Belgian Virtual Tumourbank: Catalogue module (BVTc)

User manual for researchers

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1. INTRODUCTION

This manual describes how to use the online catalogue module of the Belgian Virtual Tumourbank, the BVTc. The user should be able to retrieve the samples he/she is looking for, using the available search criteria. The concept of the BVT applications will be explained to give some insights to obtain better search results.

2. CONTACT INFORMATION

Belgian Cancer Registry (BCR) - Biobank Project:

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02/250.10.12

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biobank@kankerregister.org

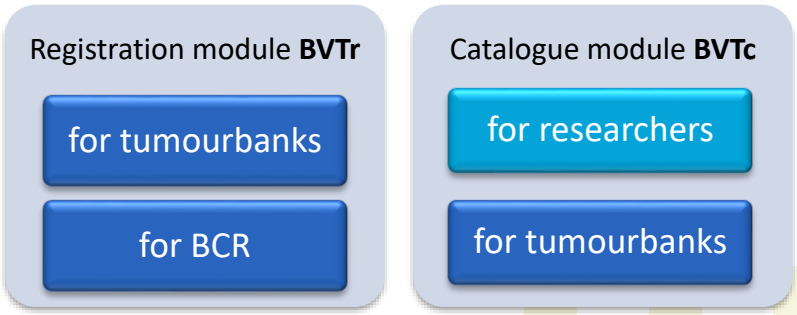
www.virtualtumourbank.be

If you have questions or remarks about the online BVTc application, please do not hesitate to contact us.
We are looking forward to receiving your feedback, since it is our purpose to keep improving the BVT catalogue and service to the users.

3. CONCEPT OF THE APPLICATION

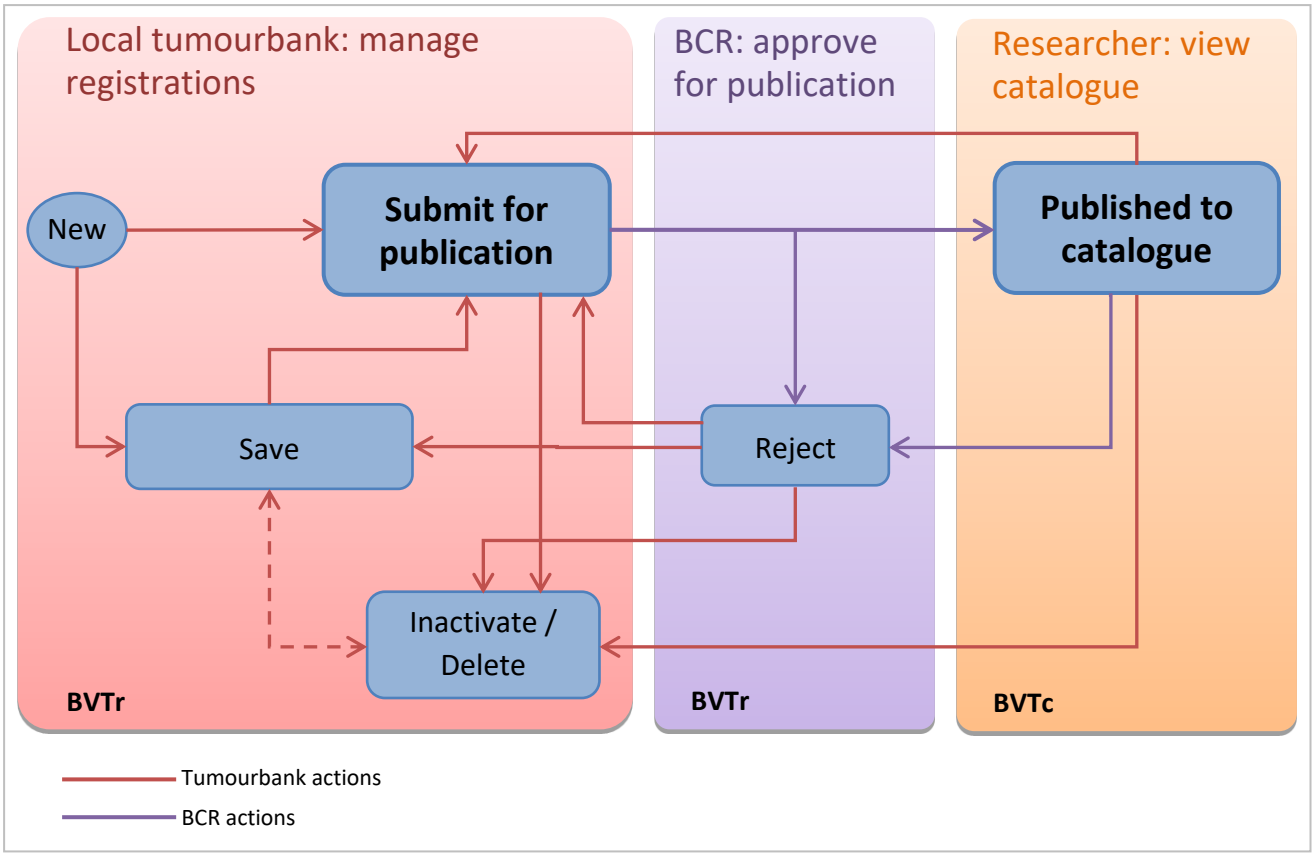
3.1. General

The application of the Belgian Virtual Tumourbank (BVT) is divided into 2 modules: the BVTr and the BVTc.



This manual contains information about the **BVTc for researchers**.

3.2. Data flow in the BVT applications



Each sample registration has a well-defined state (see blue boxes in the scheme above), which defines the specific actions that are allowed to be executed. The BVTr application (registration module) allows the local tumourbank and the BCR to populate the catalogue with tumour sample registrations. Some important principles:

- Each local tumourbank is able to view all its registrations, but is not able to view registrations from another local tumourbank.
- Each local tumourbank is responsible for its own registrations.
- The BCR is able to view all registrations from all local tumourbanks, except for the “saved” (incomplete) registrations.
- The BCR verifies the submitted registrations and approves them for publication to the catalogue. If registrations are erroneous, questionable or identifiable towards the donor, they are rejected and sent back to the local tumourbank for correction or inactivation/deletion.
- All published registrations are available in the catalogue for query. The data in the catalogue is coded, i.e. it is not possible for a researcher to re-identify the donor.
- Data are structured using a predefined dataset, with minimal required fields. Historical data (i.e. data of samples taken before 2010) have less required fields.

3.3. Dataset and data content/validation

Data Element (Variable Name)	Required	Required for historical data (before 2010)	Visible in catalogue
General variables			
Laboratory	(automatically)	(automatically)	X
Reference ID	(automatically)	(automatically)	X
Patient variables			
SSIN	X	SSIN / Biopsy nr.	
Gender	X	X	X
Birth date	X	X	
Age			X
Patient Opposition	X	X	
Technical variables			
Sample ID	X	X	X
Biopsy number	X	Biopsy nr./ SSIN	
Sample Date	X	X	X (only year)
Conservation mode	X		X
Comment if other conservation mode			X
Conservation delay	X		X
Autopsy?			X
Available materials	X		X
Comment if other available materials			X
Technical remarks			
Oncological variables			
Sample type (lesion type)	X	X	X
Comment if other sample type			X
Sample localisation	X	X	X
Localisation primary tumour if meta			X
Laterality			X
Morphology	X	X	X
Behaviour	X	X	X
Differentiation grade			X
Prefix			X
pT			X
pN			X
pM			X
Oncological remarks			
BCR variables			
cT			X
cN			X
cM			X
Quality Control Result			
BCR Comment			
Error Comment			

Every variable in the dataset has its own defined format and validation rules. You can find more information about the variables in appendix 1 (see chapter 5).

3.4. Classifications

The tumours in the Belgian Virtual Tumourbank are classified according to the internationally acknowledged ICD-O classification (International Classification of Diseases – Oncology) and the TNM of the UICC (http://www.uicc.org/resources/tnm). These classifications are available in several editions, and the use of each edition depends on the year in which the tumour is discovered:

<table>
<tr><th>Sample Year</th><th>ICD-O</th><th>Sample Year</th><th>TNM</th></tr>
<tr><td>…</td><td rowspan="5">ICD-O-2</td><td>…</td><td rowspan="2">TNM 4</td></tr>
<tr><td>1998</td><td>1998</td></tr>
<tr><td>1999</td><td>1999</td><td rowspan="3">TNM 5</td></tr>
<tr><td>2000</td><td>2000</td></tr>
<tr><td>2001</td><td>2001</td></tr>
<tr><td>2002</td><td rowspan="13">ICD-O-3

→ Warning: update of 2011![1]</td><td>2002</td></tr>
<tr><td>2003</td><td>2003</td><td rowspan="7">TNM 6</td></tr>
<tr><td>2004</td><td>2004</td></tr>
<tr><td>2005</td><td>2005</td></tr>
<tr><td>2006</td><td>2006</td></tr>
<tr><td>2007</td><td>2007</td></tr>
<tr><td>2008</td><td>2008</td></tr>
<tr><td>2009</td><td>2009</td></tr>
<tr><td>2010</td><td>2010</td><td rowspan="3">TNM 7</td></tr>
<tr><td>…</td><td>…</td></tr>
<tr><td>2016</td><td>2016</td></tr>
<tr><td>2017</td><td>2017</td><td rowspan="3">TNM 8
→ Warning: errata![2]</td></tr>
<tr><td>…</td><td rowspan="2">…</td></tr>
<tr><td>2020</td><td>ICD-O-3.2</td></tr>
<tr><td>…</td><td></td><td></td></tr>
</table>

1: The ICD-O-3 update of 2011 can be applied to all tumours from 2002 onwards. The complete list of updates can be downloaded via the following link:
http://www.kankerregister.org/media/docs/downloads/voorpathologen/20130118ICDO3Updates-vertalingNL.pdf

2: For the last version of all the changes and corrections for TNM, see:
http://www.wileyanduicc.com/pdf/Corrected_pages.pdf

4. WORKING WITH BVTc

4.1. Start

4.1.1. System requirements

This application will work best with the browsers Internet Explorer and Firefox.

4.1.2. Web address BVTc

You can reach the catalogue module of the BVT by the following link:
https://www.virtualtumourbank.be/bvtc

The link is also available via the BVT website www.virtualtumourbank.be by clicking the orange button on the right side:

4.1.3. Authentication with electronic identity card (eID)

The BVTc is a secured web application, where the identity of the user will be verified (authentication) at the moment of logging in. For this you need a valid electronic identity card (eID) or the mobile app “itsme”.

To be able to use the **eID** services, the following things should be installed on your computer:

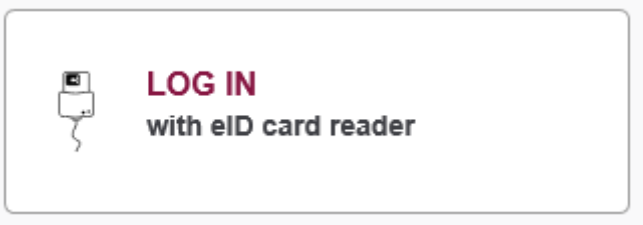
- A card reader (free to choose)
- Software to read electronic identity cards
  (free to download via http://eid.belgium.be/en/using_your_eid/installing_the_eid_software/, click on the “quick install”-icon on the right side)
- If you work with Firefox, you will also have to install the following add-on:
  https://addons.mozilla.org/en-US/firefox/addon/belgium-eid/

You will need to know the PIN code of your eID to be able to login to the BVTc with your eID.

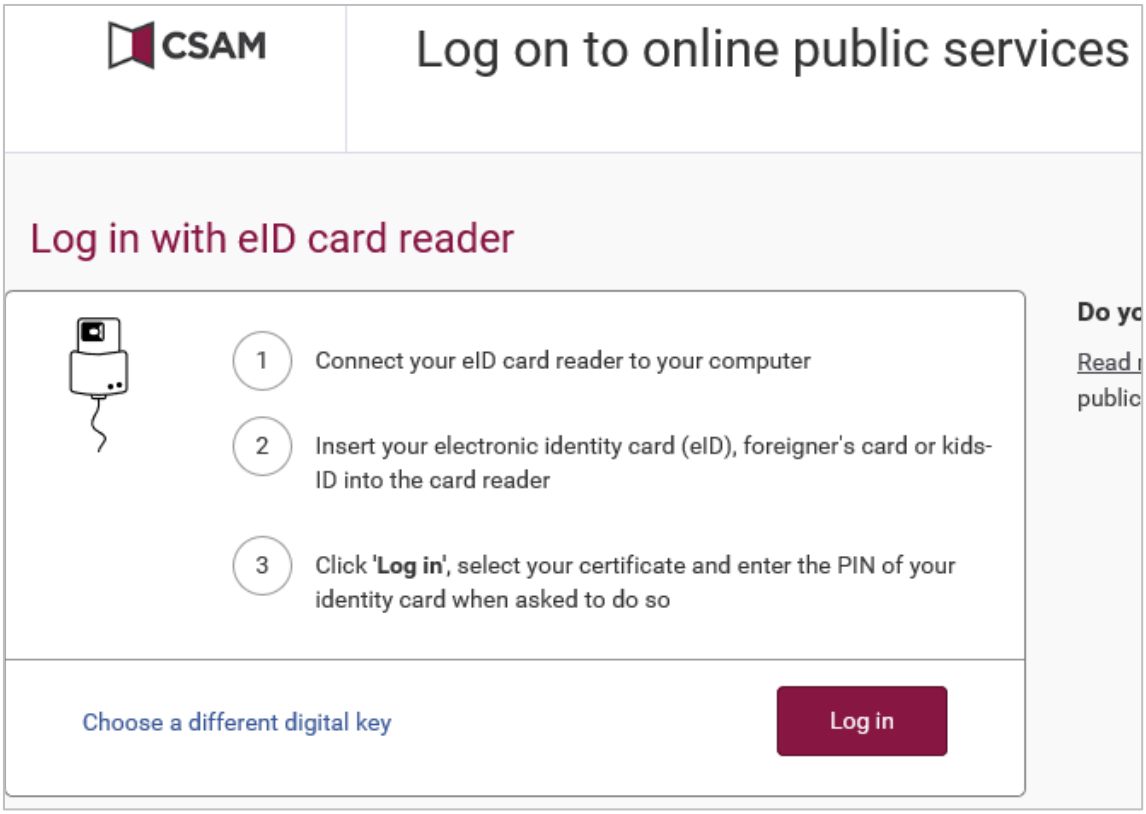
More information is also available on the eHealth website:
Dutch: https://www.ehealth.fgov.be/nl/egezondheid/hoe-krijgt-u-toegang-tot-het-portaal-egezondheid-/eidtoken
French: https://www.ehealth.fgov.be/fr/esante/acceder-au-portail-esante/eidtoken

4.1.4. Connection procedure eHealth with eID to access the application

- Enter the web address (URL) https://www.virtualtumourbank.be/bvtc in the web browser.
- Choose “Log in with eID card reader” on the page of the CSAM portal. You can change your language at the top of the page.



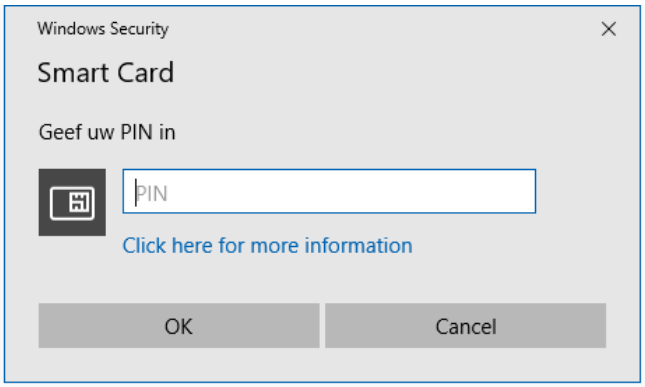
- A window of the “Federal Authentication Service” (FAS, an authentication service offered by Fedict) will appear.



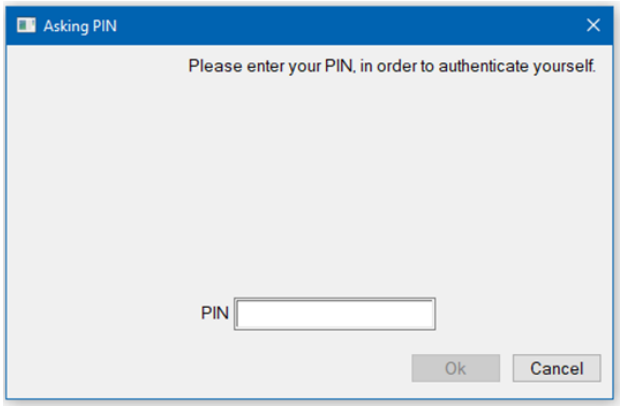
- Insert your electronic identity card (eID) in the card reader.
- Click on the red button “Log in”.

More information about FAS can be found via the following link:
Dutch: https://dt.bosa.be/nl/identificatie_beveiliging/federal_authentication_service
French: https://dt.bosa.be/fr/identification_et_securisation/federal_authentication_service

- Select your own certificate in the pop-up that appears and enter your PIN code.

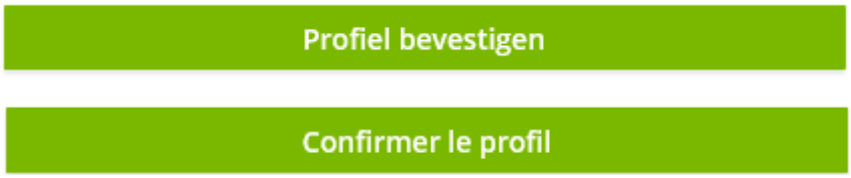


or



- Select the organisation of the Belgian Cancer Registry in the dropdown menu.

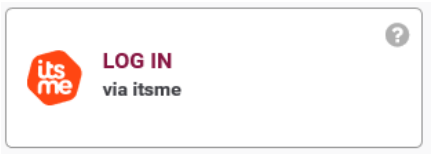
- Click on the green button "Profiel bevestigen" / "Confirmer le profil".



- You will be forwarded to the homepage of the BVTc-application.
- Please navigate throughout the application with the buttons within the application itself (not the ones from your web browser).

Error messages can occur during the connection procedure. In this case, it is advised to completely close your internet browser and to restart the connection procedure. If the problem persists, you can contact the Biobank Team of the Belgian Cancer Registry (02/250.10.12 or biobank@kankerregister.org) and mention/ take a screenshot of the displayed ticket number (if applicable).

An alternative for logging in via eID is via the mobile app "itsme". For this you will need a smartphone with the itsme-app installed. Choose "Log in via itsme" on the page of the CSAM portal:



Next, a window of itsme will appear where you should insert your mobile phone number. Then you should open the itsme-app on your smartphone and confirm your identity with the security code. Finally, a window will open on your computer where you should select and confirm the Belgian Cancer Registry as your institution, just as during the procedure via eID.

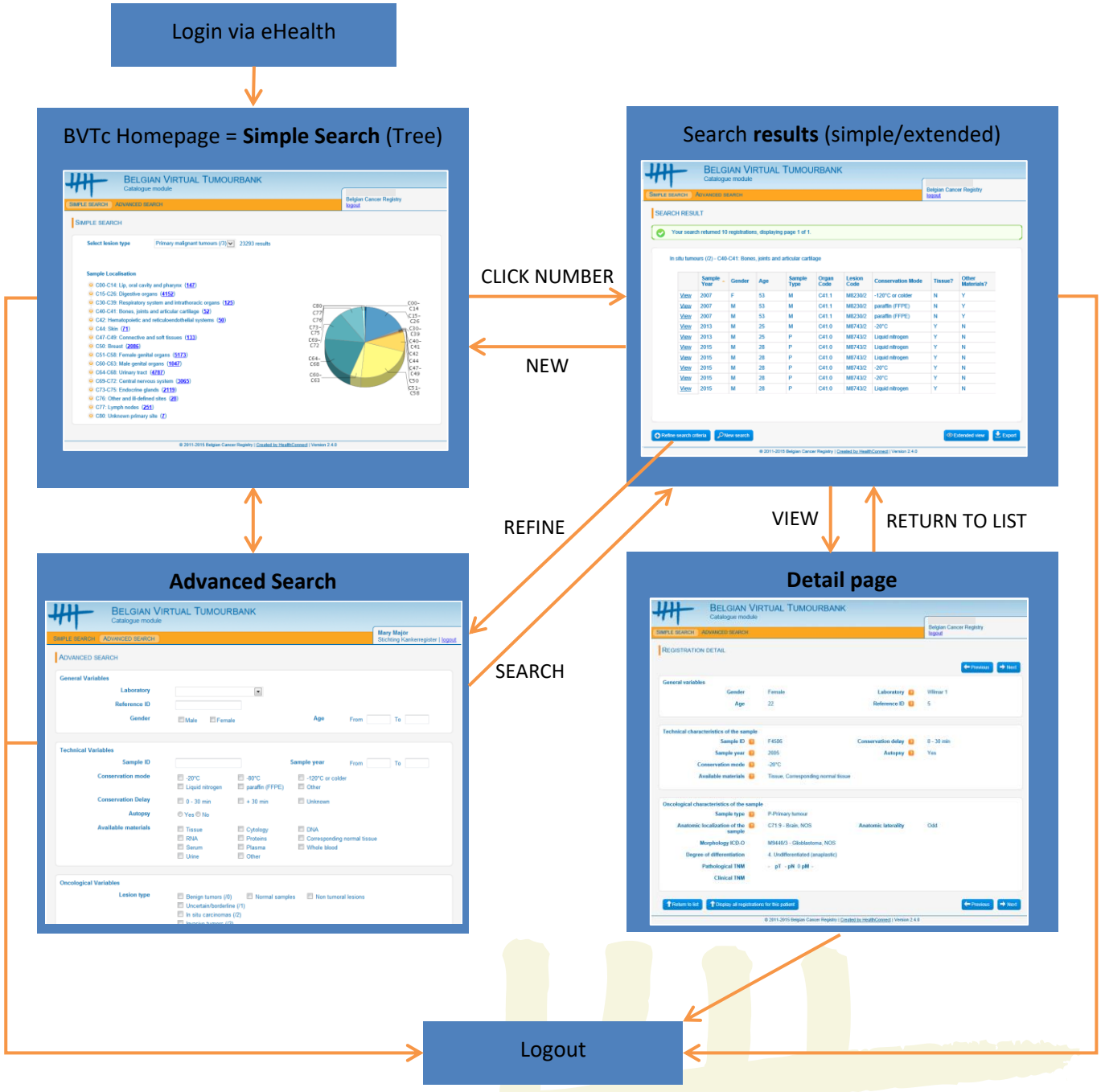
To log out completely from the BVTc-application, you should:

- click on “logout”, in the right upper corner of the application (see screenshot below), and,
- close all pages of the web browser to completely end the eHealth-session.

When the application is not used for 30 minutes, the session will automatically expire and you will be disconnected from the BVTc-application.
Attention! After these 30 minutes the eHealth-session will still be active. To completely end this eHealth-session, all pages of the web browser should be closed. Otherwise, unauthorized persons can obtain access to the BVTc-application in your name on that computer, without having to re-enter your PIN code.

4.1.5. BVTc Navigation

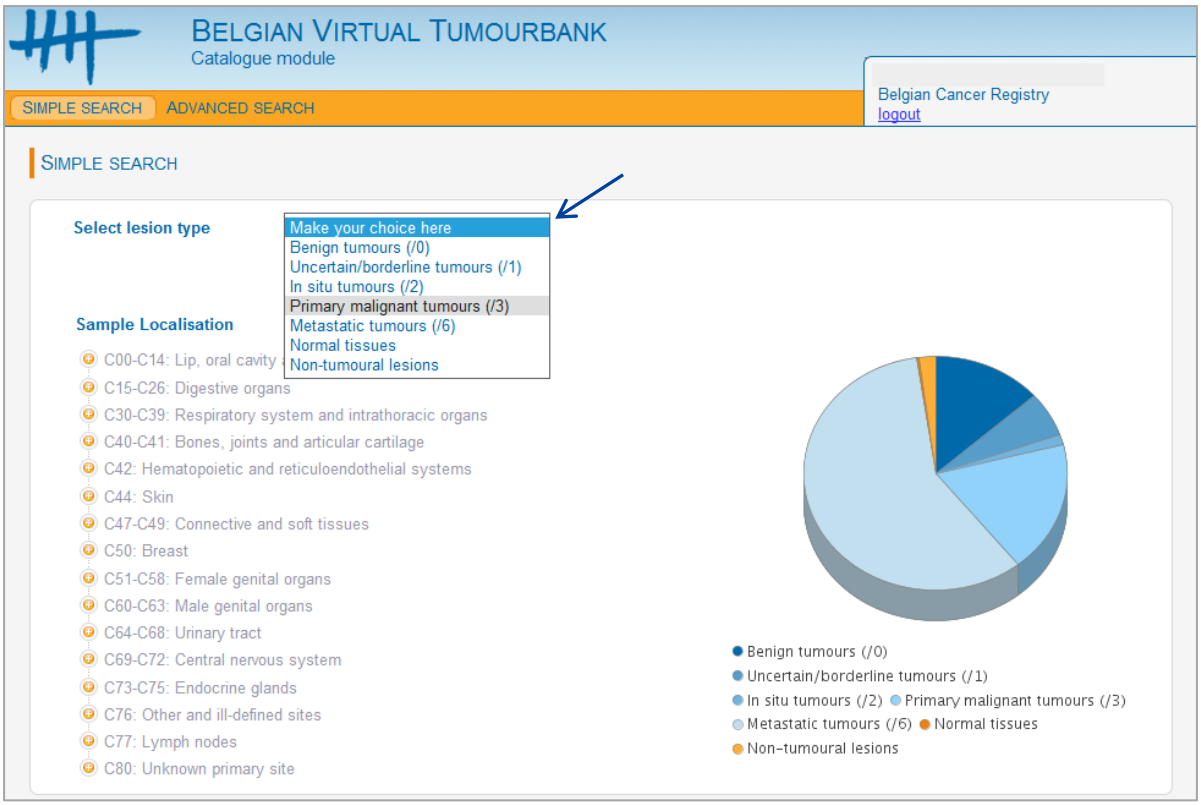
The navigation in the BVTc is quite simple and intuitive: you can perform a quick simple search in the homepage, or you can select other (multiple) criteria in the advanced search section. These two menus are always accessible via the links in the orange toolbar. The results are displayed as a list that can be downloaded to an Excel file.



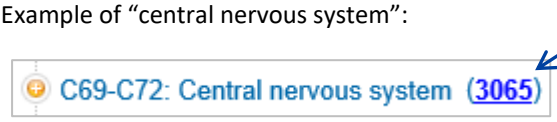
4.2. Simple Search

On the simple search page, you can visualize the distribution of the samples available in the virtual tumourbank, according to the type of lesion and the organ localisation (using ICD-O classification).

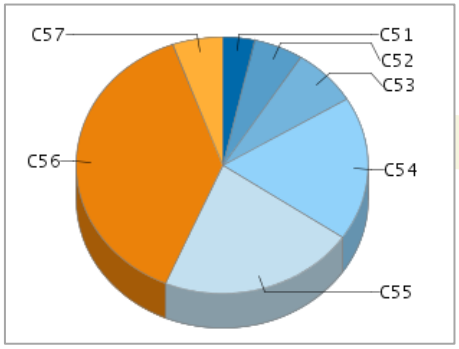
First select the lesion type of interest and then click in the tree structure on a plus sign or category name to expand the different levels (organ category – organ – sub-localisation).



The number of samples available for the given organ category, organ or sub-localisation is displayed between brackets. Simply click on this number to go to the result list and view the individual registrations.
Example of "central nervous system":



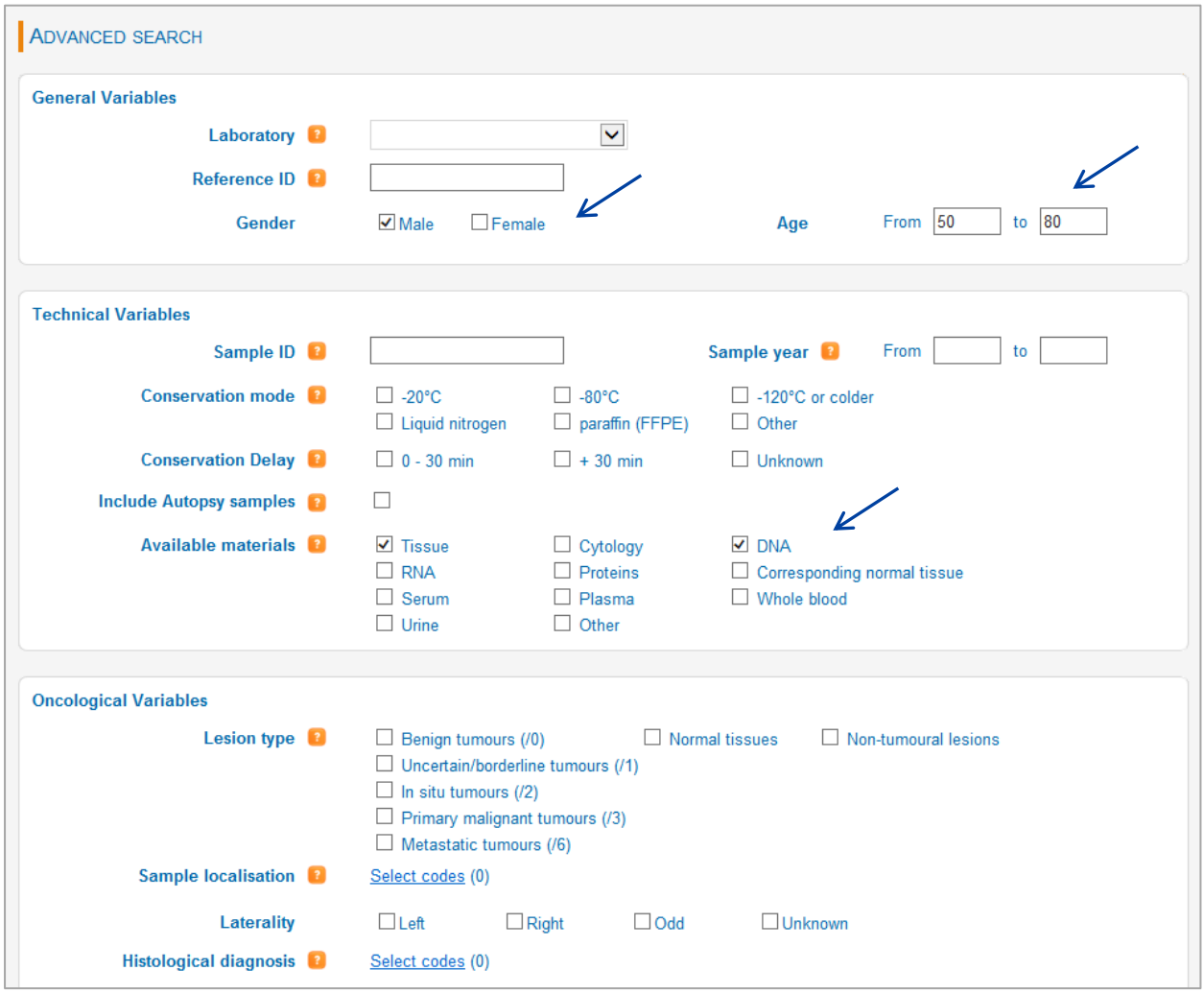
When expanding a certain organ (Cxx) or organ category (Cxx-Cyy) in the tree structure, the pie graph on the right side will show the distribution of the numbers of tumours (i.e. number of registrations without duplicates; see chapter 4.3 for the definition of duplicates) within the selected organ or organ category and according to the different organs (Cxx) or sub-localisations (Cxx.x). Example of the organ category "female genital organs":



4.3. Advanced Search

You can access the advanced search-page by clicking in the orange toolbar on “Advanced search”, or by clicking “Refine search criteria” when you already performed a search action (this last option remembers your previously entered search criteria).

Example of advanced search page with certain search criteria entered:



All the searchable variables are displayed on the screen. Every filled in or selected variable will be integrated in the search action, with:

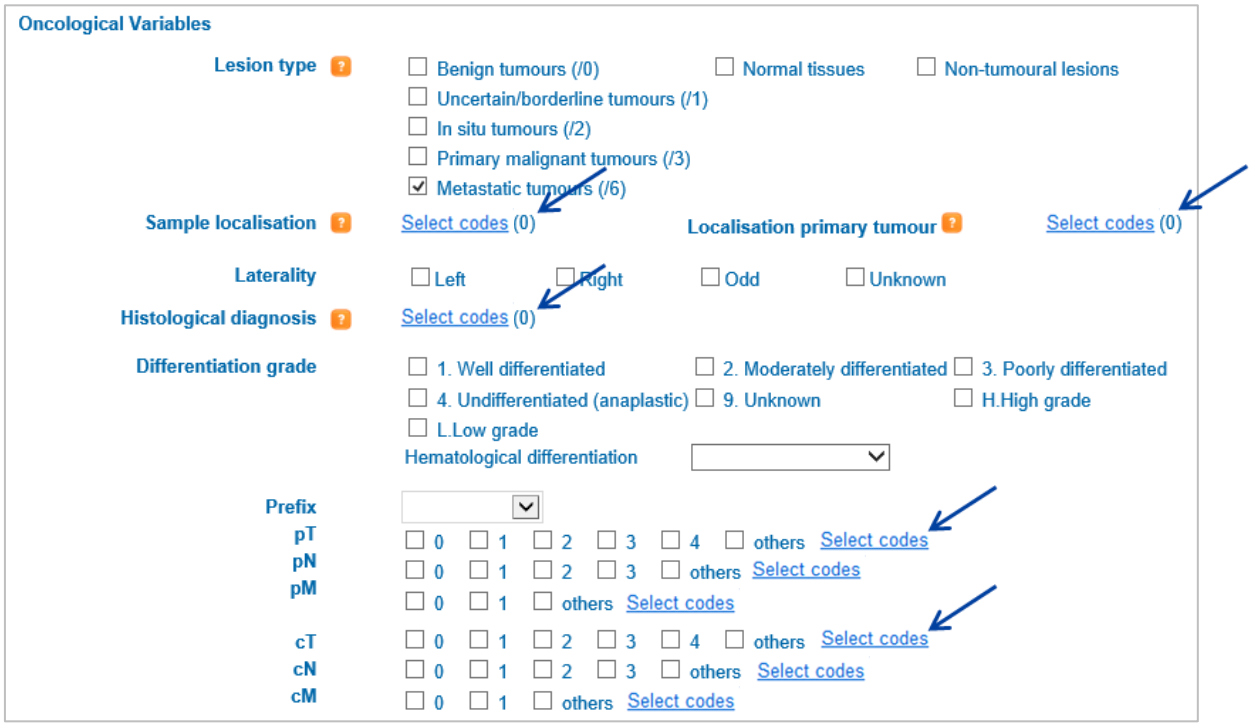
- the “AND”-logic between the parameters
  e.g. "male" AND "from 50 to 80 years" = all males from 50 to 80 years
- and the “OR”-logic between the selected options within a parameter
  e.g. "Tissue" OR "DNA" in Available materials = all tissue samples and all DNA samples

When you included all the parameters of your interest, you can click on the blue “search”-button to perform the search action.

Select codes

On the advanced search-page there are multiple options to select codes (see blue arrows in screenshot below):

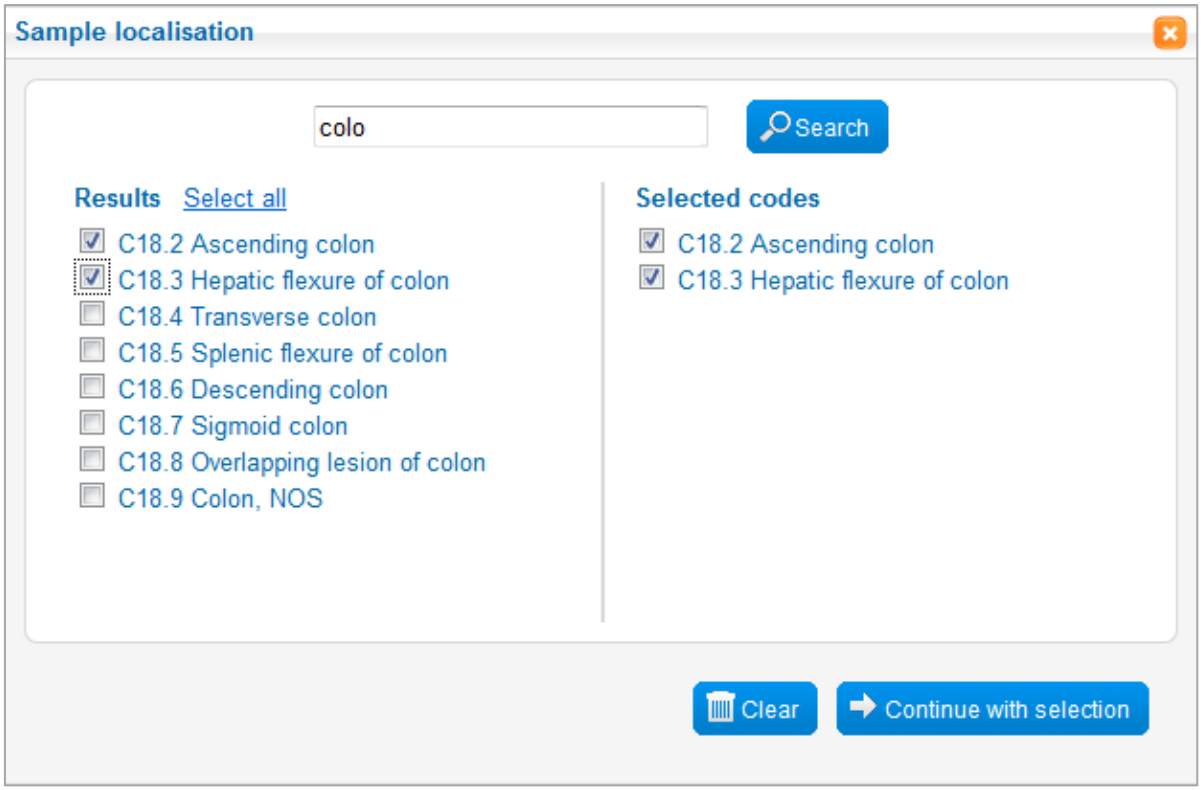
- for the sample localisation,
- for the localisation of the primary tumour (in case you are looking for a sample of a metastasis),
- for the histological diagnosis,
- for the pTNM and
- for the cTNM.



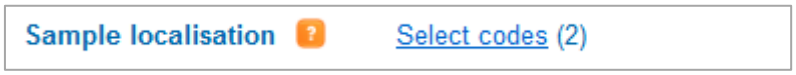
When clicking "Select codes" next to one of these parameters, a pop-up window appears that allows you to search and select the organs, morphologies, pTNM or cTNM of your interest.

- For pTNM and cTNM you should first select one or more checkboxes (0, 1, 2, 3, 4 or "others").
- In the pop-up of sample localisation and histological diagnosis you should first enter a (part of a) description or an (part of an) ICD-O code in the search field, and click on search, before you will be able to select the codes of your interest.

In the example on the next page a search is shown on sample localisation to retrieve colon samples. By entering the first letters (e.g. "*colo*") and clicking the blue "search"-button in the pop-up, the application will give you all possible codes with these letters in the description (in this example the colon). Afterwards the codes of interest can be selected by clicking the checkboxes next to the codes (e.g. ascending colon and hepatic flexure of colon). The selected codes appear in the right list of the pop-up. All selected codes will be included in the search if "continue with selection" is clicked.



After selecting codes in the pop-up and closing the pop-up, the number of selected codes is indicated between brackets next to the parameter ("2" in the example below) on the advanced search-page.



Buttons

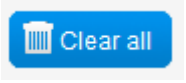
If the search is performed with the checkbox "Hide duplicates" ON, it means that the result list will NOT contain duplicate registrations. Two registrations are duplicates from each other when they are from the same laboratory and if they have the same SSIN (Social Security Identification Number), biopsy number, sample date, sample type and sample localisation.

➔ Choose this option if you want to see only one registration per tumour.

If the search is performed with the checkbox "Hide duplicates" OFF, it means that the result list WILL contain duplicate registrations.

➔ Choose this option if you do not mind to see multiple registrations from the same tumour.

If you click the "Clear all"-button, at the bottom of the advance search-page, all filled in search criteria will be erased to allow you to start a completely new advanced search.



Search tips

- Make sure that the lesion type and the selected behaviour in the pop-up for histological diagnosis are compatible. E.g. lesion type “Primary malignant tumours /3” + Mxxxx/2 = not possible (zero results will be shown in the result list).
- When the lesion type “metastatic tumours (/6)” is selected, an extra search parameter appears in the advanced search page: “localisation of the primary tumour”.
- The behaviour and differentiation grade mentioned in the BVTc corresponds with the behaviour and differentiation grade of the tumour and not always with the behaviour and differentiation grade present in only a part of the tumour present in the sample. An evaluation of each sample can be done by the local tumourbank for requested samples if needed by the researcher.
- If you are looking for tumour tissue with corresponding normal tissue, do NOT search on lesion type “normal tissues”, but search on available materials “corresponding normal tissue”.

4.4. Viewing search results

4.4.1. Result list

At first, the search results will always be displayed in a simple result list (limited number of columns; without scrollbar).
The total number of registrations and the total number of pages are indicated in the message above the result list, as well as the selected search criteria in case of a simple search.
When the result list contains more than 20 registrations, you can navigate to other pages by clicking the arrows or the page numbers at the bottom of a result list.

You can switch to extended view to see more parameters for the registrations in the result list (horizontal scrollbar at the bottom of the list). Afterwards you can click on “Simple view” to see the result list with fewer columns again.

It is possible to download an Excel version of this result list by clicking on “Export”.

➔ Attention: A result list and an export list are limited to 2000 registrations (i.e. 100 pages). If a search resulted in more than 2000 registrations, it is indicated in the message above the result list and some results will not be shown.

For some parameters, the results in the list can be sorted by clicking once (A-Z) or twice (Z-A) on the title of that column (not possible for all parameters in the result list).

You can click on “View” on the left side of each registration to view the detail page of a specific registration (see chapter 4.4.2).

From this selection, you can also refine your search with other or additional criteria or start a new search.

When you move your cursor to a specific code or abbreviation in the result list (a sample type, an organ code or a lesion code), the description of that code will be displayed above the cursor (i.e. a mouse-over).

Example of a result list in simple view in the BVTc-application, sorted on organ code (indicated by the small orange triangle):

SEARCH RESULT

Your search returned 132 registrations, displaying page 1 of 7.

Primary malignant tumours (/3) - C47-C49: Connective and soft tissues

	Sample Year	Gender	Age	Sample Type	Organ Code	Lesion Code	Conservation Mode	Tissue?	Other Materials?
View	2010	F	45	P	C47.2	M9540/3	-80°C	Y	N
View	2011	M	63	P	C48.1	M8850/3	-80°C,paraffin (FFPE)	Y	N
View	2011	M	63	P	C48.1	M8850/3	-80°C,paraffin (FFPE)	Y	N
View	2011	M	63	P	C48.1	M8850/3	-80°C,paraffin (FFPE)	Y	N
View	2010	M	45	P	C48.1	M8812/3	-80°C	Y	N
View	2010	M	45	P	C48.1	M9687/3	-80°C	Y	N
View	2009	F	63	P	C48.2	M8020/3	-80°C	Y	N
View	2008	F	50	P	C48.2	M8310/3	-80°C	Y	N
View	2010	M	45	P	C48.8	M9500/3	-80°C	Y	N
View	2009	F	63	P	C49.0	M9380/3	-80°C	Y	N
View	2011	M	55	P	C49.0	M8070/3	-80°C	Y	N
View	2008	M	50	P	C49.0	M8004/3	-80°C	Y	N
View	2007	F	61	P	C49.0	M8833/3	-80°C,paraffin (FFPE)	Y	N
View	2007	M	61	P	C49.0	M8000/3	-80°C,paraffin (FFPE)	Y	Y
View	2008	M	50	P	C49.1	M8800/3	-80°C	Y	Y
View	2008	M	50	P	C49.1	M8800/3	-80°C,paraffin (FFPE)	Y	Y
View	2008	F	50	P	C49.1	M8900/3	-80°C	Y	Y
View	2009	M	61	P	C49.1	M8800/3	-80°C	Y	N
View	2009	M	61	P	C49.1	M8800/3	-80°C	Y	N
View	2010	M	45	P	C49.1	M9044/3	-80°C	Y	N

1 2 3 4

Refine search criteria | New search | Extended view | Export

4.4.2. Detail page

The detail page displays all available data of one registration in a coded form (i.e. without identifying information to ensure privacy of individuals). From this page you can navigate from one registration to another (“Previous” - “Next”) and you can return to the search result list.

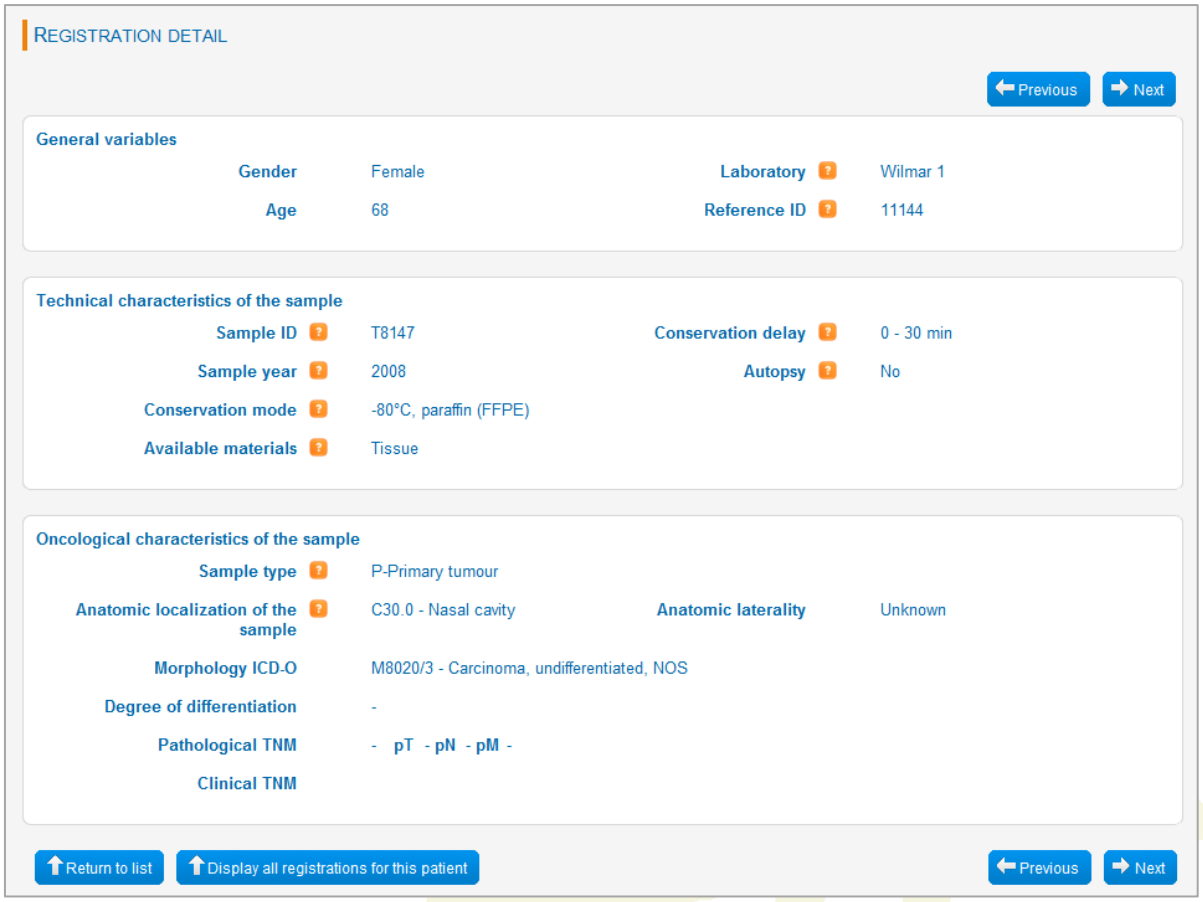
If you click on “Display all registrations for this patient”, you can see all available registrations from the same donor.

By moving your mouse to an orange icon with a question mark ?, a tooltip with more information about the corresponding parameter will pop-up.

A hyphen “-” is shown for variables that have not been filled in.

Attention: Letters with accents and special signs written in the free fields (e.g. other conservation mode or other available material) will sometimes appear as a question mark (“?”) in the BVT applications.

Example of a detail page of a fictive registration in the BVTc-application:



4.5. Additional step of data quality control before sample request?

To receive access to the samples itself, please follow the next steps:

1. Search in the BVTc the samples of your interest. Note down the **reference IDs** (= unique number within the BVTc) and the **sample IDs** of these samples.

2. If you are interested in an additional quality control on the data, send a mail to the biobank team of the BCR with the list of reference IDs of the sample of your interest. If not, proceed with step 4.

3. The biobank team of the BCR runs **an additional step of data quality control on the information of the samples** selected for your research purposes **(through linkage with available cancer registry data).** → Note: this is not possible for benign tumours and very recent tumours.

4. Contact the biobank coordinator(s) or biobank manager(s) of the local biobank(s) hosting your samples of interest. The biobank team of the BCR will be pleased to provide you the contact information (i.e. e-mail address(es) and/or telephone number(s)) of the local biobank coordinator(s) or biobank manager(s). Communication with the local tumourbank about the samples should be done with the **Sample ID** (=unique number within the local tumourbank). **The decision about sample exchange is up to the local tumourbank and details about the samples should be discussed with the biobank coordinator.**

5. Each local tumourbank has its own procedures concerning the transfer of samples (e.g. human material transfer agreement (HMTA)). Additional documents or information might be requested by the local tumourbank.

5. APPENDIX: The different search variables in the BVTc

Variable Name	Type	Possible values		Description
General variables				
Laboratory	dropdown list			The laboratory (local tumourbank) that physically stores the sample(s)
Reference ID	text box (numeric)			Unique code for this registration in the Belgian Virtual Tumourbank; to be used during communications between the researcher and the Belgian Cancer Registry
Gender	checkboxes	Male	M	Gender of the patient
		Female	F	
Age	range			Age of the patient at the time of resection. When 1 or 2 values are filled in, a range of ages will be shown.
Technical variables				
Sample ID	text box			Unique and non-identifying code of the sample within the local tumourbank; to be used during communications between the researcher and the local tumourbanks
Sample Year	range			Year at which the sample was removed from the patient. When 1 or 2 values are filled in, a range of sample years will be shown.
Conservation mode	checkboxes	-20°C		Indicates the conservation mode used for the tumour tissue sample in the local tumourbank
		-80°C		
		-120°C or colder		
		Liquid nitrogen		
		Paraffin (FFPE)		
		Other		
Conservation delay	checkboxes	0 - 30 min		Indicates the time elapsed between the removal from the patient and the fixation of the tumour tissue sample
		+30 min		
		Unknown		
Include autopsy samples	checkbox	(checkbox on or off)		Indicates whether the search should include autopsy samples or not
Available materials	checkboxes	Tissue		Indicates which various types of materials are available in the tumourbank, that correspond to the tumour tissue sample
		Cytology		
		DNA		
		RNA		
		Proteins		
		Corresponding normal tissue		
		Serum		
		Plasma		
		Whole blood		
		Urine		
		Other		

Variable Name	Control type	Possible values		Description
Oncological variables				
Lesion type	checkboxes	Benign tumours	/0	Indicates the lesion type of the sample in the local tumourbank
		Uncertain/borderline tumours	/1	
		In situ tumours	/2	
		Primary malignant tumours	/3	
		Metastatic tumours	/6	
		(Normal Tissues)		
		(Non-tumoural lesions)		
Sample localisation	pop-up window	ICD-O code lists (see also chapter 3.4)		Anatomic localisation of the sampled specimen. In case of a metastasis, this localisation is different from the primary tumour localisation
Localisation primary tumour if meta	pop-up window	ICD-O code lists (see also chapter 3.4)		Anatomic localisation of the primary tumour in case the sample was taken from the metastasis; appears only when lesion type “metastatic tumours” is selected
Laterality	checkboxes	Left		Anatomic side from which the sample was taken
		Right		
		Odd		
		Unknown		
Histological diagnosis	pop-up window	ICD-O code lists		Morphology and behaviour of the sampled tumour
Differentiation grade	checkboxes + dropdown list	Well differentiated	1	Tumour differentiation: 1-4 or high grade or low grade for most tumours; 5-8 for haematological tumours. Be aware, particularly in case of haematological diseases, that the differentiation grade is not always filled in by the tumourbank.
		Moderately differentiated	2	
		Poorly differentiated	3	
		Undifferentiated (anaplastic)	4	
		T-cell	5	
		B-cell	6	
		Null-cell	7	
		NK-cell	8	
		Unknown	9	
		High grade	H	
		Low grade	L	

Variable Name	Control type	Possible values		Description
Oncological variables (continued)				
Prefix	dropdown list	pTNM during or after neoadjuvant therapy	y	
		pTNM of a recurrent tumour	r	
		pTNM determined at autopsy	a	
pT	checkboxes + pop-up window	TNM code lists (see also chapter 3.4)		Pathological TNM. The selected digit(s) represents tumours with a category starting with this digit. More precise codes can be selected in the pop-up window.
pN				
pM				
cT	checkboxes + pop-up window	TNM code lists (see also chapter 3.4)		Clinical TNM. The selected digit(s) represents tumours with a category starting with this digit. More precise codes can be selected in the pop-up window.
cN				
cM				