
<https://cdr.chic-vph.eu/api/objects/7833/download>

CDR.Kidney.XX.F.MR.7834.000.dcm  
Type: DICOM\_SERIES, # Files: 80  
<https://cdr.chic-vph.eu/api/objects/7834/download>

CDR.Kidney.XX.XX.MINIML.8022.000.xml  
Type: GENOMICS, # Files: 1  
<https://cdr.chic-vph.eu/api/objects/8022/download>

CDR.Kidney.XX.XX.CDISC\_ODM.8042.000.xml  
Type: CLINICAL, # Files: 1  
<https://cdr.chic-vph.eu/api/objects/8042/download>

Fig. 5.1.3: At the next step one can select a patient and available data of the patient are shown.

CRAF :: Clinical Research Application Framework

GO BACK
NEXT >

Cancer Topic > Nephroblastoma > Patient Selection > Hypermodel for the selected Patient

Please select a hypermodel

☒ **Nephroblastoma multimodeller hypermodel**  
Nephroblastoma hypermodel description

☐ **Nephroblastoma phenomenological hypermodel**  
Phenomenological hypermodel

☐ **Hello World Test Model**  
A Hello World test for VPHHF

[CREATE A NEW HYPERMODEL AT THE CHIC "HYPERMODEL EDITOR"](#)

Fig. 5.1.4: At the next step one can select a hypermodel for that patient.

The screenshot shows the CRAF Clinical Research Application Framework interface. At the top, there is a blue header with a menu icon, the text 'CRAF :: Clinical Research Application Framework', a 'GO BACK' button, and an 'EXECUTE' button with a green arrow. Below the header, a breadcrumb trail reads: 'Cancer Topic > Nephroblastoma > Patient Selection > Hypermodel for the selected Patient'. The main title is 'Nephroblastoma multimodeller hypermodel'. Below this, there are two tabs: 'INPUT' (selected) and 'OUTPUT'. The 'Input parameters' section contains two toggle switches: 'Show required' (checked) and 'Show editable' (unchecked). The parameters are arranged in two columns:

diff_nec_rate 0.05 Default: 0.05 , Range: 0-1	stem_g0_to_g1_fraction 0.01 Default: 0.01 , Range: 0-1
limp_g0_to_g1_fraction 0.01 Default: 0.01 , Range: 0-1	vcr_time_A 7 Default: 7 , Range: 0-..
vcr_time_B 14 Default: 14 , Range: 0-..	vcr_time_C 21 Default: 21 , Range: 0-..
vcr_time_D 28	dt_posttreatment_scan 1

Fig. 5.1.5: At the next step input and output parameters can be seen and one can start the execution of the application.

After the execution results will be made available in a PDF file as provided by the stand alone tool. See figure 4.3.1.8.

At the end of the evaluation the end-user will be asked to answer an evaluation questionnaire that was developed for that reason. This questionnaire will be the same as for the stand-alone application (see Appendix 3).

A second reason for setting up such a virtual evaluation workshop is the possibility to enhance the workshop with other hypermodels and to continue evaluations over a longer period of time. In addition this virtual platform can serve also as a demonstration area for the CHIC platform and the hypermodels and is an excellent way for exploitation and dissemination of the CHIC project. This virtual platform can be enhanced with videos demonstrating how to use the platform and the hypermodels.

## Appendix 1 – Questionnaire used at the evaluation workshop of the German School of POH



### **‘in silico’ Modelling for Decision Support in WT** **Söllereck – GPOH - January 2016**

Age: \_\_\_\_\_

Profession: \_\_\_\_\_

**Prior experience with ‘in silico’ Modelling of Tumours:**

*Not at all*      1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10      *very experienced*

**‘in silico’ models will be an important technology in health care in the future**

*Not at all*      1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10      *highest degree*

**‘in silico’ models will be useful for decision support in the future**

*Not at all*      1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10      *highest degree*

**Physicians need to use ‘in silico’ models for decision support in the future**

*Not at all*      1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10      *highest degree*

**‘in silico’ models must be intuitive to work with (like an App)**

*Not at all*      1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10      *highest degree*

**‘in silico’ models need to guarantee data safety and security**

*Not at all*      1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10      *highest degree*

**‘in silico’ models need to be understandable in all details by physicians**

*Not at all*      1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10      *highest degree*

**‘in silico’ models need to run without further interaction by physicians besides the selection of the model and the patient**

*Not at all*      1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10      *highest degree*

**The result of the ‘in silico’ model should be reproducible and precise**

*Not at all*      1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10      *highest degree*

**The result of the ‘in silico’ model must be better than the weather forecast of today to use it in clinical care as decision support service**

*Not at all*      1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10      *highest degree*

**The result of the ‘in silico’ model must be given clearly and easy to understand (e.g. visualization of tumour shrinkage)**

*Not at all*      1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10      *highest degree*

**The ‘in silico’ model application should also be able to demonstrate the patient how treatment affects his tumour**

*Not at all*      1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10      *highest degree*

---

**The following features need to be integrated in ‘in silico’ models to be useful for clinicians:**

**General comments:**

---

***Thanks***

## Appendix 2 – Evaluation questionnaire for the CDR



### CHIC clinical data repository evaluation

*Thank you for participating in this evaluation! Before you start, we would like to highlight the user guide, which can be found on the top right corner of the clinical data repository web application when logged in.*

\*Required

#### Purpose and Content

Is the purpose of the web application clear? \*

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

Is the content provided by the web application understandable? \*

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

Comments related to "Purpose and Content". (optional):

---



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## Accessibility

Is it displayed correctly in different browsers? \*

	Yes	No	Not tested
Chrome	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Firefox	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Safari	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Opera	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Internet Explorer	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Edge	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Does it load quickly? \*

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

Comments related to "Accessibility". (optional)

---



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## User Experience

Is the design consistent across the web application? \*

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

Does the design allow for easy navigation? \*

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high



**Is it visually appealing? \***

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

**Is the page design overwhelming or confusing? \***

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

**Is the font readable? \***

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

**Comments related to "User Experience". (optional)**

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## Creativity and Innovation

**How unique is the clinical data repository? \***

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

**Is it distinguishable from other similar web applications? \***

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

**Is the repository distinct and memorable? \***

	1	2	3	4	5
--	---	---	---	---	---

Low ☐ ☐ ☐ ☐ ☐ high

**Does the repository offer features not found elsewhere? \***

1 2 3 4 5  
Low ☐ ☐ ☐ ☐ ☐ high

**Comments related to "Creativity and Innovation". (optional)**

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## User Task Analysis

**How obvious and easy is for the user to view and browse the content of the clinical data repository? \***

1 2 3 4 5  
Low ☐ ☐ ☐ ☐ ☐ high

**How obvious and easy is for the user to download data? \***

1 2 3 4 5  
Low ☐ ☐ ☐ ☐ ☐ high

**How obvious and easy is for the user to enter information about the data (descriptive information, permissions, comments, etc.)? \***

1 2 3 4 5  
Low ☐ ☐ ☐ ☐ ☐ high

**How obvious and easy is for the user to delete part of the content of the clinical data repository? \***

1 2 3 4 5  
Low ☐ ☐ ☐ ☐ ☐ high

**What feature do you like, miss or want to be improved? (optional)**

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## Overall

**How would you rate your overall impression of the clinical data repository? \***

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

**Any final comment is very welcome. (optional)**

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## Appendix 3 – Evaluation questionnaires for the Nephroblastoma Hypermodels and CRAF



### CHIC hypermodel and CRAF evaluation

*Thank you for participating in this evaluation!*

\*Required

#### Questionnaire A

Can the application perform the required tasks? \*

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

How satisfied are you with the performance of the application? \*

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

Do you know other similar tools? If yes is this tool better than the other you know? \*

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

It is easy to understand the functionality of the application? \*

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

**Have you managed to familiarize yourself with ease in the handling of the application? \***

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

**How long did it take you to learn the handling of the application? \***

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

**Can you use the application without much effort? \***

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

**Does the interface look good? \***

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

**Does the interface provide all required information? \***

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

**Is the usage of the application intuitive? \***

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

**Do you think your data are secure? \***

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

**How complete is the application for the intended use? \***

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

**Does the application satisfy the perceived achievement of pragmatic goals? \***

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

**How satisfied are you of the application? \***

	1	2	3	4	5	
Low	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	high

## Questionnaire B

**I think that I would like to use this system frequently \***

	1	2	3	4	5	
Strongly disagree	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Strongly agree

**I found the system unnecessarily complex \***

	1	2	3	4	5	
Strongly disagree	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Strongly agree

**I thought the system was easy to use \***

	1	2	3	4	5	
Strongly disagree	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Strongly agree

**I think that I would need the support of a technical person to be able to use this system \***

	1	2	3	4	5	
Strongly disagree	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Strongly agree

**I found the various functions in this system were well integrated \***

	1	2	3	4	5	
Strongly disagree	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Strongly agree

**I thought there was too much inconsistency in this system \***

	1	2	3	4	5	
Strongly disagree	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Strongly agree

**I would imagine that most people would learn to use this system very quickly \***

	1	2	3	4	5	
Strongly disagree	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Strongly agree

**I found the system very cumbersome to use \***

	1	2	3	4	5	
Strongly disagree	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Strongly agree

**I felt very confident using the system \***

	1	2	3	4	5	
Strongly disagree	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Strongly agree

**I needed to learn a lot of things before I could get going with this system \***

	1	2	3	4	5	
Strongly disagree	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Strongly agree

## Appendix 4 – Abbreviations and acronyms

<i>CDR</i>	Clinical Data Repository
<i>COG</i>	Children's Oncology Group
<i>CRAF</i>	Clinical Research Application Framework
<i>RTSG</i>	Renal Tumour Study Group
<i>SIOP</i>	International Society of Paediatric Oncology