CHANGE-MRI

CTEPH DIAGNOSIS EUROPE

OpenClinica

User Manual

Content

1 Log in to OpenClinica

Access to OpenClinica is provided via a web browser (Mozilla Firefox or Microsoft Internet Explorer)

via the webpage: www.change-mri.de

(then klick on “zur Datenbank”/“database an then „login“)

Or using directly the following link:

https://simpc2.mh-hannover.de:8443/OpenClinica/MainMenu

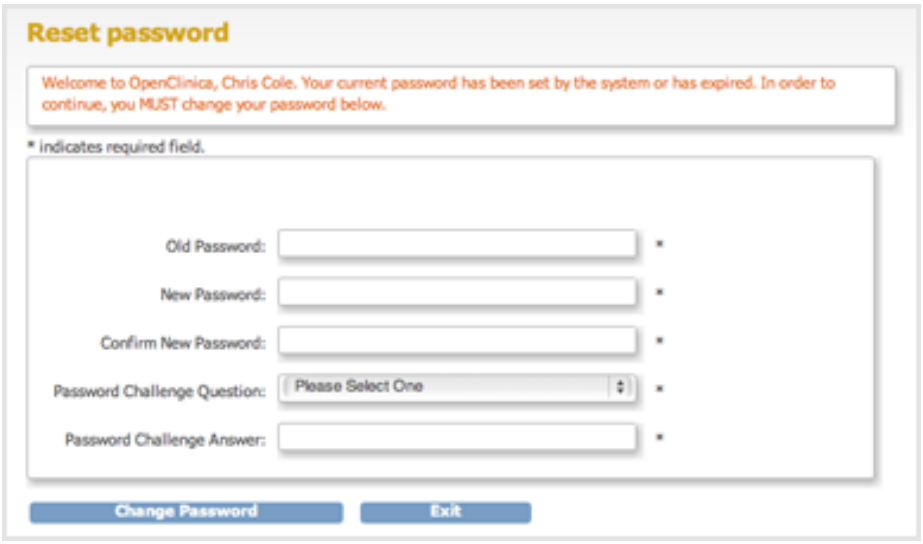
Browser configuration:

- JavaScript must be enabled
- Pop-up blockers must be disabled

Provide user name and password you received via e-mail and click Login.

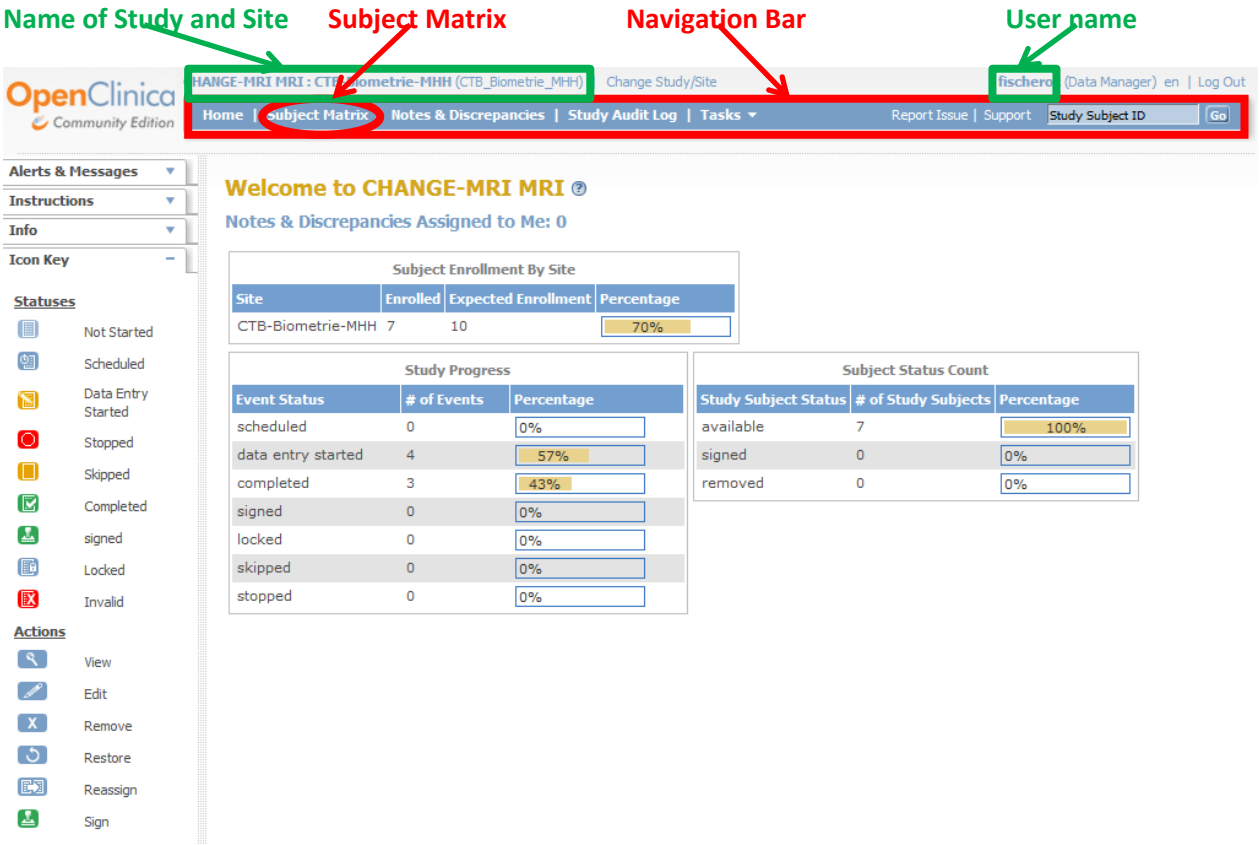
Reset password

For security purposes you have to reset your password at first log in. Your new password must be at least eight characters long.



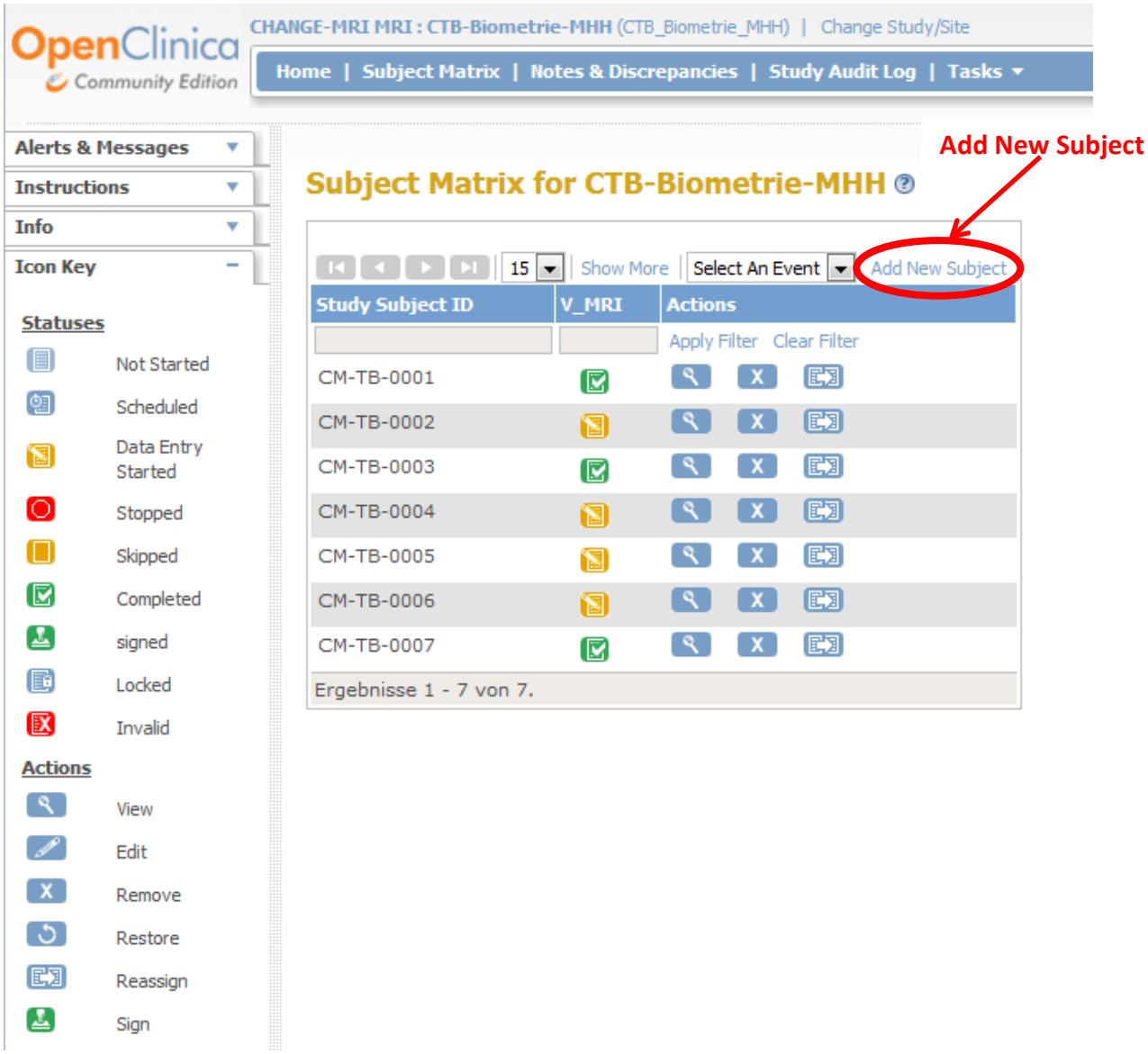
2 OpenClinica homepage

The OpenClinica homepage is the main page for the current study or site. It is displayed when you log in or when you click "**Home"** in the navigation bar. The navigation bar provides access to the main features in OpenClinica. The page contains your user name, the study name, name of the study site and a summary of subjects entered by your site. To manage subjects click "**Subject Matrix**".



3 Subject Matrix

The "**Subject Matrix**" is a table with event information for all subjects. You can view, enter, and change information.



3.1 Add a new subject from Subject Matrix

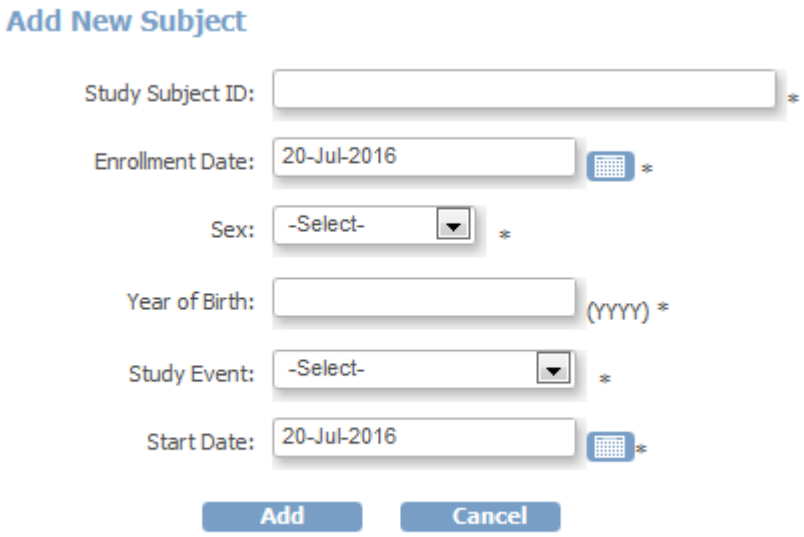
To add a new subject and schedule the first event follow steps below:

1. Click "**Add New Subject"** link in the "**Subject Matrix**".
   The "**Add New Subject**" page opens. Complete the information on the page as described in the following steps. Some of the information might be optional, an asterisk (*) indicates a mandatory field.

2. Enter the "**Study Subject ID"**.

3. Enter "**Enrollment Date"** in the specified format, or click the calendar icon to select it. (Date of enrollment = Date of signed informed consent).

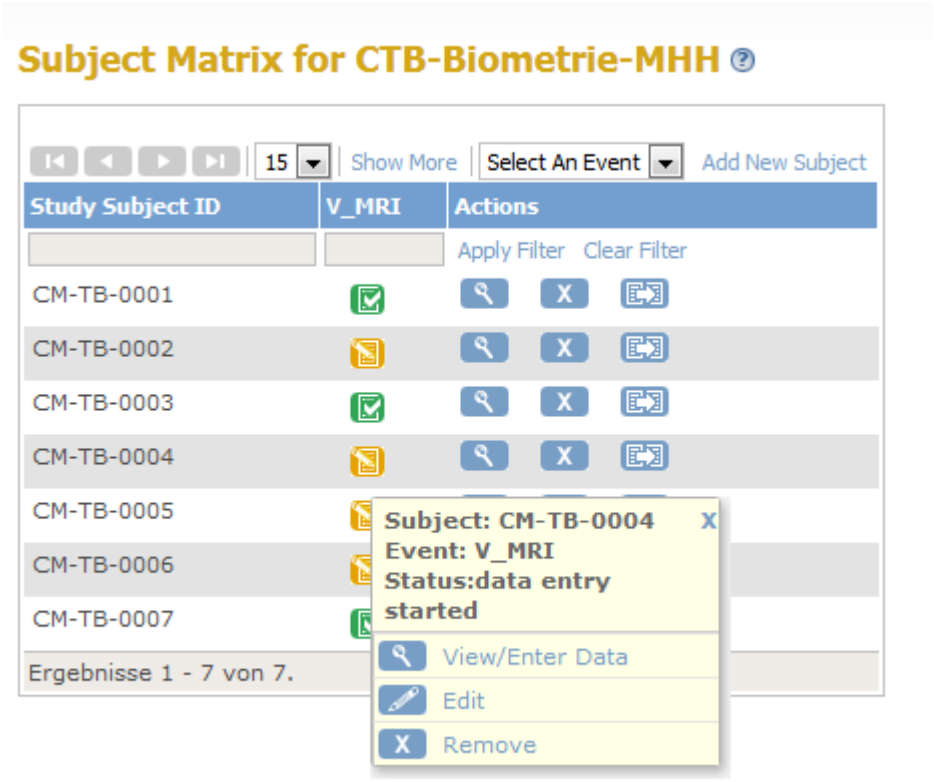
4. Select „**Sex“**.
5. Enter “**Year of Birth”**.
6. Select first “**Study Event”** from the drop-down list.
7. Enter “**Start Date”** for the event, or click the calendar icon to select it.
   (Start Date = e.g. date of MRI, SPECT…)
8. Click “**Add”** to create the new subject or click “**Cancel**” to discard entered information.



3.2 View and enter event data in Subject Matrix

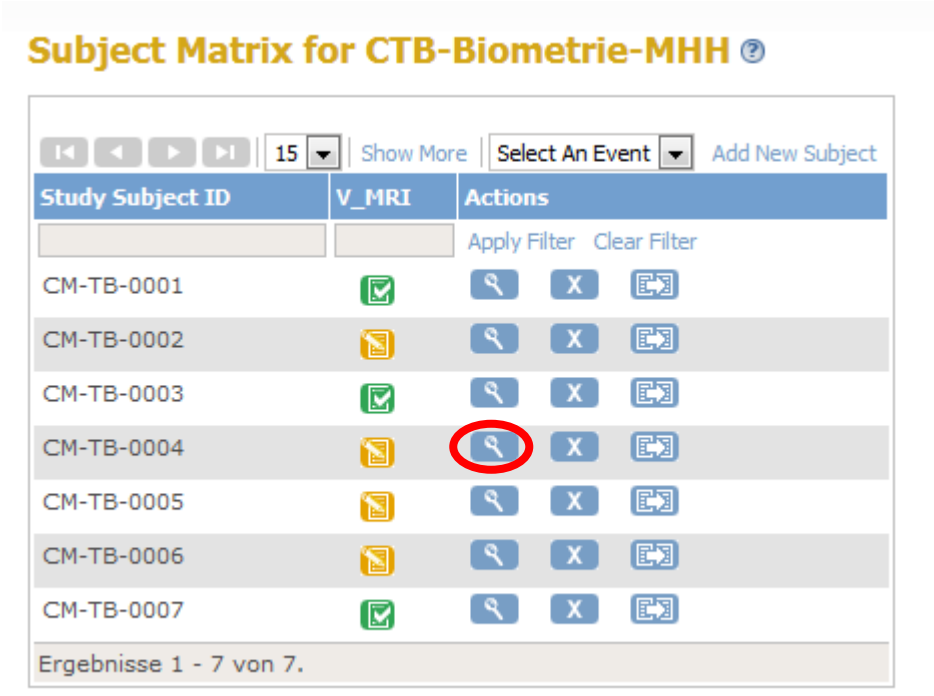
Each cell in the “**Subject Matrix”** contains a status icon of the event: green – data entry complete; yellow - data entry incomplete; blue – event not scheduled. In the “**Subject Matrix**” you are able to perform following actions depending on your role and access rights for the study: “**Schedule**”, “**View**”, “**Enter Data**”, “**Edit**”, “**Remove**”, or “**Add Another Occurrence**”. Click on the status icon to choose the action.

Subject Matrix after Clicking the Icon in the V_MRI-Column for Subject ID CM-TB-0004:

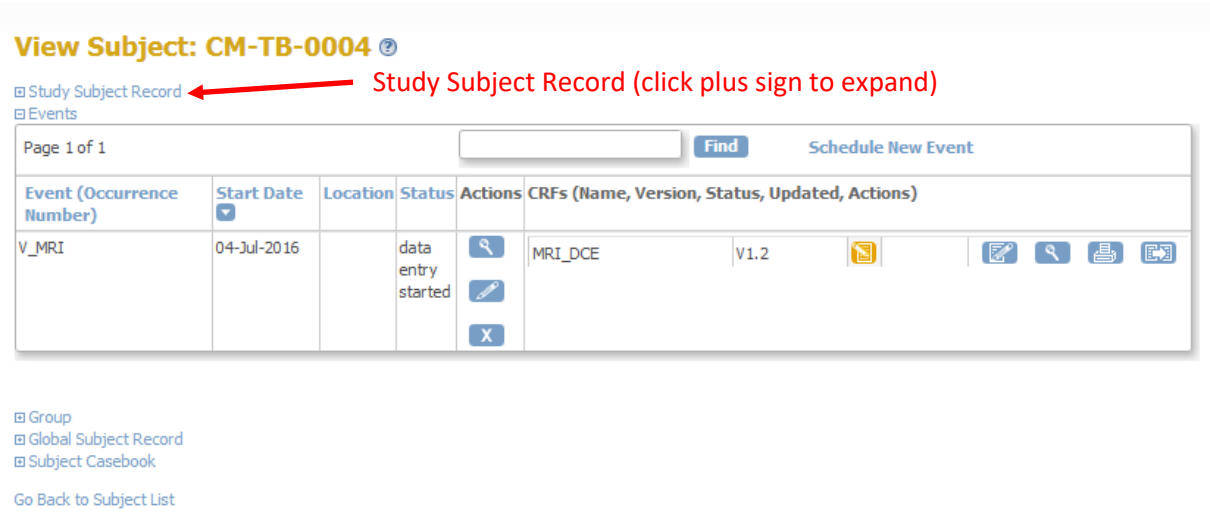


3.3 View and edit details for a subject in subject casebook

To view detailed information for a subject, click the view icon  in the "**Actions**" column.

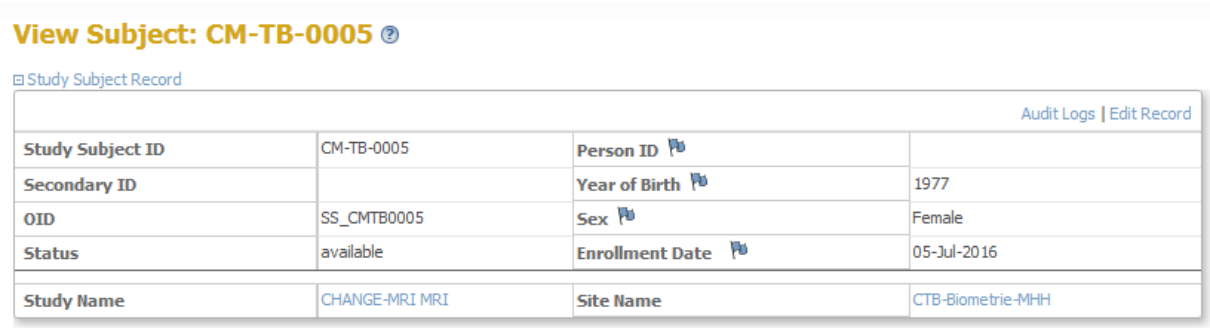


The subject casebook opens with the sections "**Study Subject Record**" and "**Events**". To show or hide a section, click plus or minus. The event section is shown by default.



Study subject record section

The "**Study Subject Record**" section provides overall information about the subject. To make changes for the study subject, click "**Edit Record"**, which opens the "**Update Study Subject Details**" page.



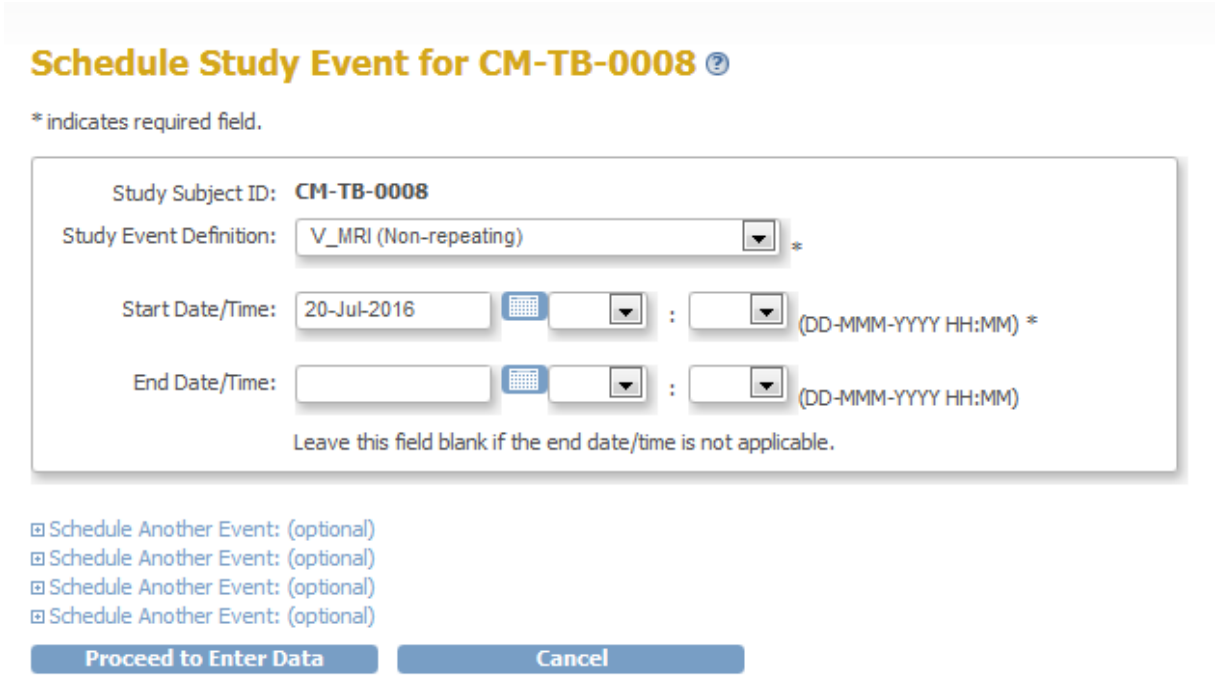
4 Study events

In OpenClinica study events are associated with type, date(s), status, and a package of case report forms (CRFs).

4.1 Schedule a study event

1. 1. To create a new event click "**Schedule New Event**" in the event section.

2. Enter information in the "**Schedule Study Event**" page. Time boxes can be left blank. As each event in the Change MRI study is performed only in one day and no events are planned to be split please leave the "**End Date**" boxes empty.

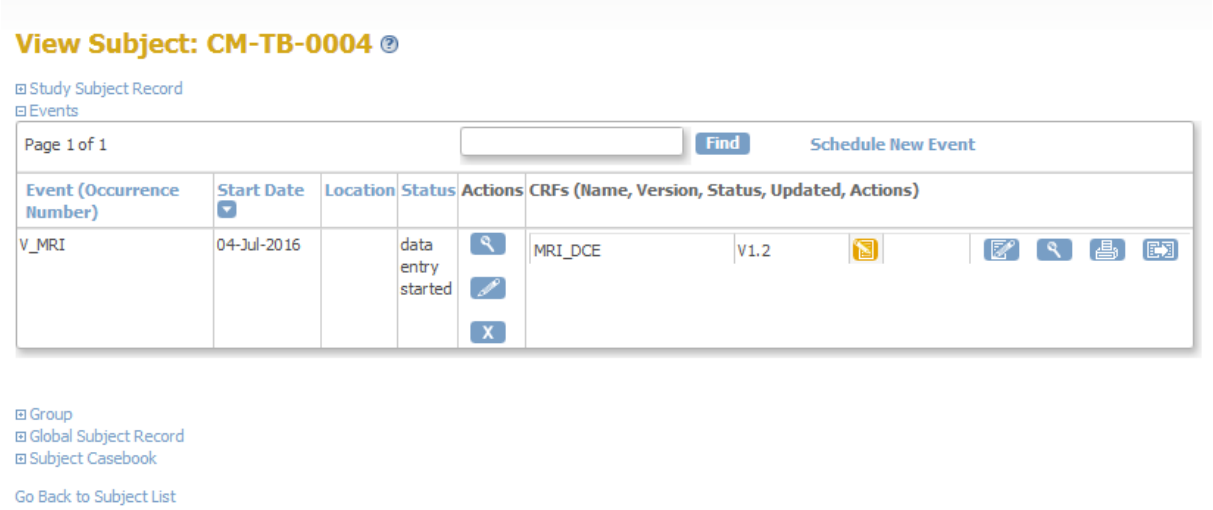


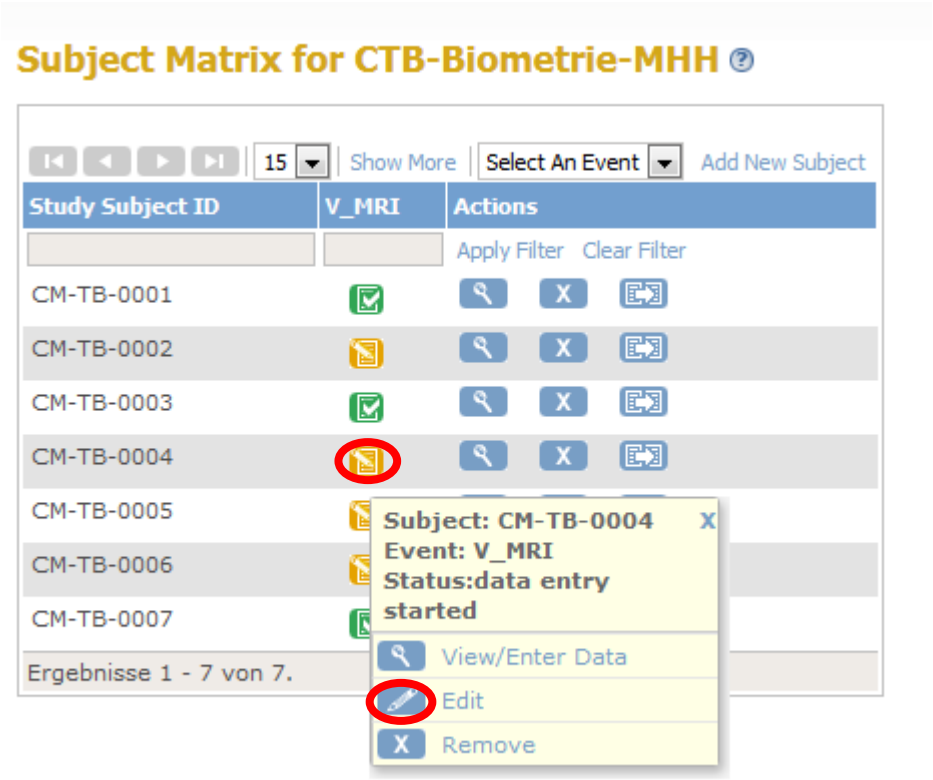
3. After completion of scheduling information you can schedule another event or select the option to enter data.

4.2 Update study events

You can update information for an event, such as the date or status:

1. In the "**Subject Matrix**", click the respective **event-item** and the "**Edit"** icon.



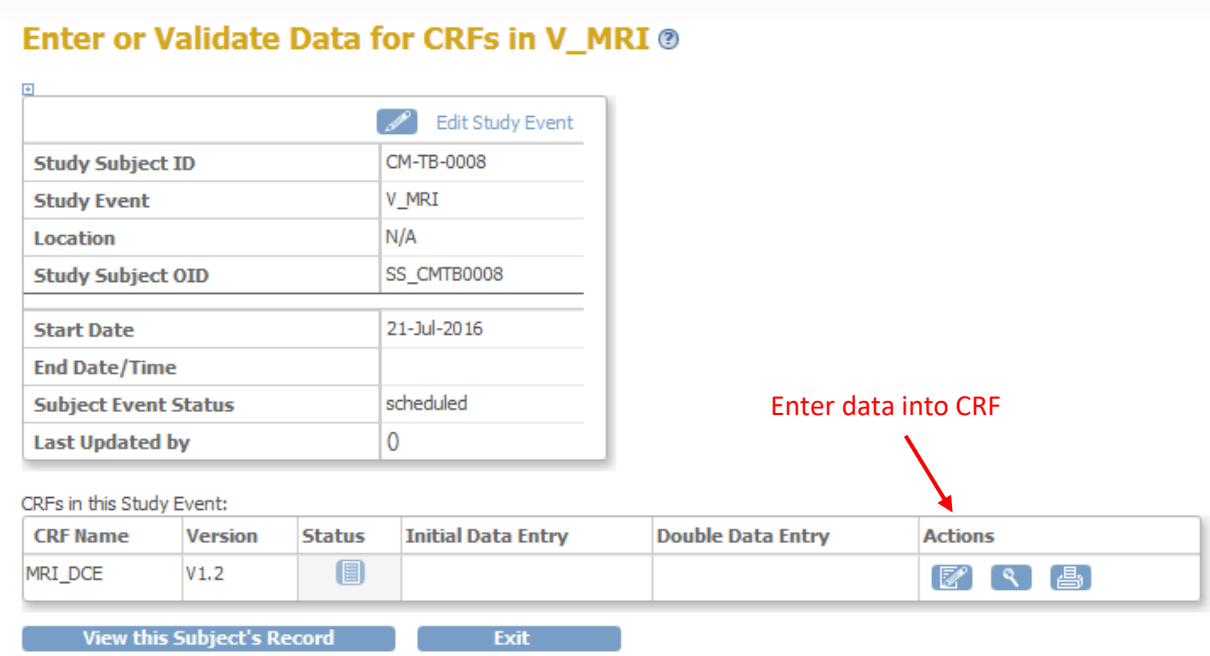


2. The "**Update Study Event**" page opens. Change the date or other information.
3. Click "**Submit Changes**". The "**View Subject**" page opens, showing the updated information for the event.

5 Enter data into a CRF

To view and enter data of a study event, click "**View/Enter Data"** in the "**Subject Matrix**" (remember that events have to be scheduled first).

In the following "**Enter or Validate Data for CRFs**" page event information is provided in a table of all CRFs in that study event.

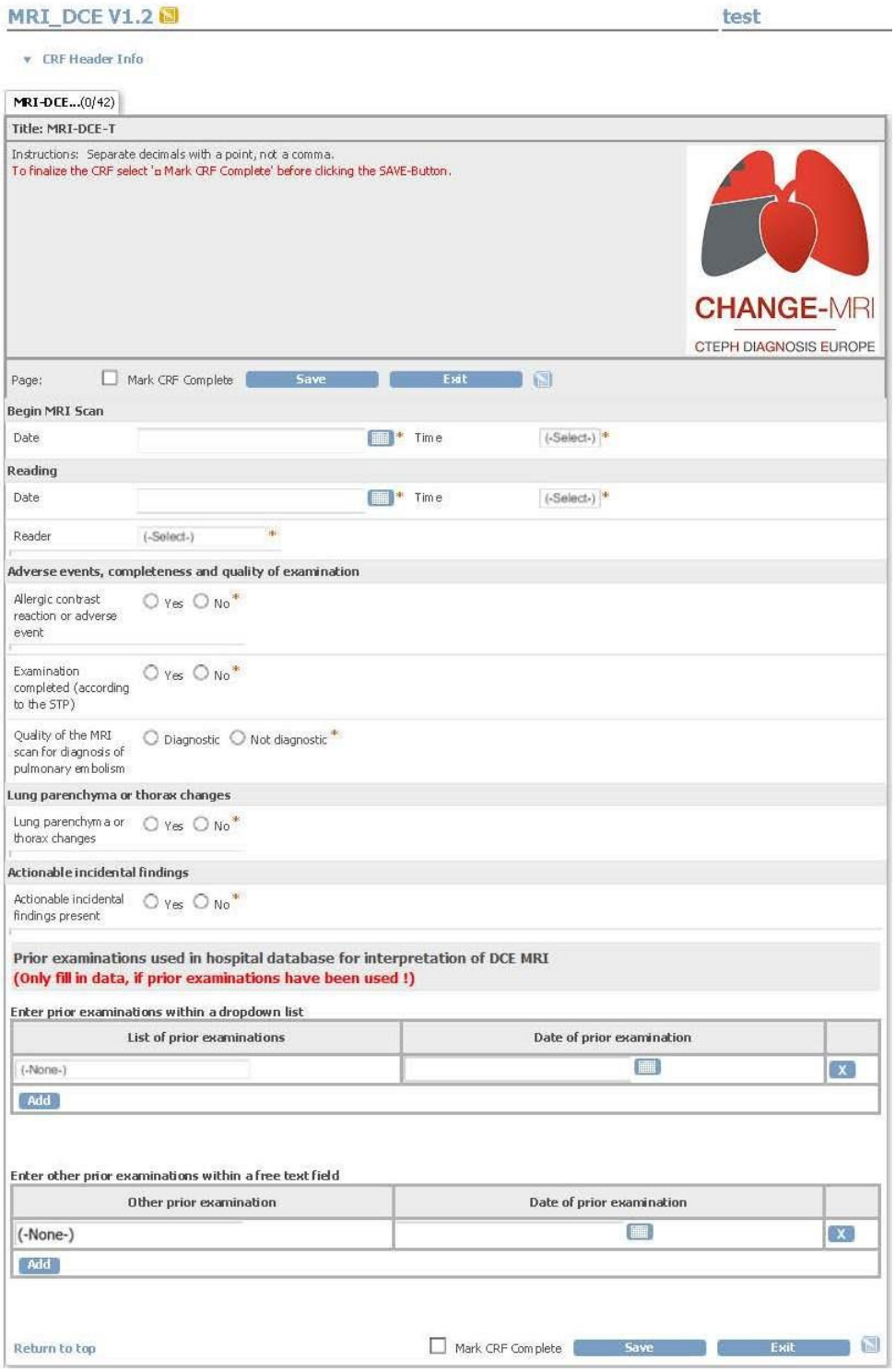


There are 3 different eCRF subtypes for the chage MRI study:

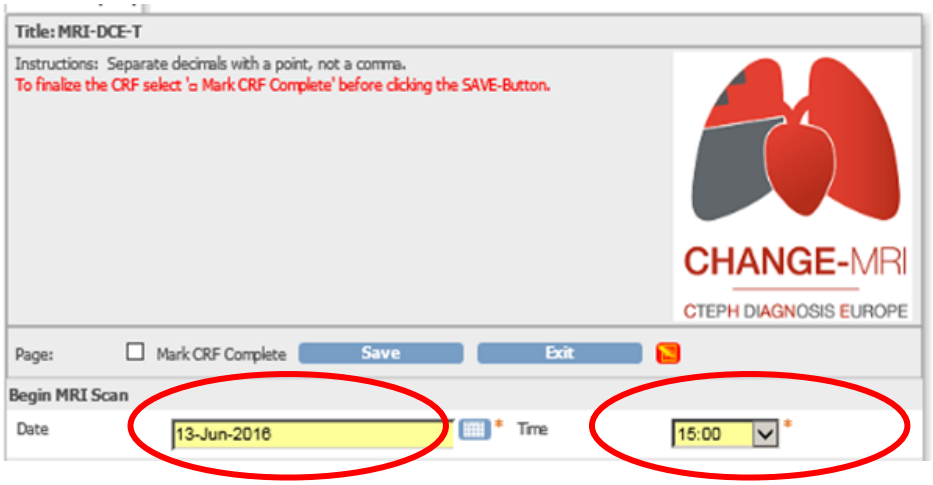
1. **MRI**
2. **SPECT**
3. **Gold standard**

5.1 MRI eCRF – Step-by-step instructions

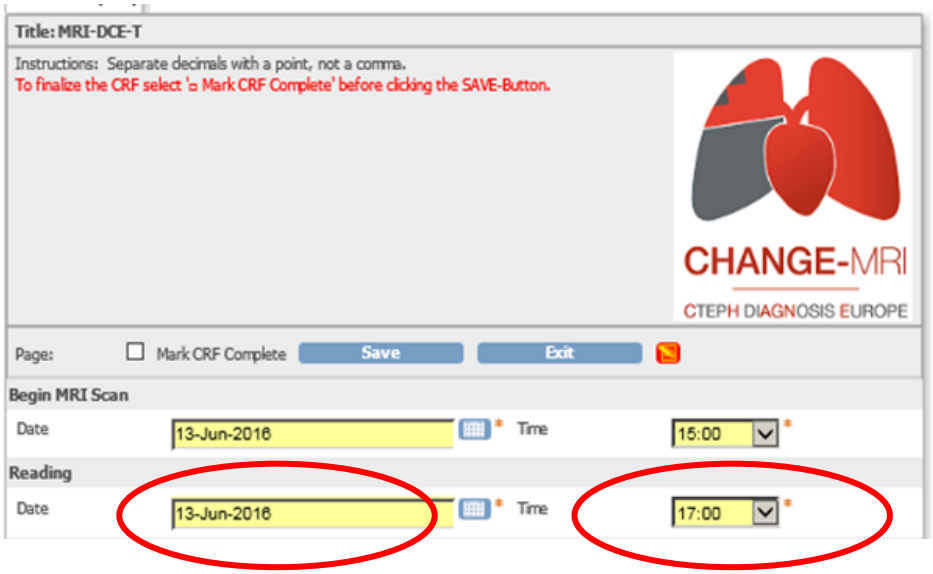
1. After clicking the **“Enter Data” icon** in the actions column for that CRF, the MRI CRF opens.



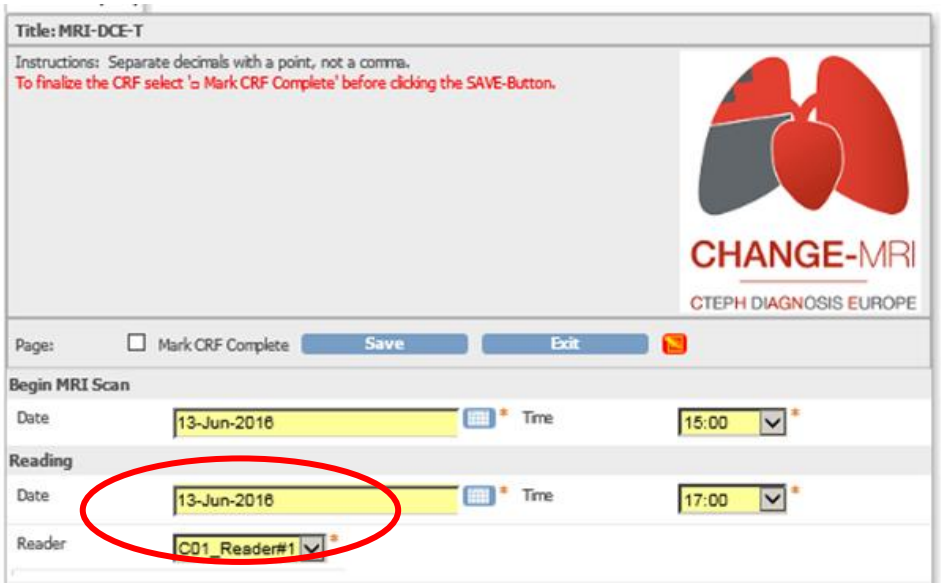
2. Select study date and time of imaging from the drop-down menu.



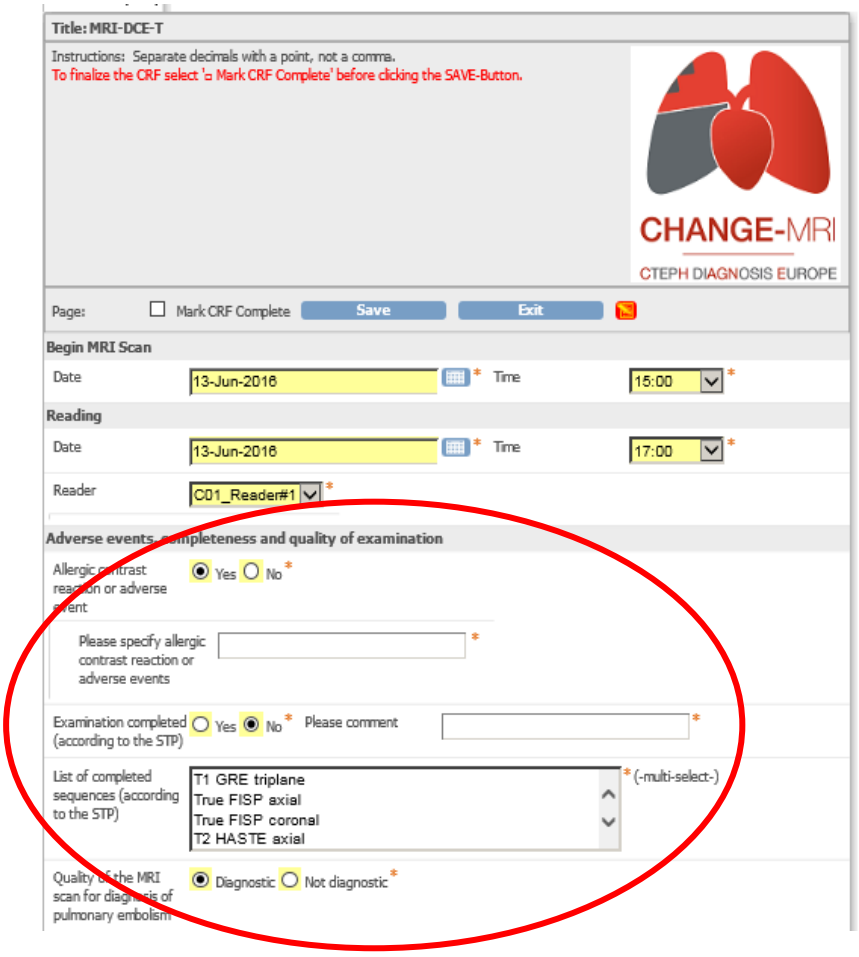
3. Select date of reading and time of reading from the drop-down menu.



4. Select the name of reader, or enter your name, if necessary.

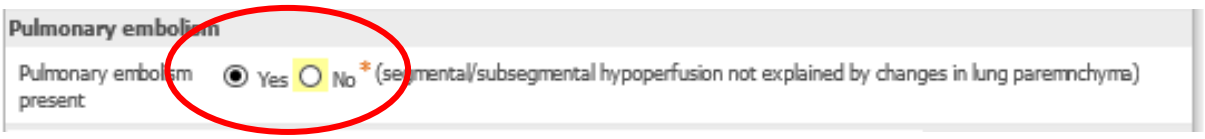


5. Answer all items concerning adverse events, completeness and quality of examinations.



- Allergic contrast reaction or adverse events related to administration of contrast material?
- Examination complete? (According to the study protocol)
- Quality of Imamges (Diagnostic vs. non.diagnostic)

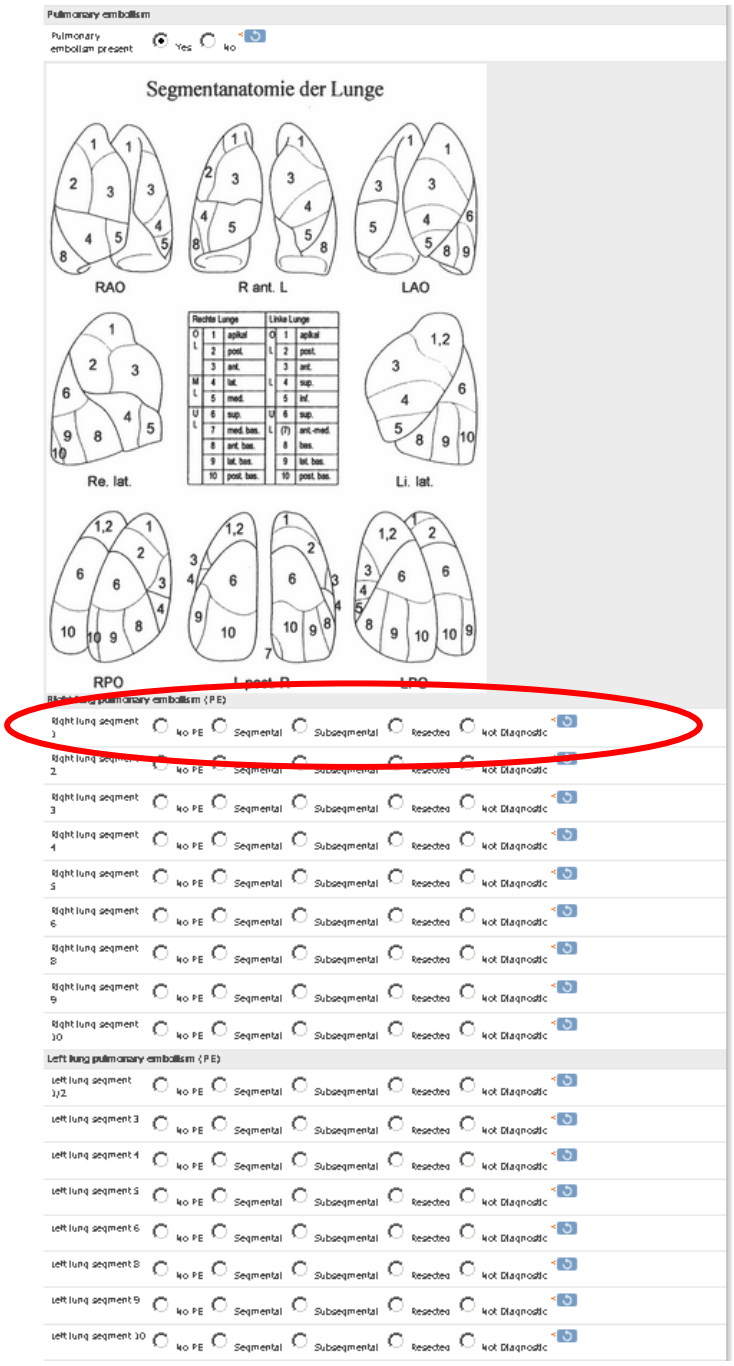
6. Pulmonary embolism present? (Do net select “yes” if perfusion defects seen on the scan are not caused by emboli)



If you select “yes”, an illustration of the segmental anatomy of the lungs will appear, and you will have to decide for each segment if pulmonary embolism is

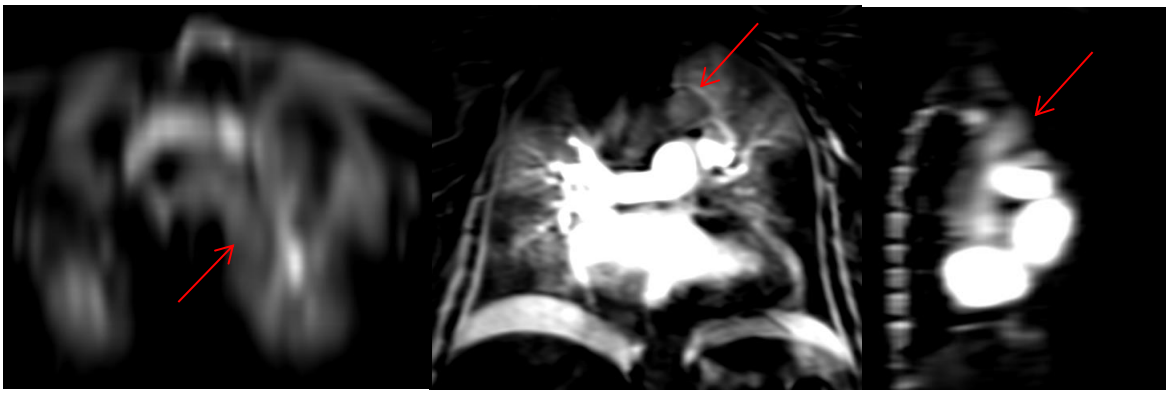
- Absent (“no”)
- Segmental pulmonary embolism

- Subsegmental pulmonary embolism
- Or if the segment has been resected previously.
- Or if the study is non diagnostic (segment cannot be scored, e.g. because of artifacts)

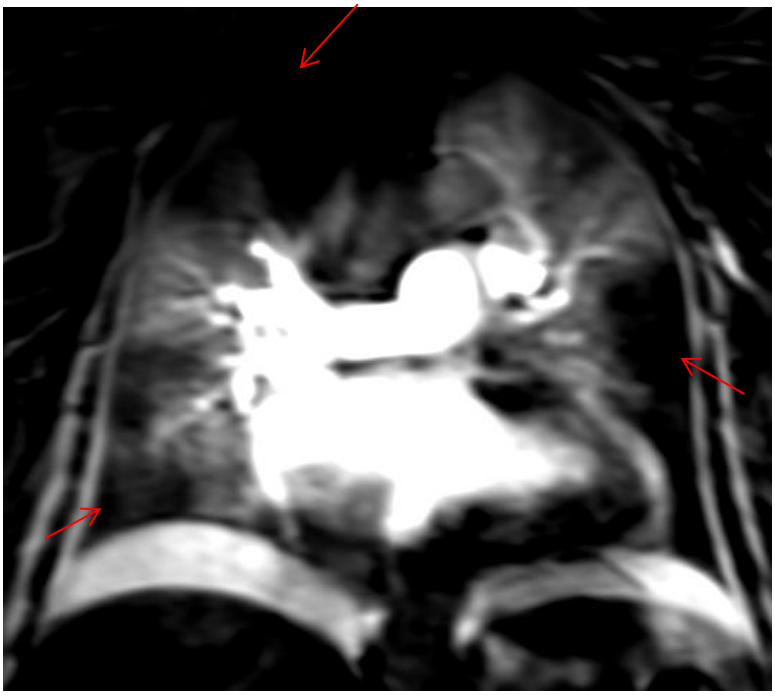


Suggestions how to read dynamic contrast enhanced MRI

- Read in 3D at maximum intensity projection (**15mm slices MIP**).
- Use **subtracted** images
- Choose the best frame/parenchymal phase with **early contrast in aorta**

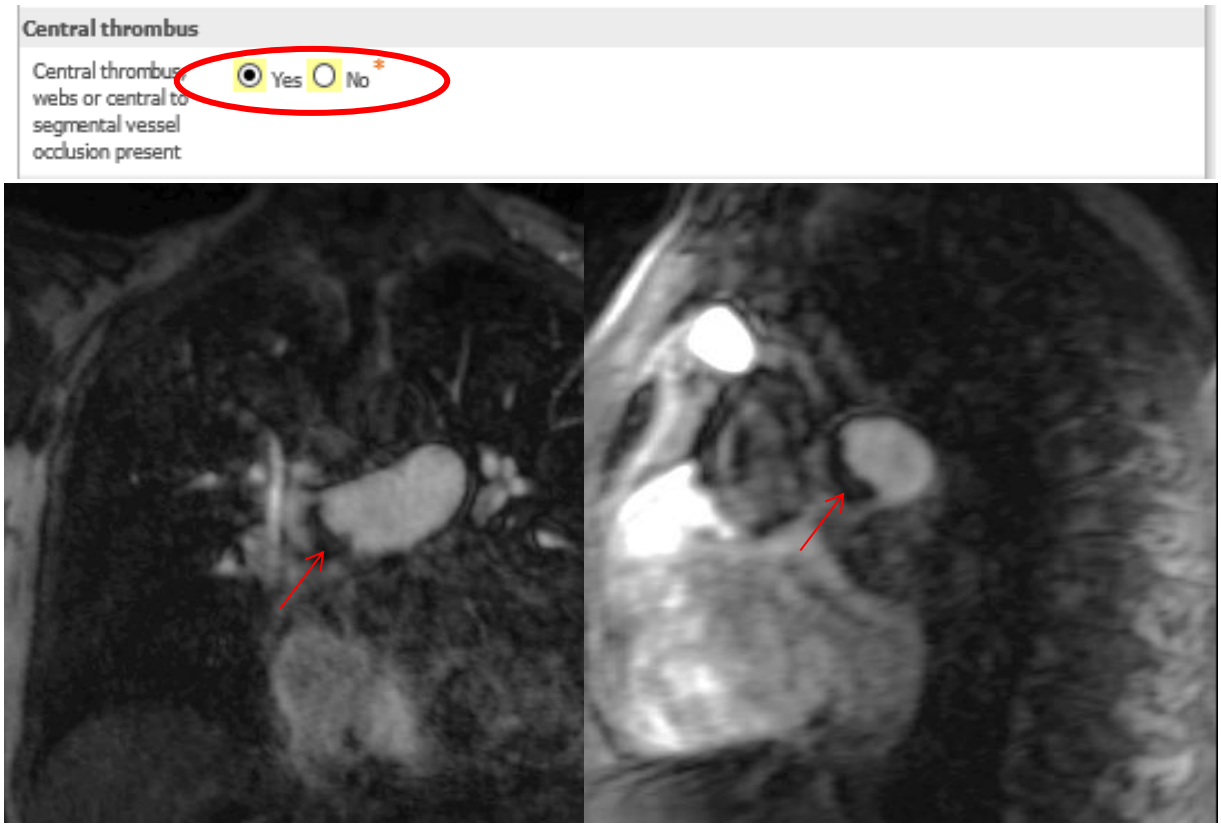


- If hypoperfusion in a segment is uncertain utilize the other dynamic enhancement frames over time to determine if hypoperfusion is present
- Use anatomic lung map in eCRF as reminder for segment anatomy

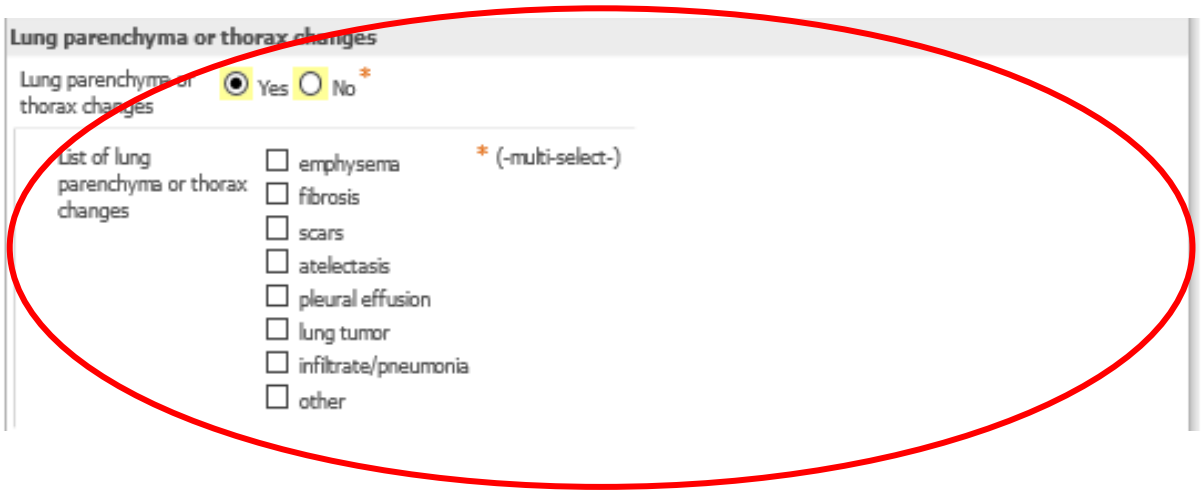


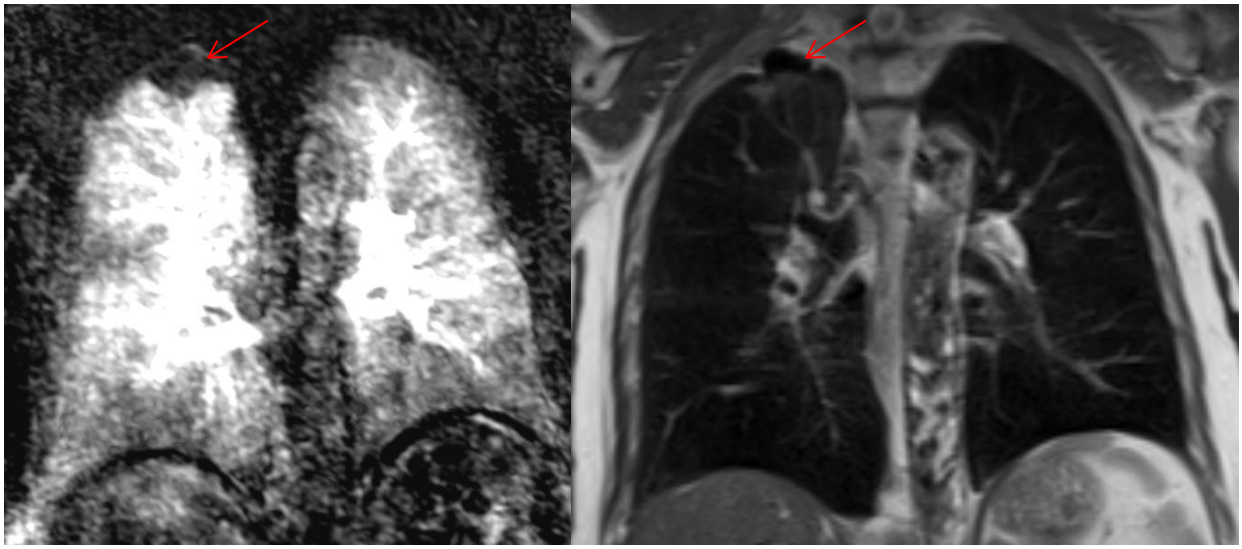
Example of CTEPH with hypoperfused segments

7. Mark if you observe presence of **central thrombus, webs or central to segmental vessel occlusion**.



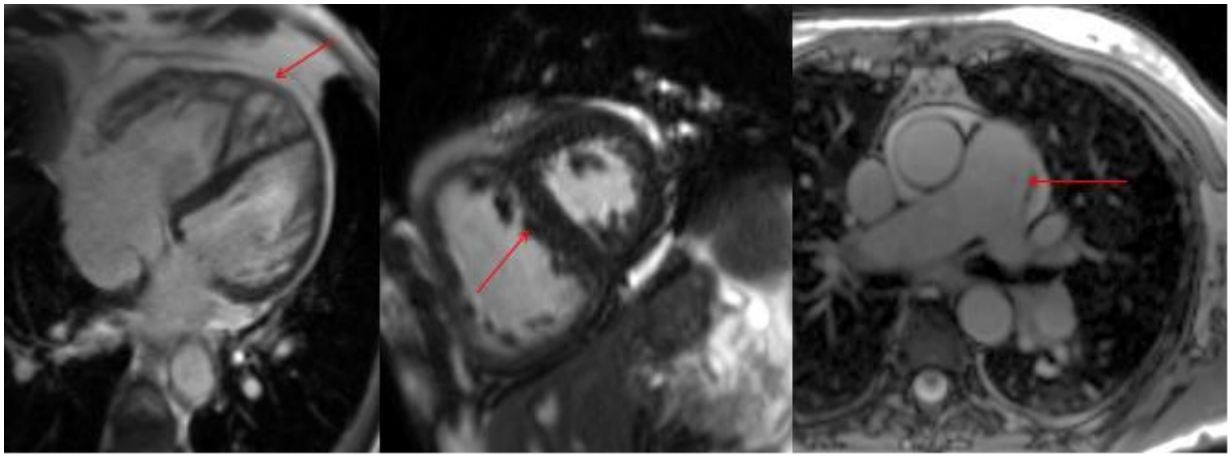
8. Select lung and thorax changes that may be the cause for hypoperfusion. If **lung parenchymal changes** are more likely to be the reason for hypoperfusion, go back to the rating of Dynamic Contrast MRI and correct.





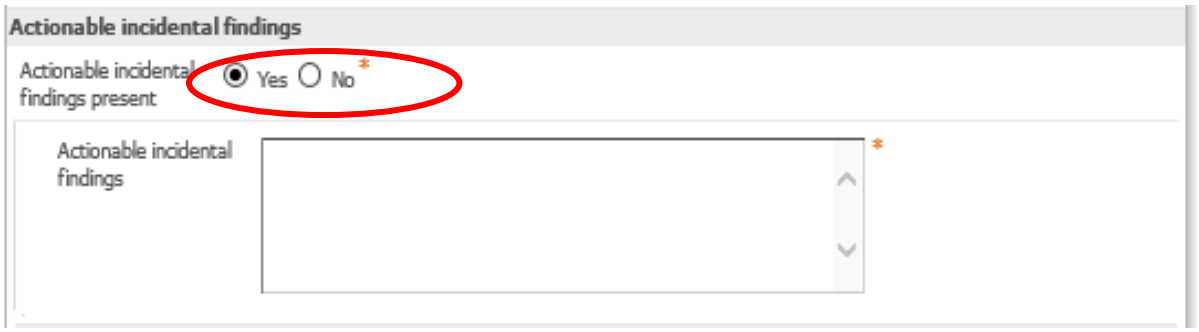
Example of subsegmental hypoperfusion due to bullae

9. Mark if **right heart strain** or pulmonary hypertension is present
    - Flattened septum
    - Paradox septal bouncing
    - RV – hypertrophy
    - RV – dilatation
    - Main pulmonary artery > 30mm diameter or diameter main pulmonary artery > diameter ascending aorta

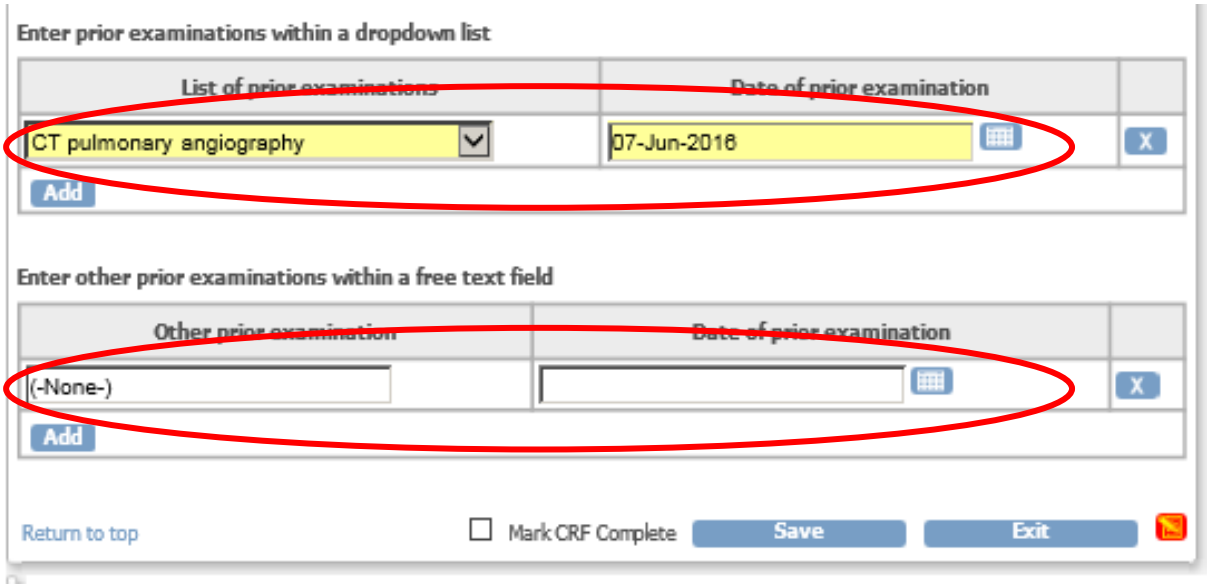


10. Diagnose CTEPH if hypoperfusion and signs of right heart strain or pulmonary hypertension are present.

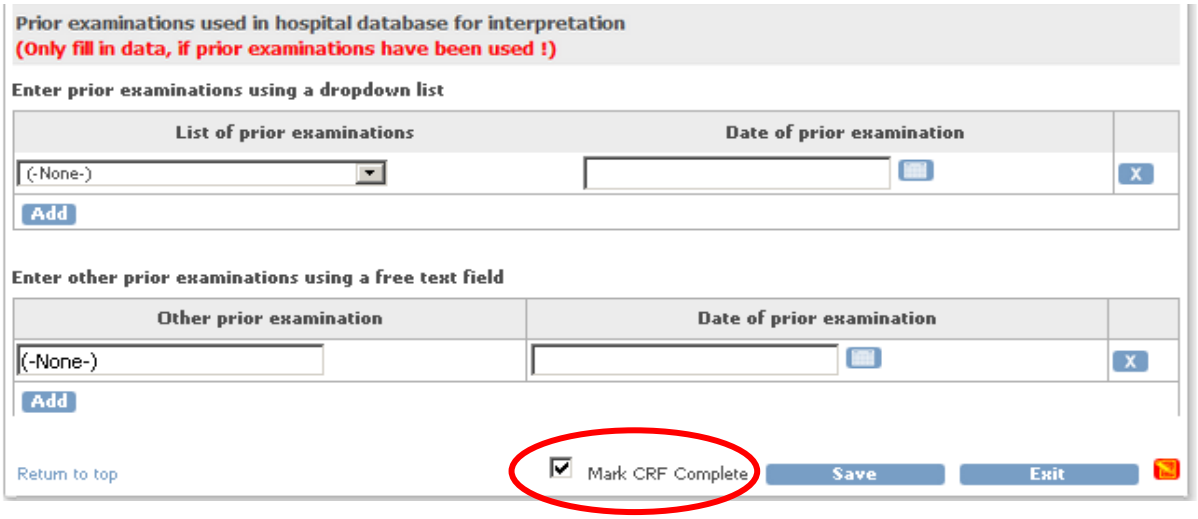
11. Enter actionable incidental findings, e.g. tumors, aneurysm…



12. Enter prior examinations (at an earlier hospital visit) that were used for the interpretation of MRI. DO NOT USE exams other than chest X ray from the current hospital visit! You may also use the free-text field below.



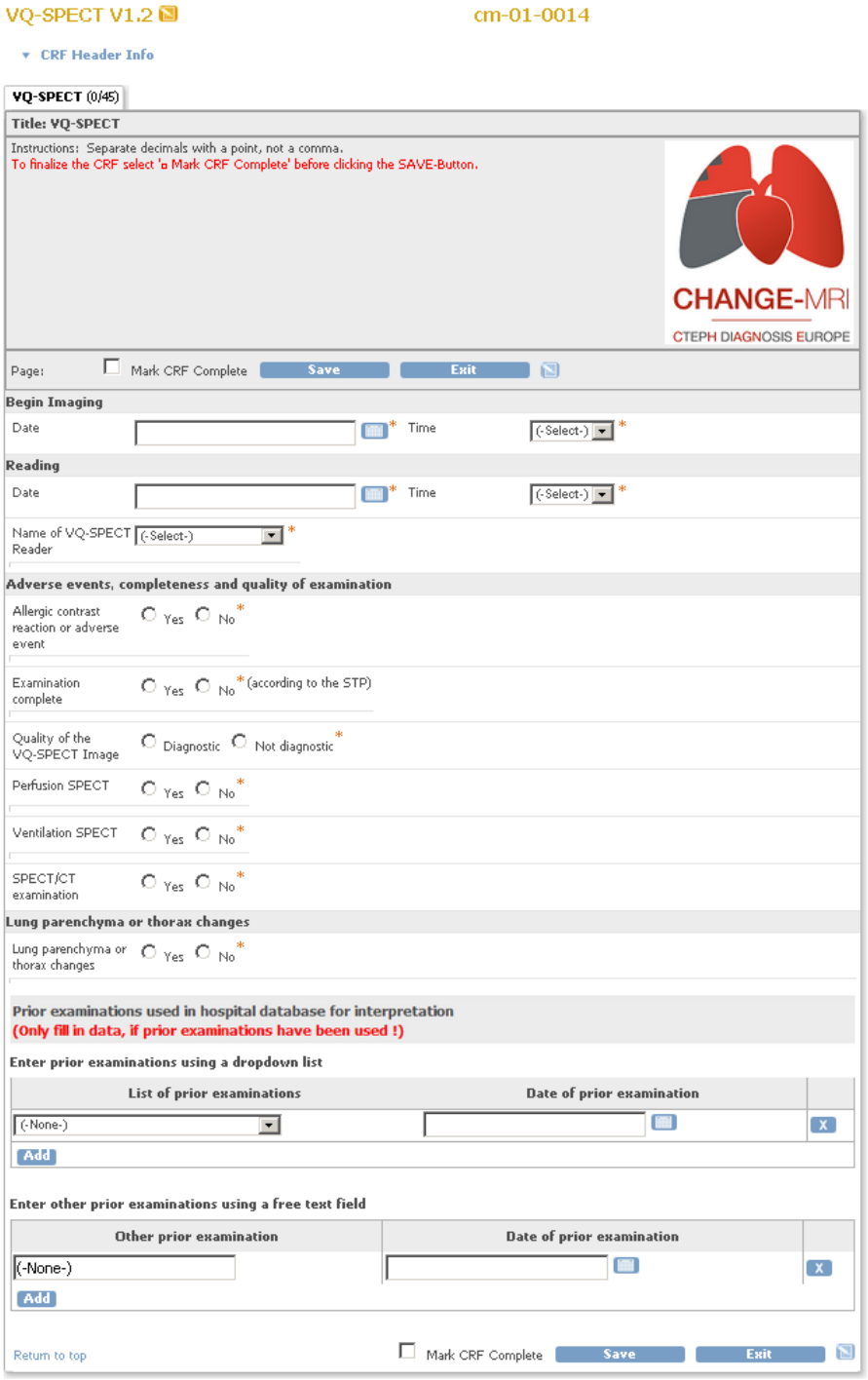
13. If you have completed the CRF, select “Mark CRF complete”.



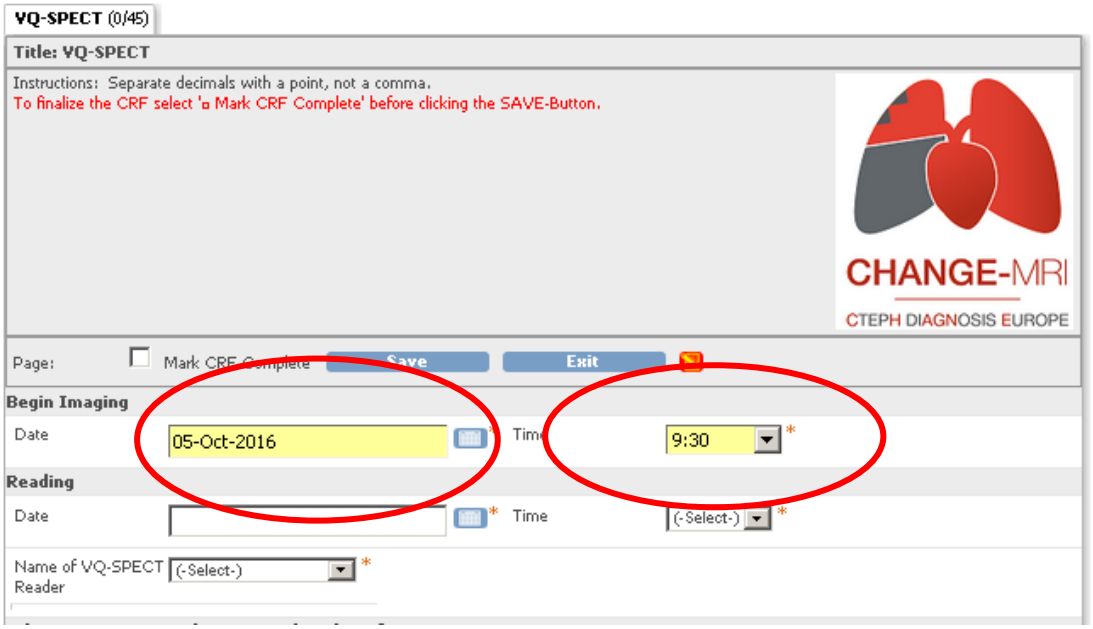
14. Press “Save“ to finish and save.

5.2 SPECT eCRF – Step-by-step instructions

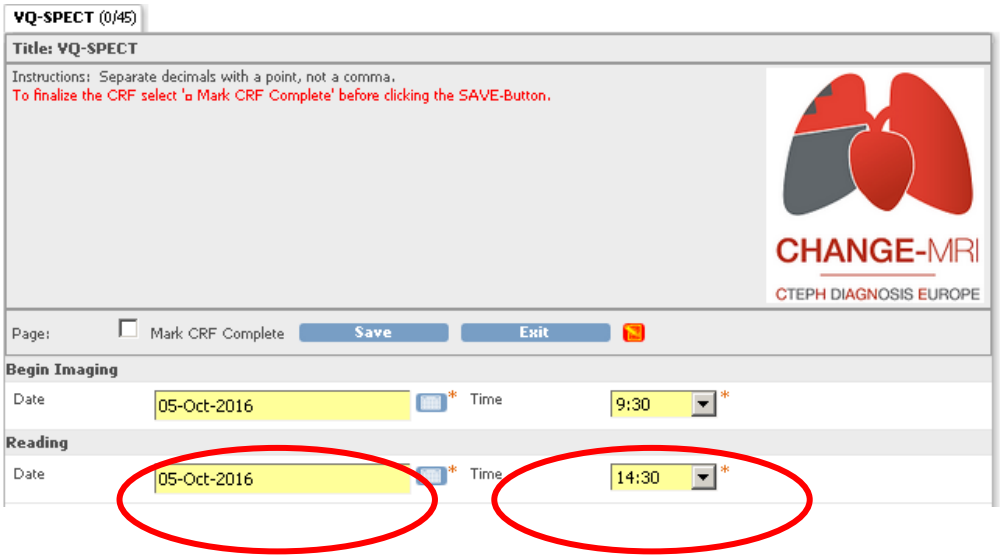
1. After clicking the **“Enter Data” icon** in the actions column for that CRF, the SPECT CRF opens.



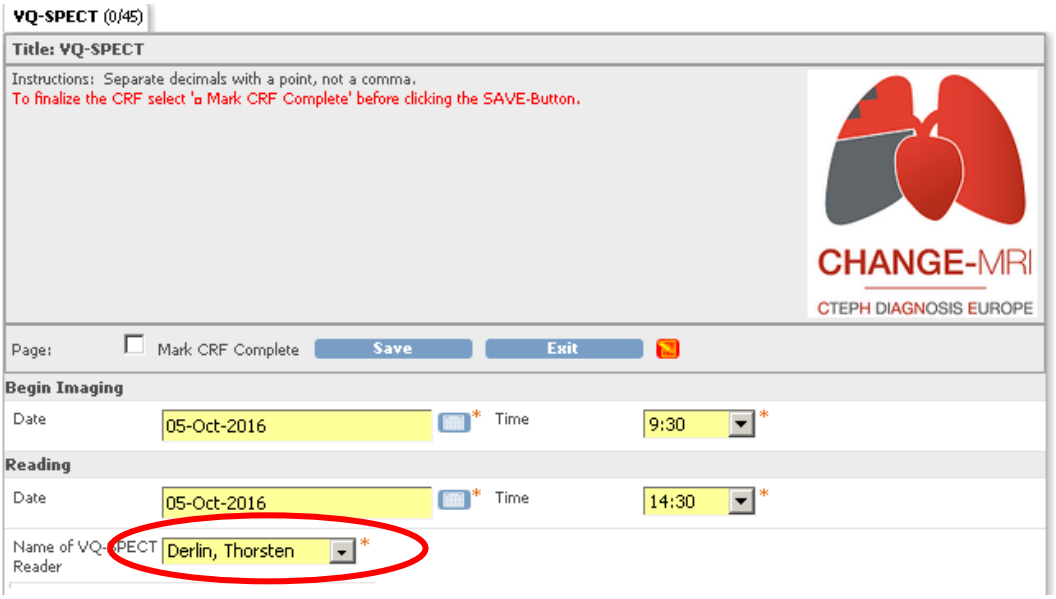
2. Select study date and time of imaging from the drop-down menu.



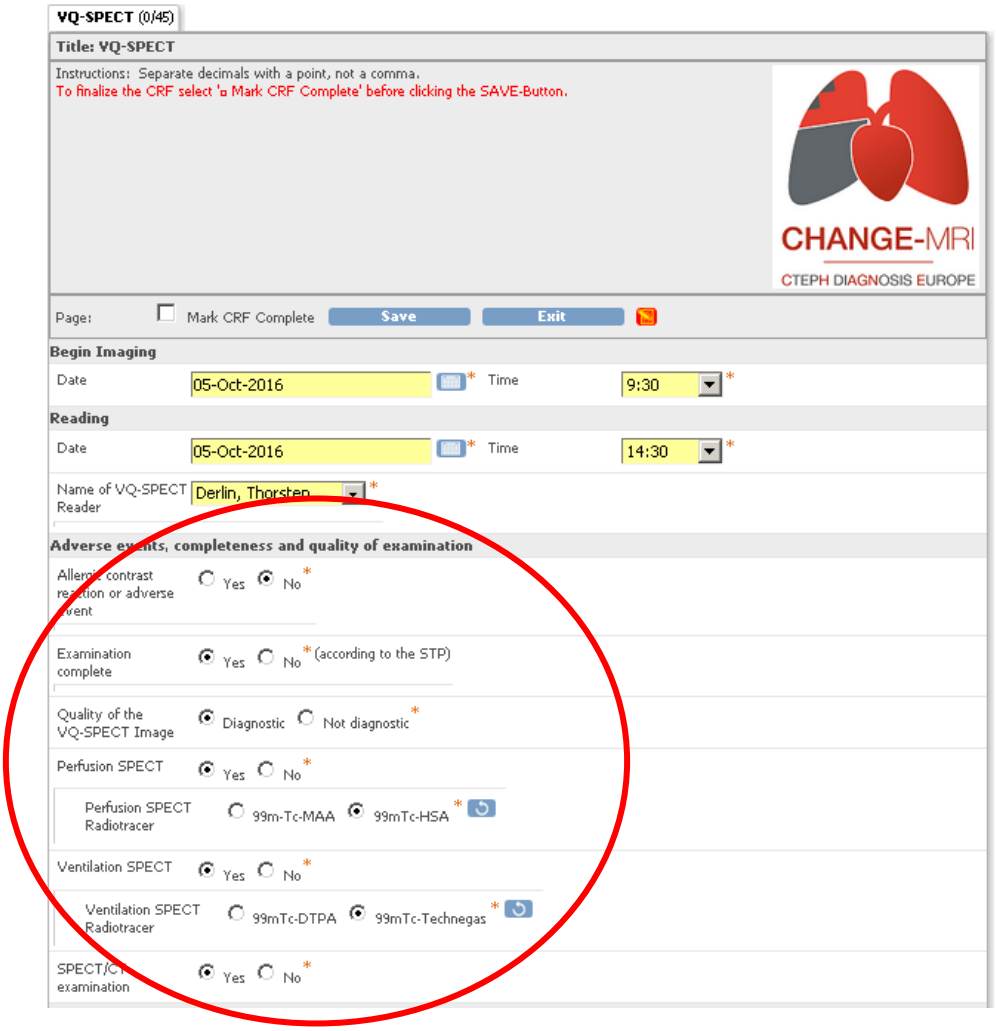
3. Select date of reading and time of reading from the drop-down menu.



4. Select the name of reader, or enter your name, if necessary.

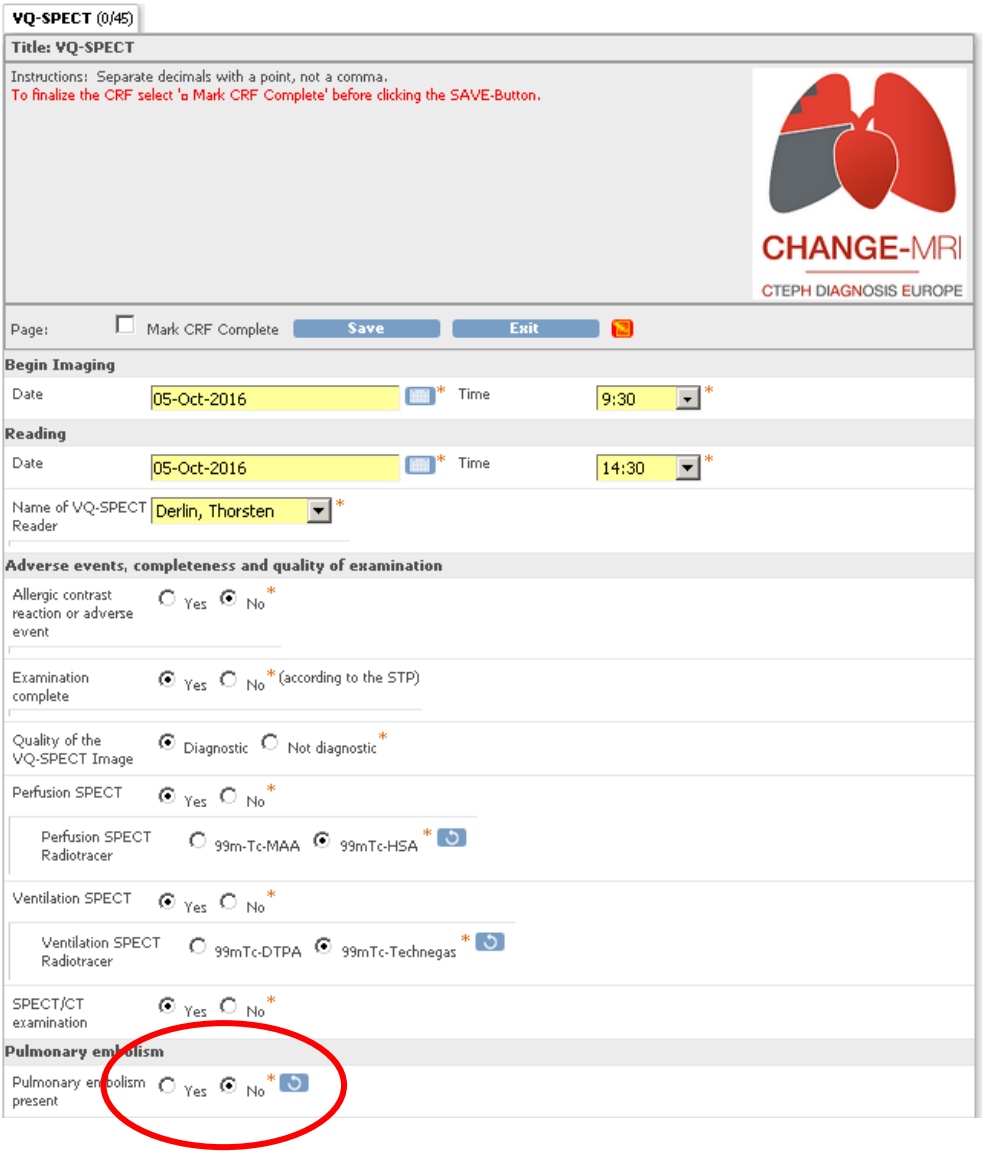


5. Answer all items concerning adverse events, completeness and quality of examinations.



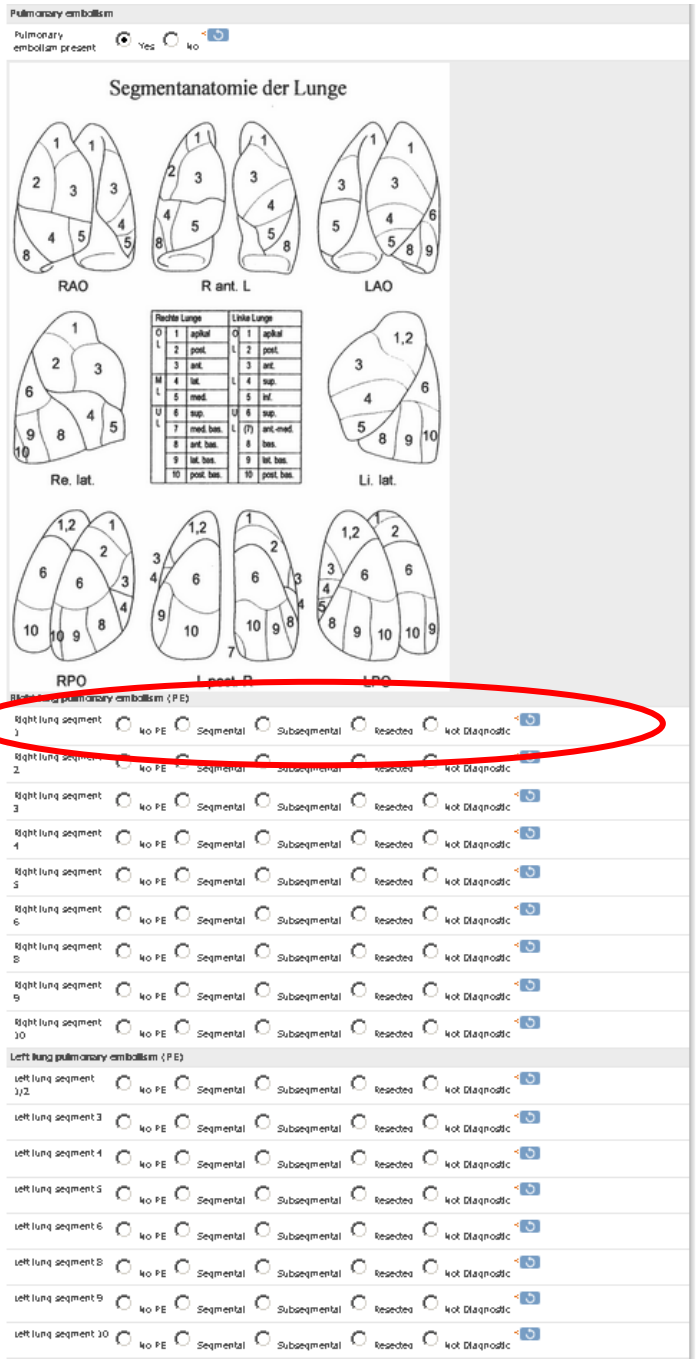
- Allergic contrast reaction or adverse events related to administration of contrast material?
- Examination complete? (According to the study protocol)
- Quality of Imamges (Diagnostic vs. non.diagnostic)
- Perfusion SPECT performed?
    - Select the radiotracer used in your institution
- Ventilation SPECT performed?
    - Select the radiotracer used in your institution
- SPECT/CT performed? (as part of either ventilation or perfusion scanning or both)?

6. Pulmonary embolism present? (Do net select “yes” if perfusion defects seen on the scan are not caused by emboli)

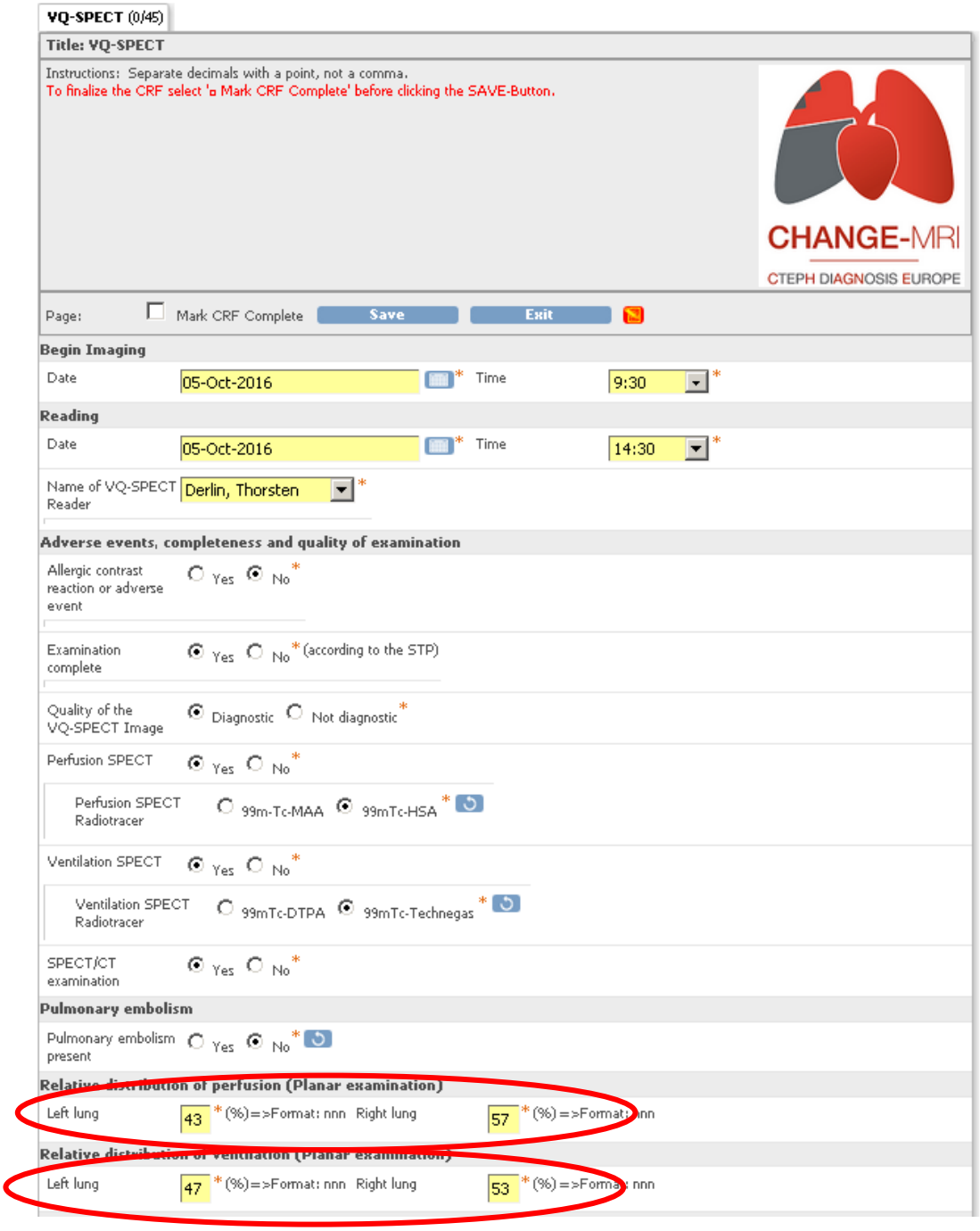


If you select “yes”, an illustration of the segmental anatomy of the lungs will appear, and you will have to decide for each segment if pulmonary embolism is

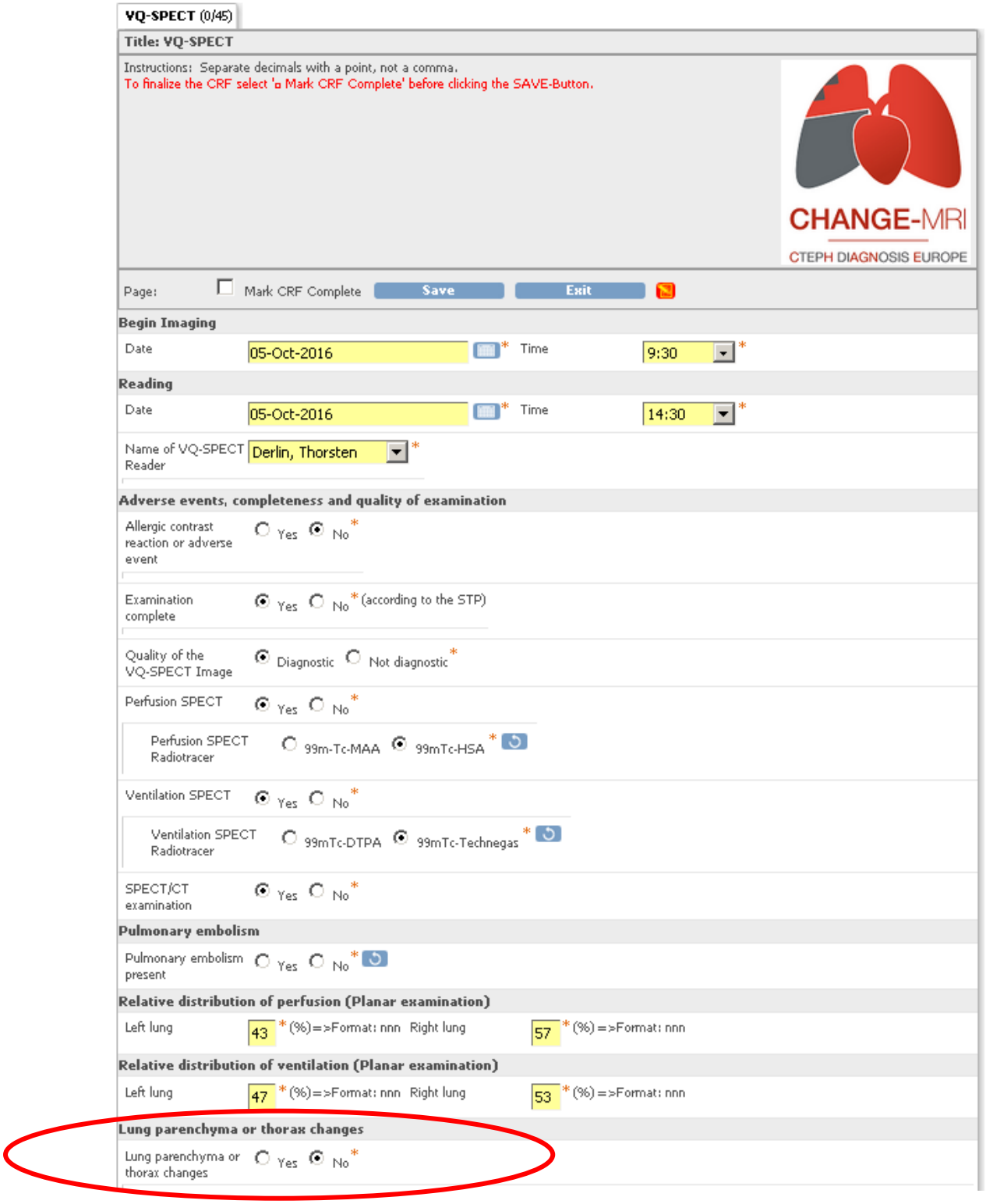
- Absent (“no”)
- Segmental pulmonary embolism
- Subsegmental pulmonary embolism
- Or if the segment has been resected previously.
- Or if the study is non diagnostic (segment can not be scored, e.g. because of artifacts)


Pulmonary embolism
Pulmonary embolism present
Yes
No
Segmentanatomie der Lunge
RAO
R ant. L
LAO
Re. lat.
Li. lat.
RPO
L post. R
LPO
Right lung pulmonary embolism (PE)
Right lung segment 1
Right lung segment 2
Right lung segment 3
Right lung segment 4
Right lung segment 5
Right lung segment 6
Right lung segment 8
Right lung segment 9
Right lung segment 10
Left lung pulmonary embolism (PE)
Left lung segment 1/2
Left lung segment 3
Left lung segment 4
Left lung segment 5
Left lung segment 6
Left lung segment 8
Left lung segment 9
Left lung segment 10
No PE
Segmental
Subsegmental
Resected
Not Diagnostic

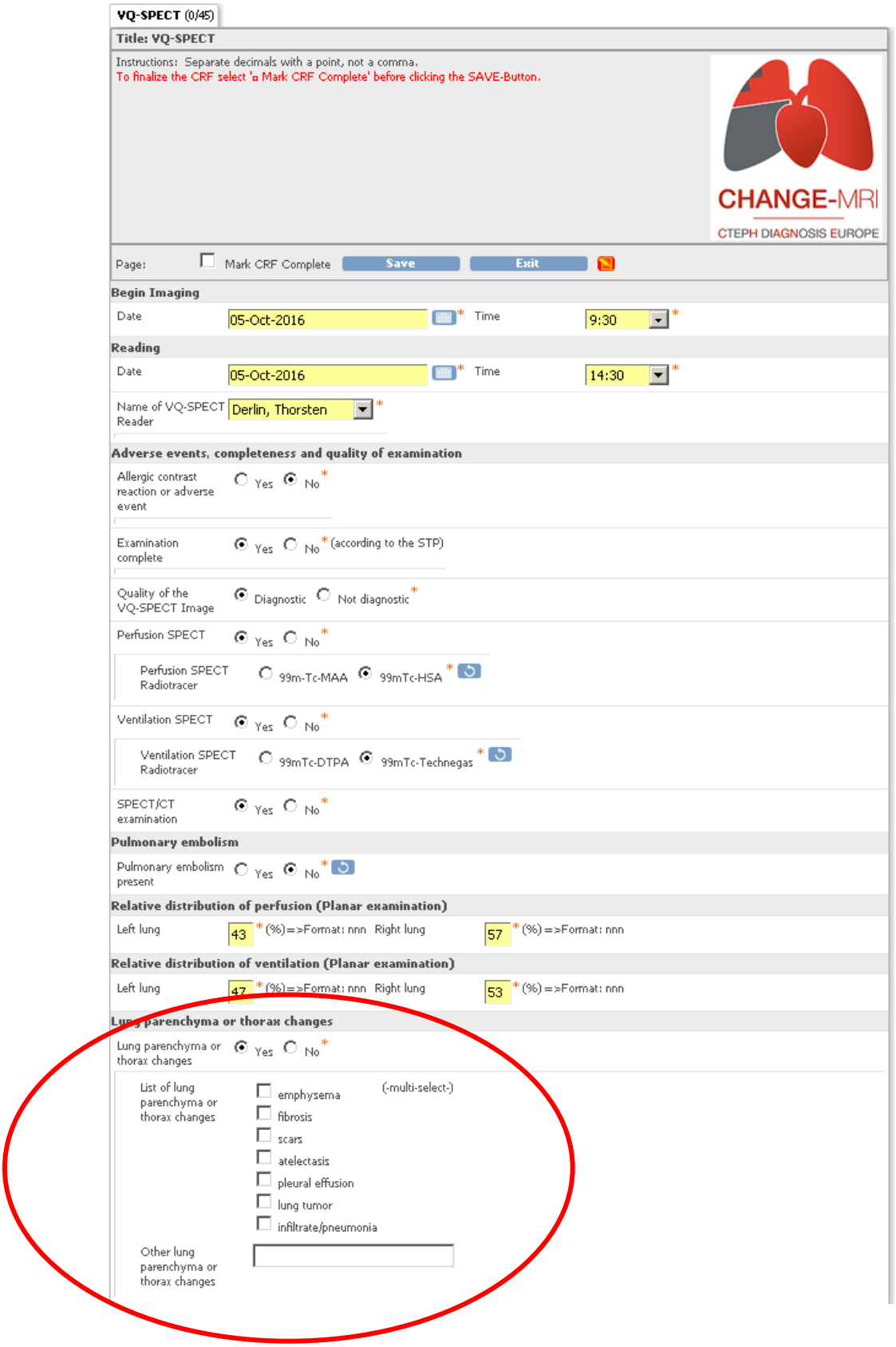
7. Enter values for the relative distribution of perfusion and ventilation, derived from planar imaging.



8. Select if lung parenchyma or thorax pathology is seen (only in case of SPECT/CT). If SPECT/CT has not been performed, select “no”.

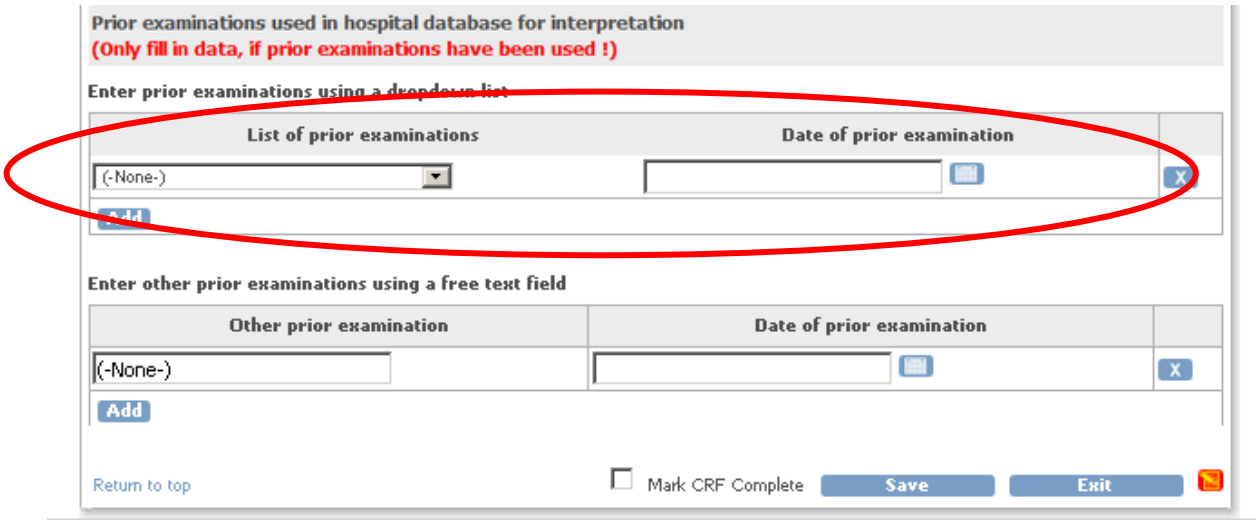


If you select “yes”, a multi-select menu will appear. Select all items you identified on the CT images.

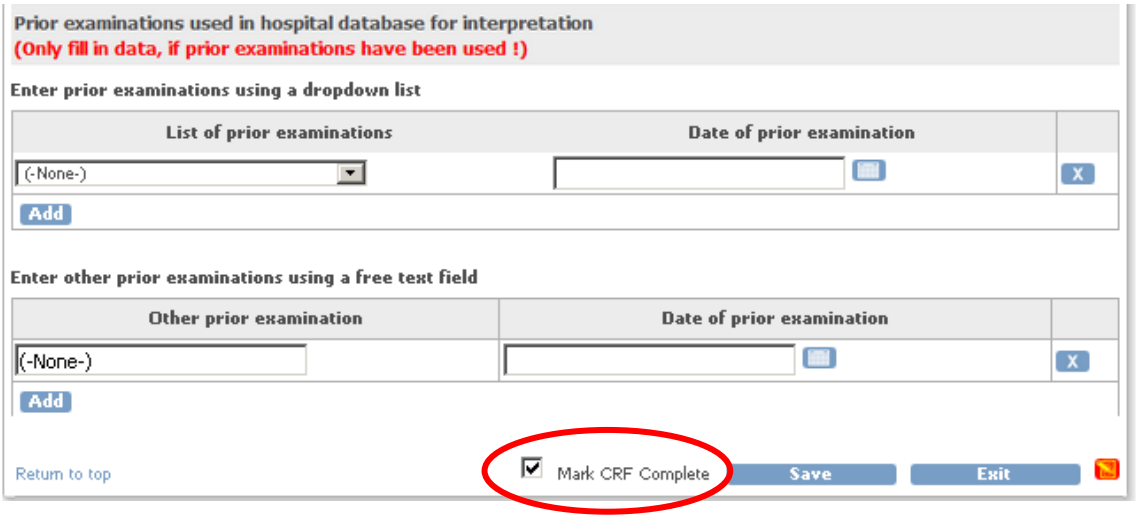


9. Select prior examinations (only if you used any)

- select type and date of prior examination used. You may also use the free-text field below.



10. If you have completed the CRF, select “Mark CRF complete”.



1. Press “Save“ to finish and save.

5.3 Goldstandard eCRF and image data storage

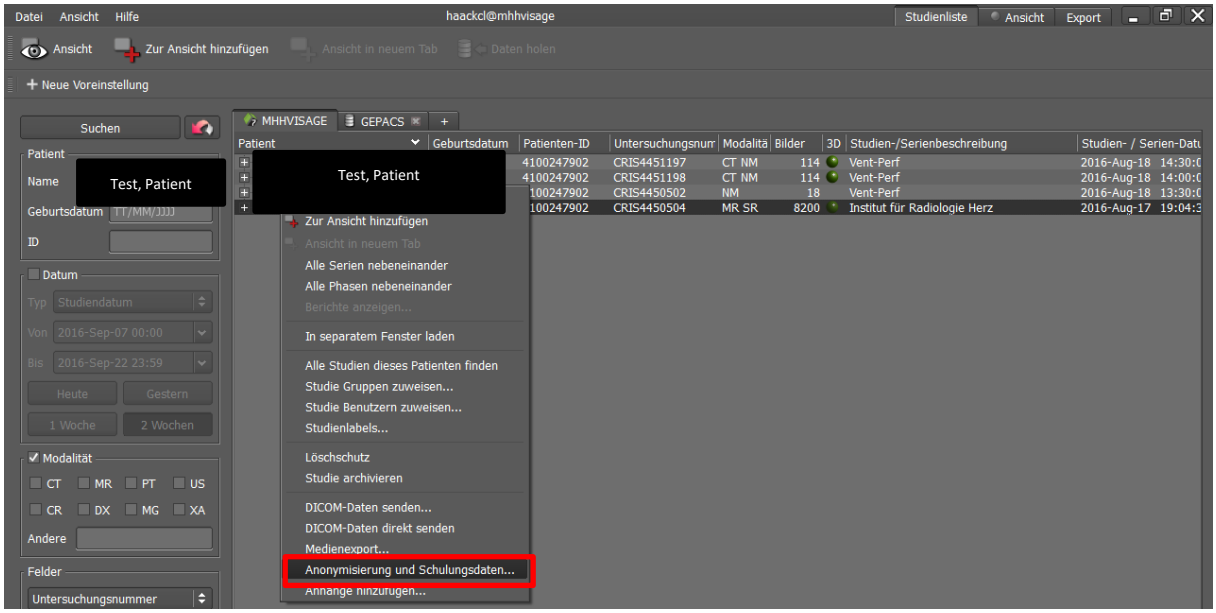
The eCRF Goldstandard has to be filled in 30 – 37 days after the MRI-scan and consists of three tasks:

- pseudonymization
- image data storage
- data entry eCRF

1. Pseudonymization

In the following example we use the program “Visage” for the pseudonymization:

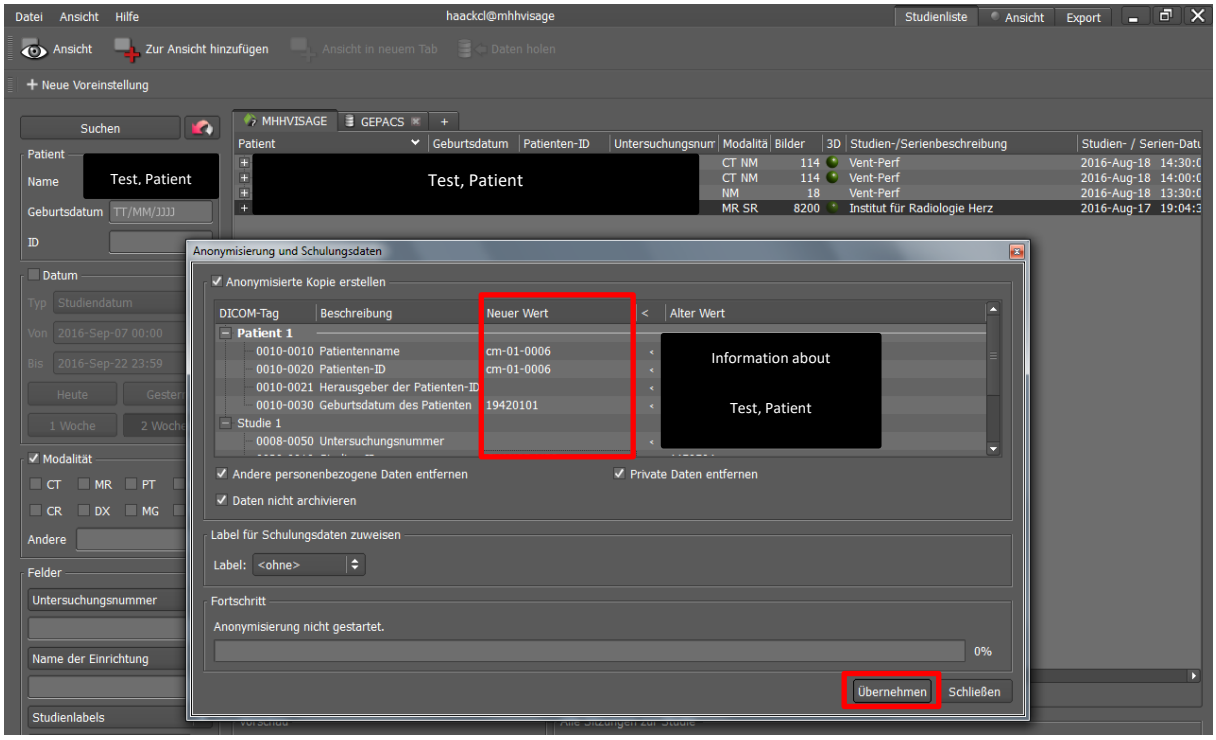
- Search the system for the patient (clear name)
- Choose the MRI scan and check the correct enrollment date (refer to pseudonym-list)
- Select “Anonymisierung und Schulungsdaten” by right mouse key



- Replace cleared patient data by following pseudonymization data in a newly opened function and confirm (refer to pseudonym-list)

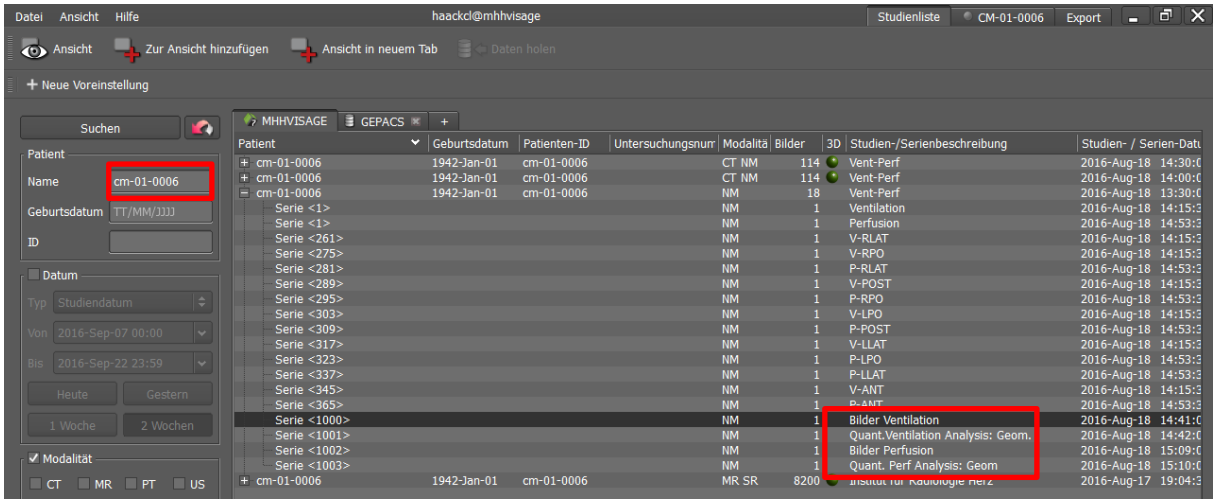
Pseudonymization data:

Patient name	subject ID of patient
Patienten-ID	subject ID of patient
Patient birth	set to 01.01. "real year of birth".
Exam number	leave field blank, or delete entries
Study- ID	Change-MRI
Study description	make no changes
Study comments	make no changes
Name of institute	make no changes

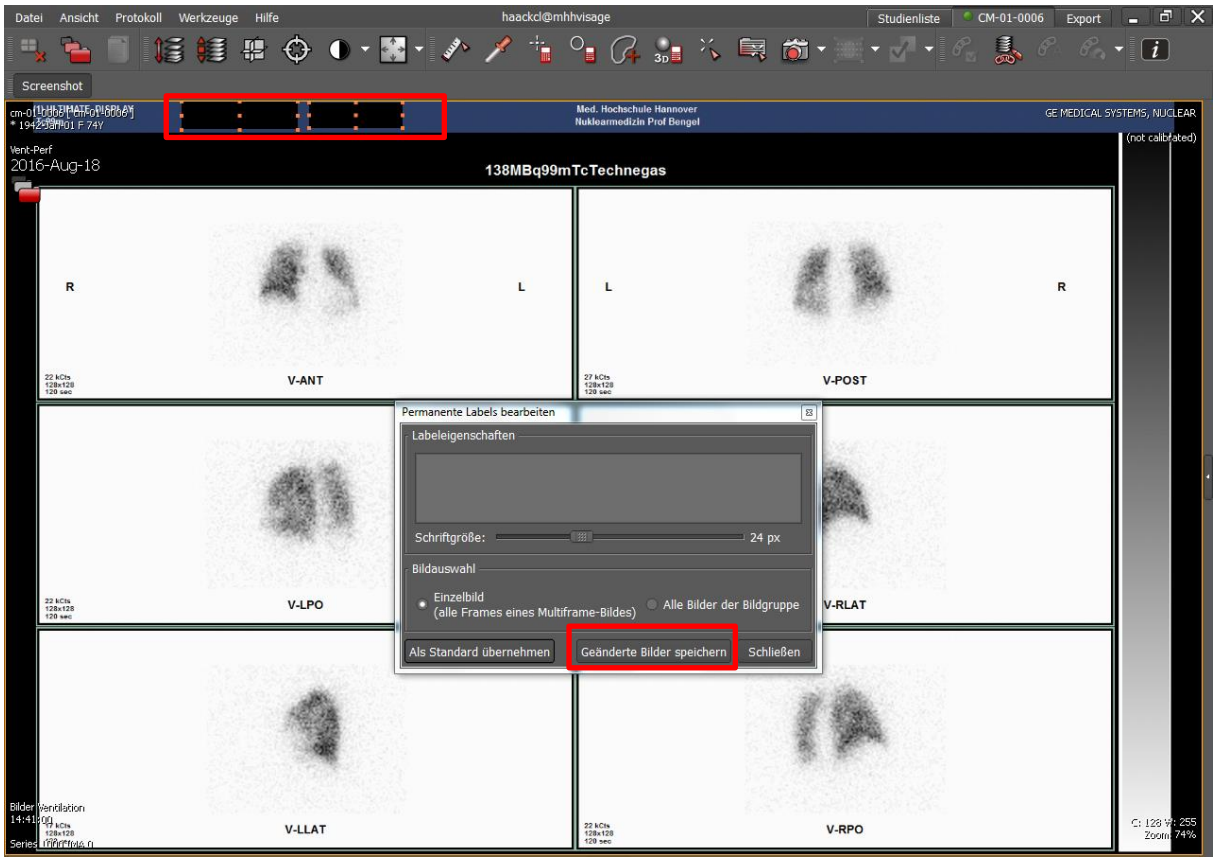


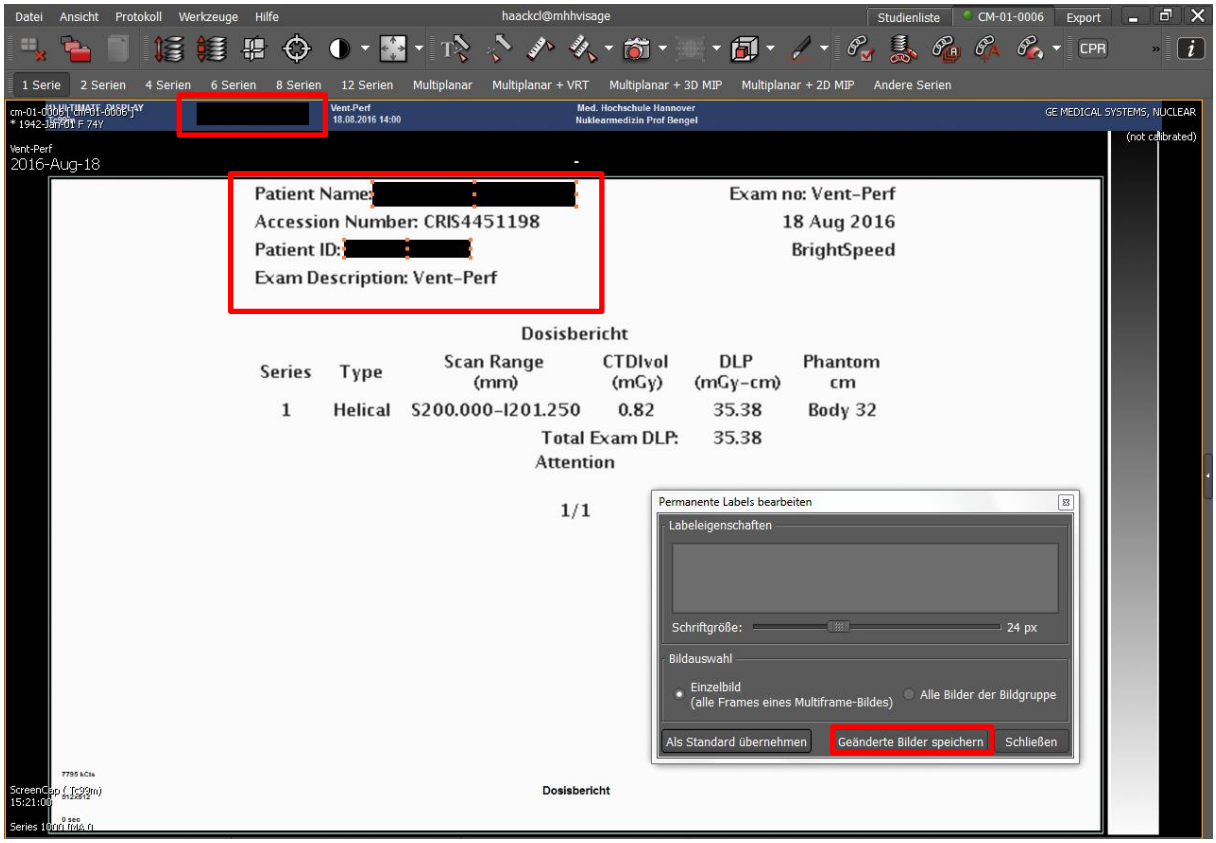
It is important to check, that all identifying patient data are completely pseudonymised or deleted. (Check data that might be stored within an image, e.g. in the dose- report.)

Search the system for patient subject ID and check all images, especially the SPECT-data, for identifying patient data.



Visage is able to black identifying patient data in the images:

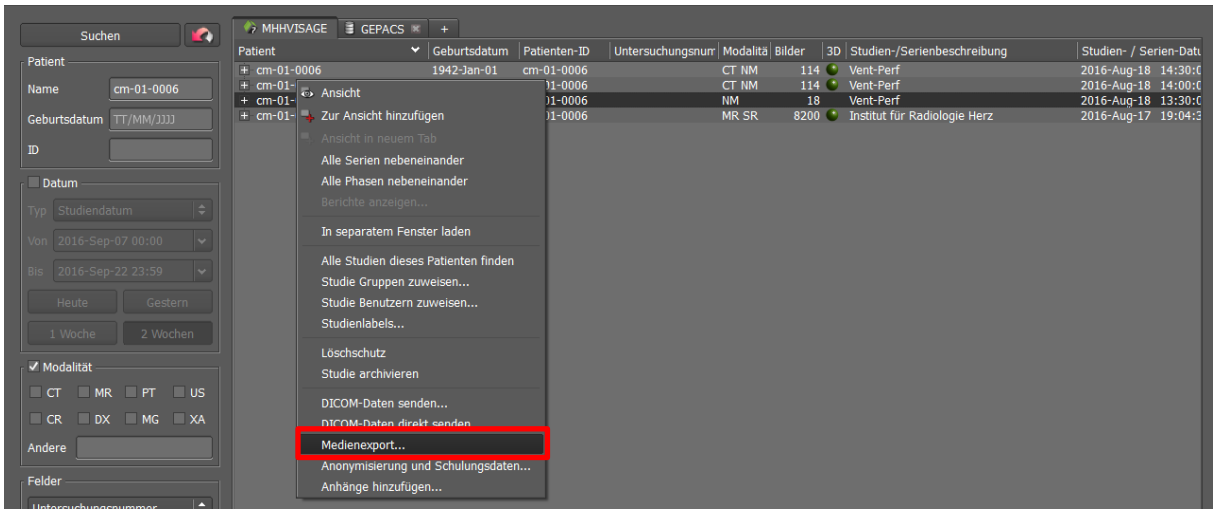


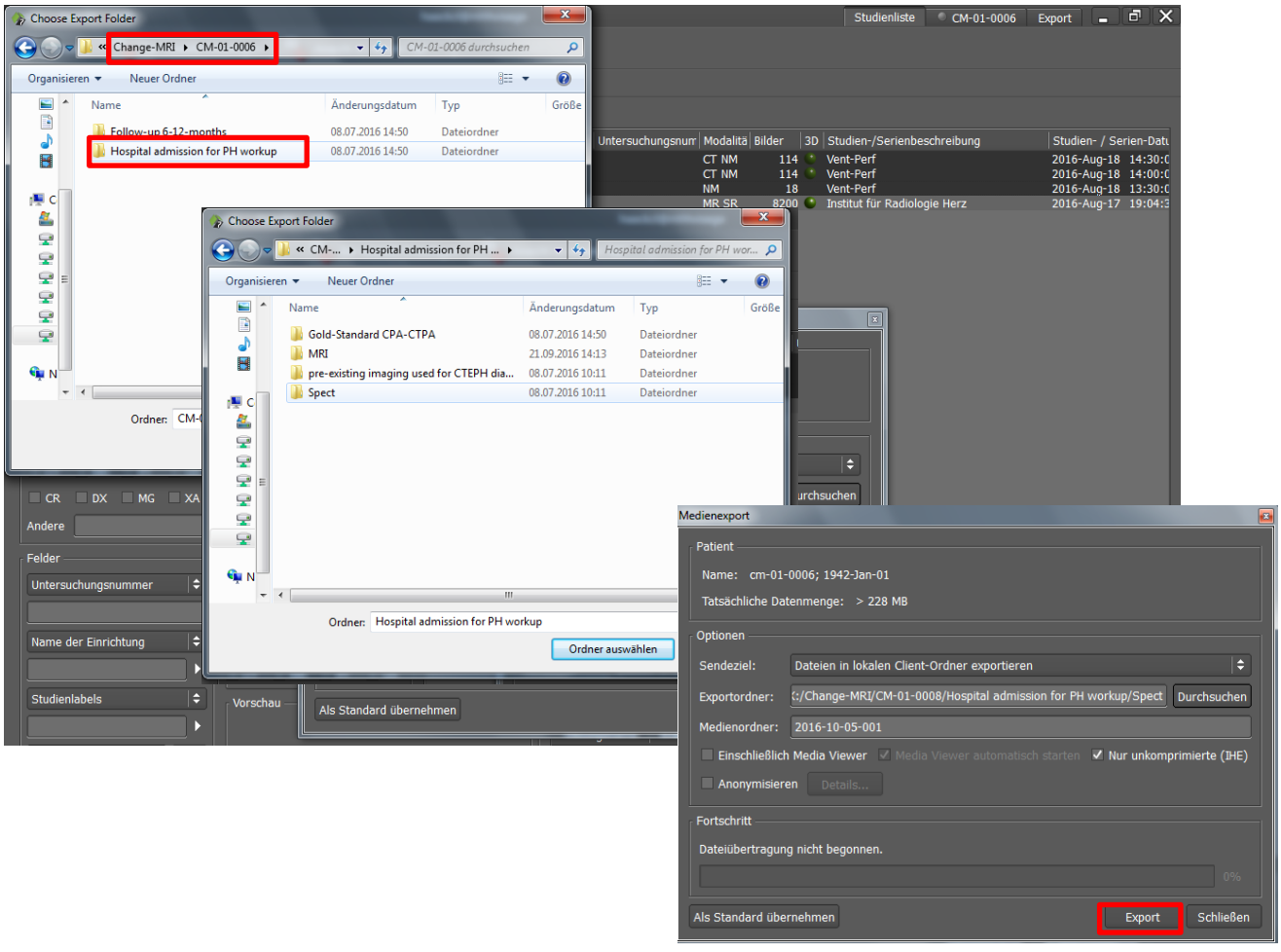


2. Image data storage

If all identifying patient data are completely pseudonymised, deleted or blacked, the image data storage can be started using Visage:

- Select MRI data by right mouse key
- Choose “Medienexport”
- Choose the folder CHANGE MRI with the correct subject ID
- Choose MRI or SPECT data storage in the hospital admission for PH workup
- select the correct folder for the image export and press “exportieren”, the data storage starts



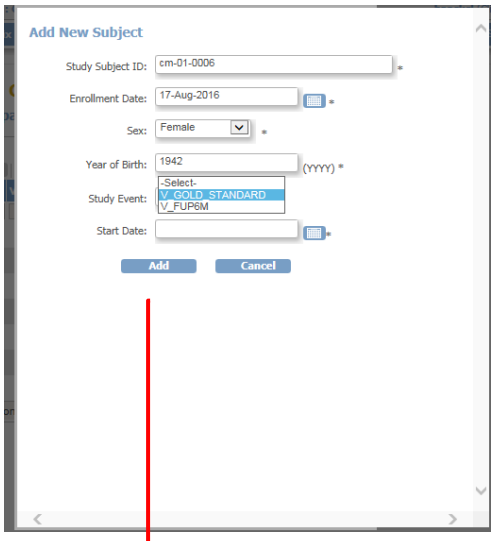


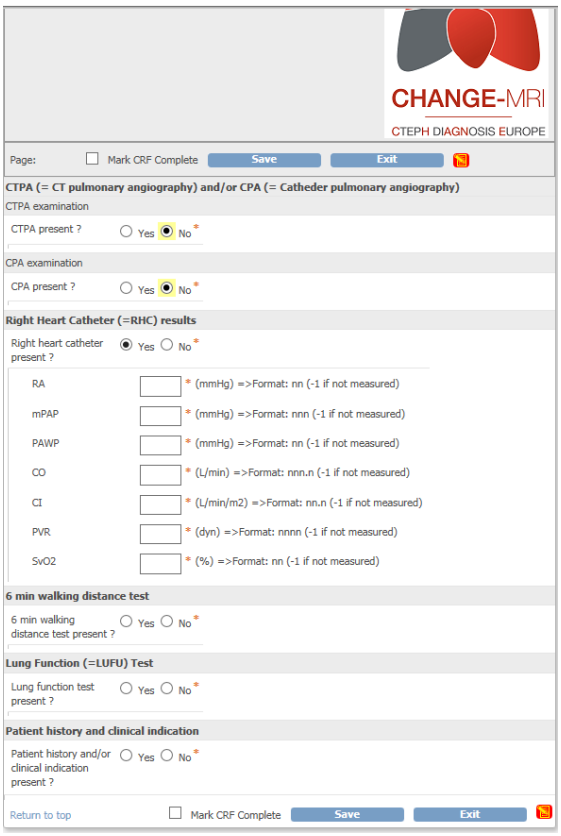
To document the data storage and backup the information for the monitoring, enter all steps in the sample excel sheet:

I	J	K	L	M	
Transfer PACS Date/sig	Transfer Image Bank Date/sig	Imagetransfer Date /sig	30d pre/post MRI Date	Imagetransfer Date/sign	30
MRI	**MRI**	**SPECT**	**CT pulmonary angiography**	**CT pulmonary angiography**	**Cathete**
10.08.2016/ch	20.07.2016/ ch	20.07.2016/ ch	n.a./ch	n.a./ch	
26.08.2016/fs	26.08.2016/fs	26.08.2016/fs	n.a./ch	n.a./ch	
09.09.2016/cj	09.09.2016/cj	09.09.2016/cj	n.a./cj	n.a./cj	
/	/	/	/	/	
06.09.2016/cj	06.09.2016/cj	06.09.2016/cj	n.a./cj	n.a./cj	
21.09.2016/cj	21.09.2016/cj	21.09.2016/cj	n.a./cj	n.a./cj	
09.09.2016/cj	09.09.2016/cj	09.09.2016/cj	n.a./cj	n.a./cj	

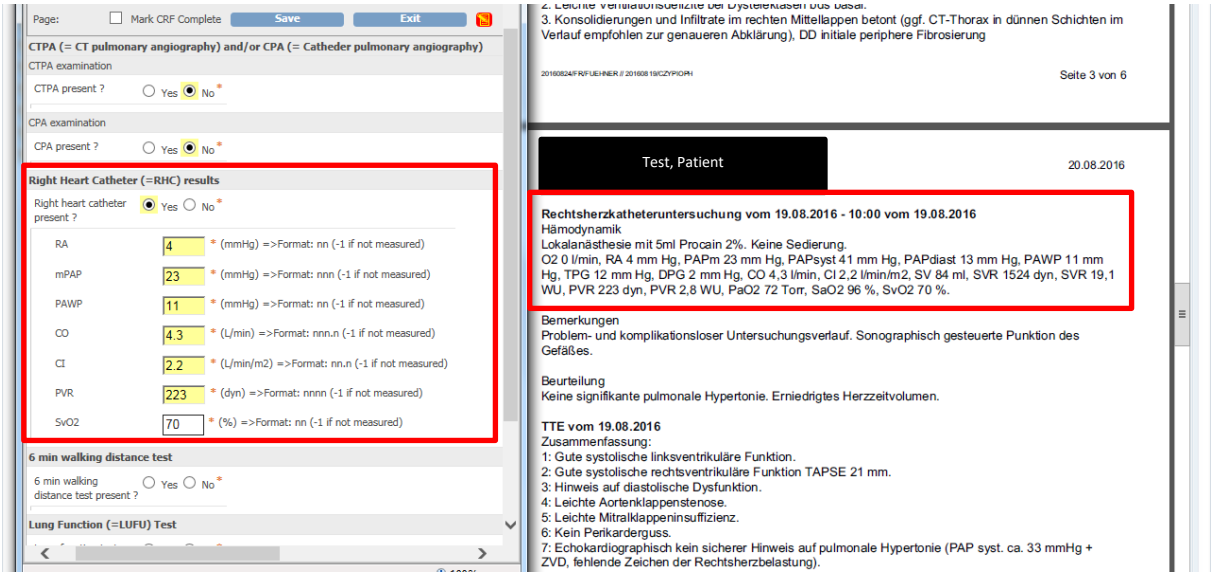
3. Data entry eCRF

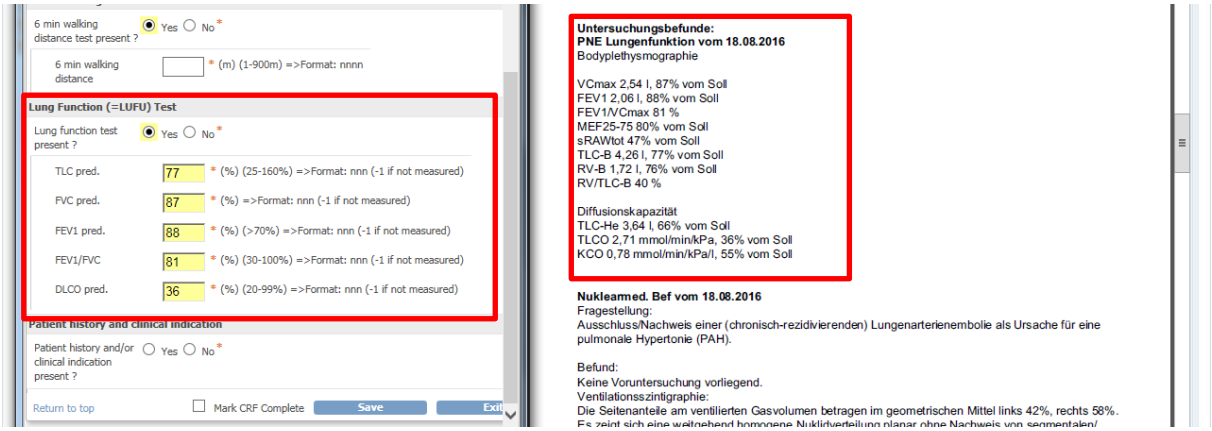
Add a new subject, equivalent to data entry for MRI or SPECT in the eCRF.





Fill in the correct clinical data from the hospital information system:





Pay attention to the different nomenclature between english (eCRF) and german (hospital information system):

Lung function:

eCRF:	hospital information system
TLC pred.	TLC-B
FVC pred.	VCmax
FEV1 pred.	FEV1
FEV1/FVC	FEV1/VCmax
DLCO pred.	TLCO

Right heart catheter:

eCRF:	hospital information system
mPAP	PAPm
PVR *(dyn)	PVR*"Wert"* **dyn**

Finish the data entry with "Save" button, don't use the „Mark CRF Complete" checkbox.

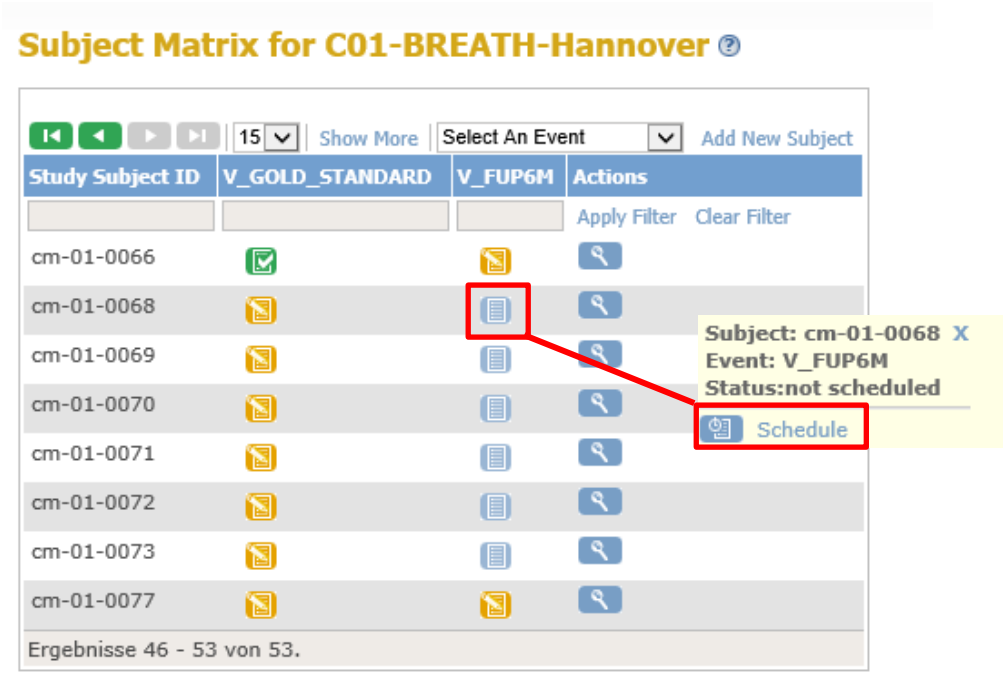
This function is used later, after the values have been checked by our biometrics.

5.4 Follow_Up6Months eCRF

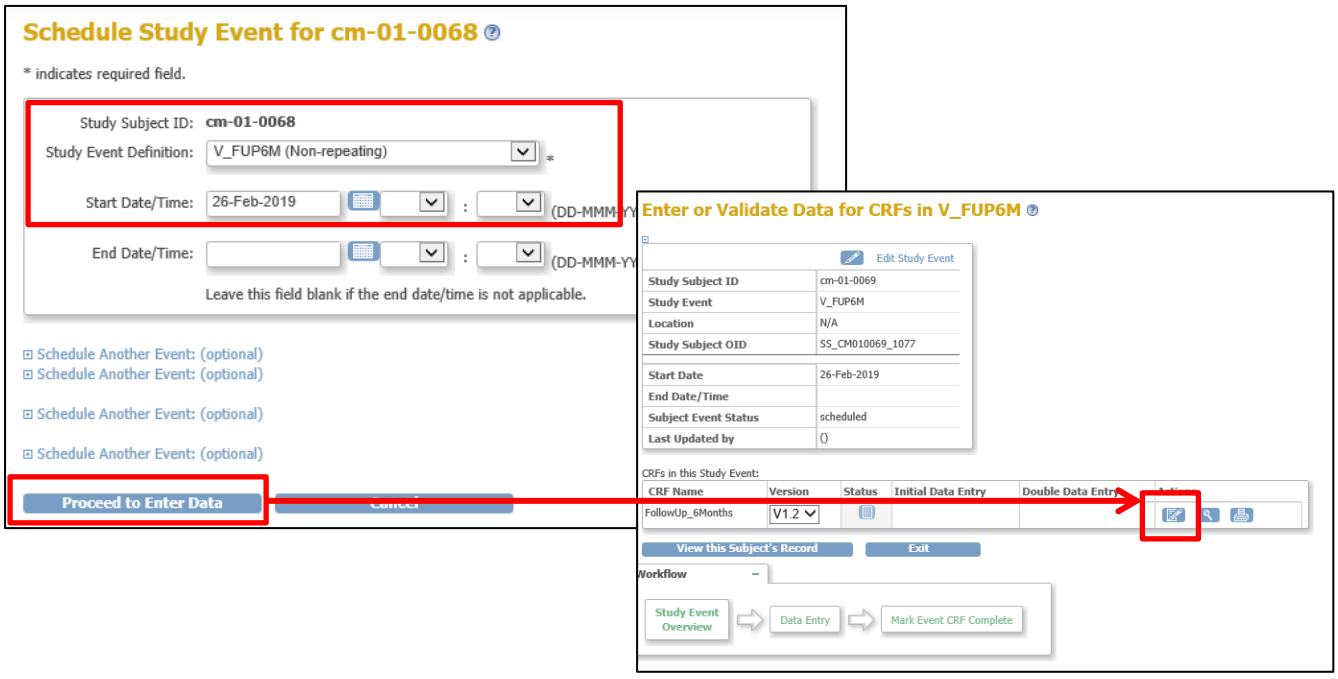
The FUP6M eCRF (6 months Follow up) has to be filled in at the period of 6 to 12 months after the MRI Scan. The earliest begin of data entry, should be started 6 months after the MRI Scan. If no data is entered after 7 months, a query will be sent as reminder.

As soon as all necessary data are available, the entry into the eCRF should be made once.

For the eCRF data entry, select the “V_FUP6M” Event at the added patients.
Use the right patient ID and choose “schedule” to get to the FUP eCRF:

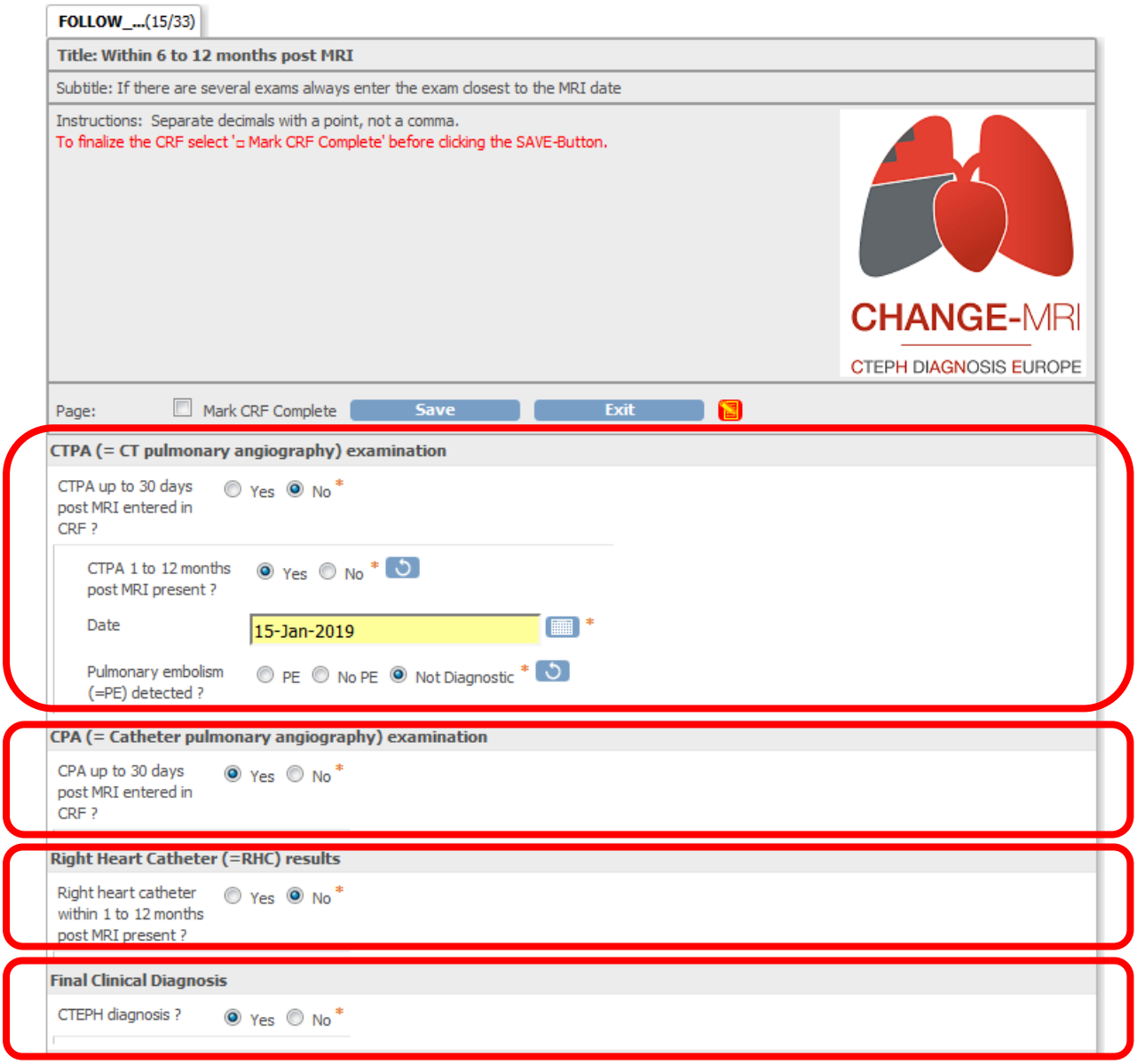


Check the right event and the date of the data entry (actual date is automatically deposited), continue with “proceed to enter data” and enter the valid data:



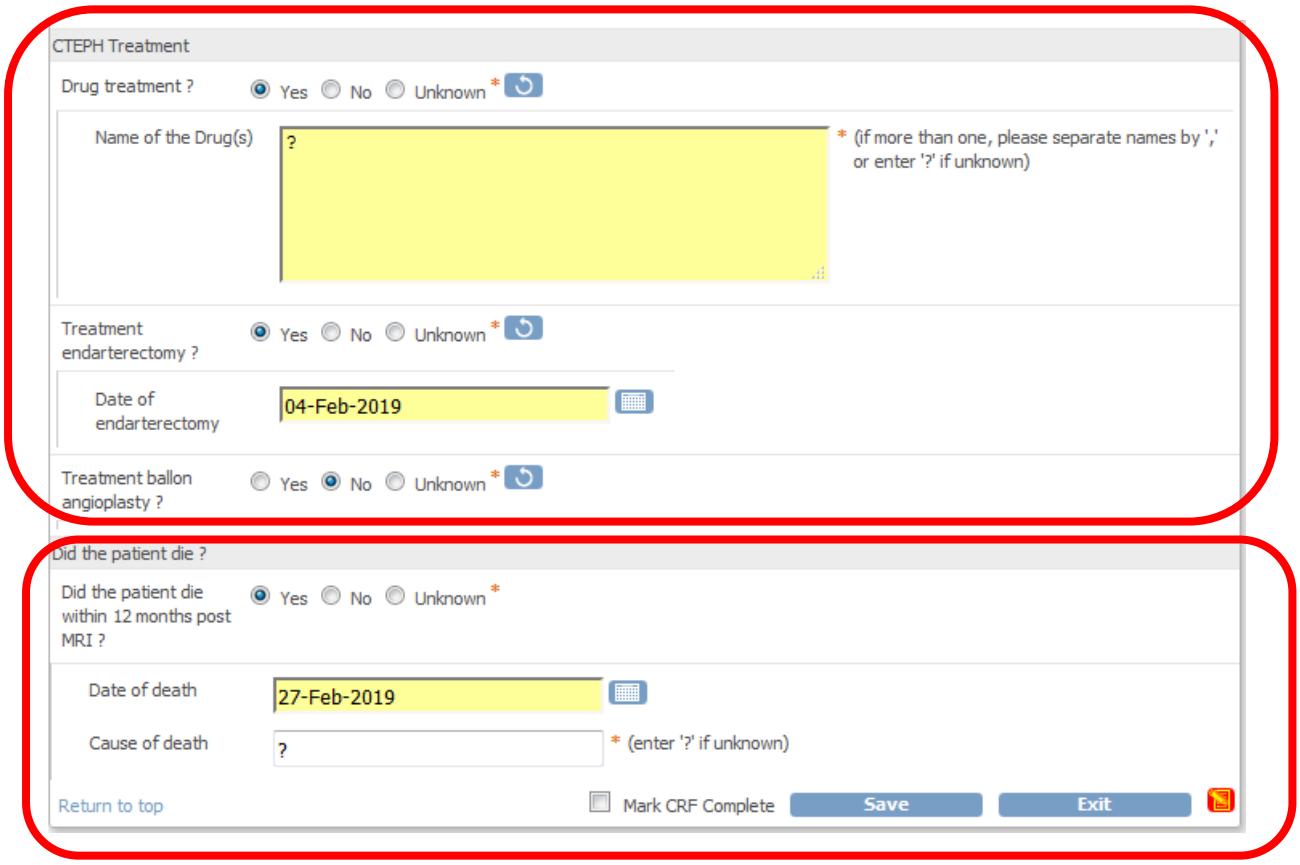
The eCRF consists of six items to be entered:

- **CTPA (= CT pulmonary angiography)** examination **must** be entered only, if a **CTPA** examination has been performed **within 1 to 12** months after MRI scan and **no CTPA** is entered within the **Gold-standard eCRF**.
- **CPA (= Catheter pulmonary angiography)** examination **must** be entered only, if a **CPA** examination has been performed **within 1 to 12** months after MRI scan and **no CPA** is entered within the **Gold-standard eCRF**.
- **Right Heart Catheter (=RHC) results** should be entered, if the examination has been performed **within 1 to 12 months** after MRI scan.
- **Final Clinical Diagnosis** this item contains the latest available clinical diagnosis, which may be **CTEPH**, **Pulmonary Hypertension** (incl. classification) or **other diagnosis**.



➔ **For the final clinical diagnosis, use the most recent medical report, if available.**

- **CTEPH Treatment** this item must be entered, if the final diagnosis is CTEPH. It may contain **Drug treatment**, **treatment endarterectomy** or **treatment ballon angioplasty**
- **Did the patient die within 12 months post MRI?** If possible enter **date** and **cause** of death.



If **pseudonymised** (see 5.3 part 1: Pseudonymization) image data are entered and present, they should be stored within the sites SFTP area in folder **…\Follow-up 6-12-months\Gold-Standard CPA-CTPA\CTPA (Computed Tomography Pulmonalis Angiography)** or in **…\Follow-up 6-12-months\Gold-Standard CPA-CTPA\CPA (catheter pulmonary angiography)**.

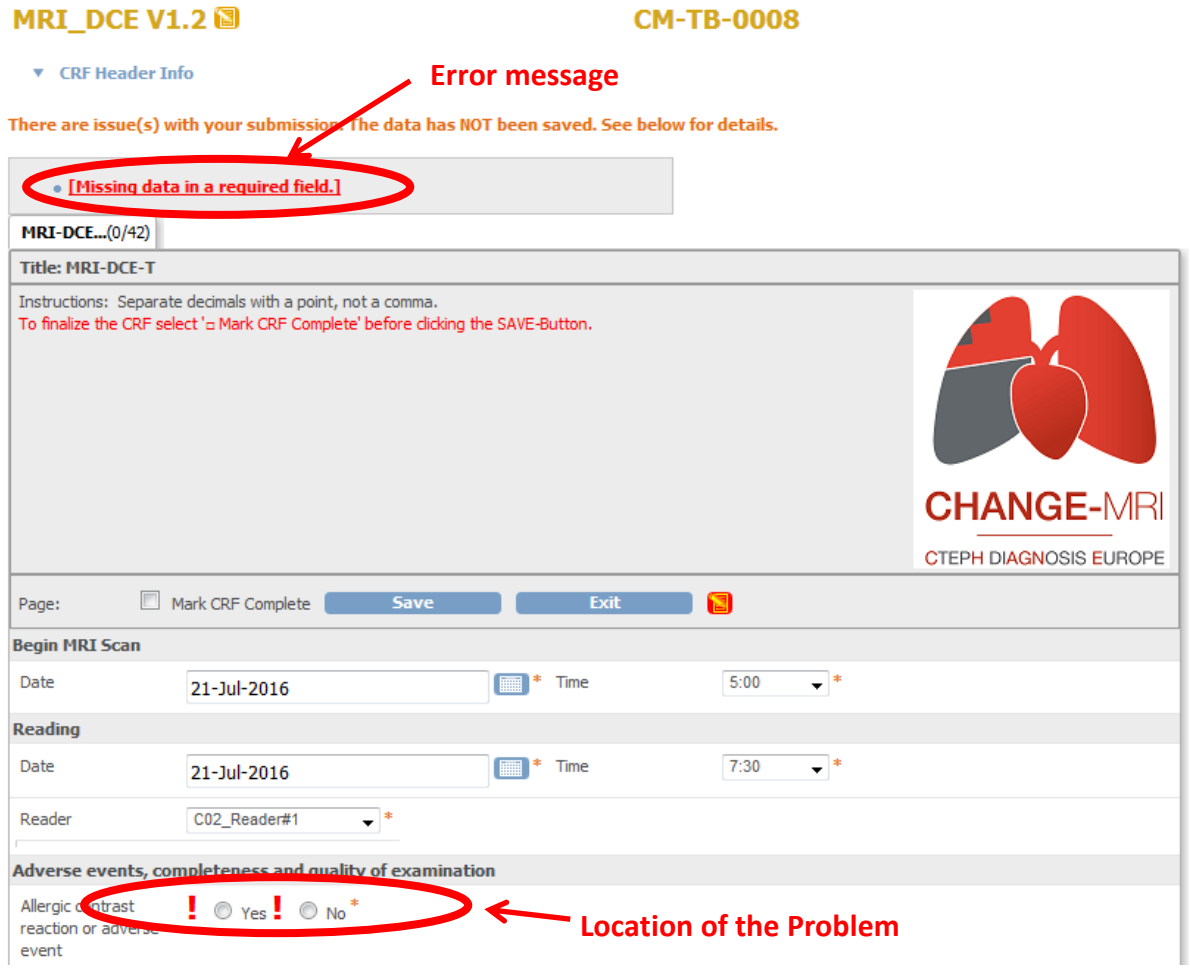
Finish the data entry with "Save" button, don't use the „Mark CRF Complete" checkbox.
This function is used later, after the values have been checked by our biometrics.

6 OpenClinica error messages

After clicking the "**SAVE**" button OpenClinica performs validation/plausibility/format checks to ensure data integrity. For each failed check OpenClinica displays an error message which may be used as a link to the respective item of the CRF (marked by one or two bold red exclamation marks). These issues have to be solved before the CRF data can be saved to the database. In the following chapters error messages are listed and solutions are provided.

6.1 Error: Missing data in a required field

This error message occurs, if a required (see asterix * right beside the item) data field is empty. The problem may be solved by entering data for the item.



6.2 Error: Only provide if ….

This error message occurs, if the previous saved version of the CRF contains data for an additional inserted item, but the cause for the insertion of the additional item in the current version of the CRF has been dropped out.

E.g. in the previous saved CRF version an allergic contrast reaction "**skin eruption**" has been entered and in the current CRF version only the radio button for "**Allergic contrast reaction**" has been switched from "**Yes**" to "**No**" but the text field still contains "**skin erythema**". To solve this class of problems, the odd item must be cleared. The method of how to clear an item depends on the type of the item:

- Text fields: Delete the entered text
- Checkboxes: Deselect all checkboxes
- Single- or multiselect dropfields: Deselect all items by **<CTRL>+<SPACE>**

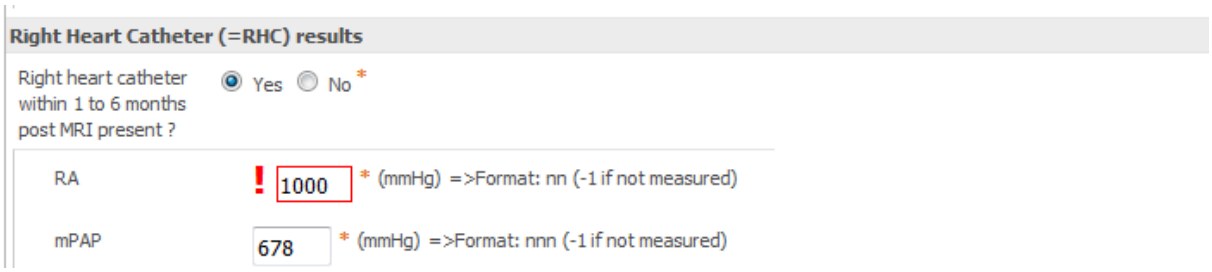
- Radio buttons: Using the blue "**UNDO**" button right beside the item

6.3 Message: MRI/SPECT PE=… has been entered! Please click "SAVE" again...

This kind of messages may occur only in MRI or SPECT CRFs. The cause for the message is a technical hint of OpenClinica to allow sending an Email to the Change-MRI Email daemon to allow in-place diagnostic. To solve the problem just click "**SAVE**" again.

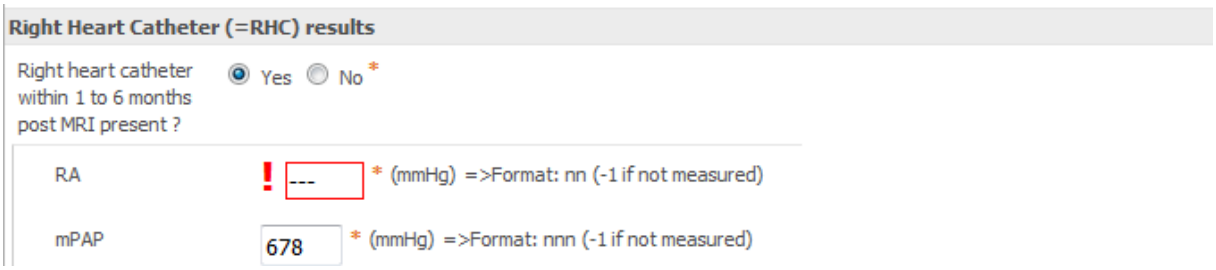
6.4 Error: Input exceeds required width=…

This error message is caused by the OpenClinica format check for numerical input data, if e.g. a numerical input field is limited to 2 digits (format: nn), but the entered data format was 4 digits (=1000). To solve the problem, the entered data must be adjusted to fit the specified format definitions.



6.5 Error: The input you provided is not an integer., Input exceeds required width=….

This error message is caused by the OpenClinica format check for numerical input data, if e.g. text is entered instead of a numerical value. To solve the problem, the entered data must be adjusted to a numerical value (e.g. -1, if not present).



.

6.6 Error: CRF Unavailable

OpenClinica prevents that more than one user enter data at the same time in one CRF. If you try to enter data during another user is already entering data OpenClinica will not show you the CRF but instead display a message that the CRF is unavailable. The message will also indicate the user currently editing the CRF. When the other user exits the CRF, you will be able to edit it.

7. Uploading of files to the SFTP area (Central pooling)

7.1 Introduction

Before a procedure is initiated please read carefully the instructions for every step of the procedure.

This SOP is intended for the data entry user of the CHANGE-MRI study. It describes the procedure for uploading of DICOM data files for central reviewing (e.g. MRI or SPECT). Additional modalities can be included if necessary. **IMORTANT: All the files must be pseudonymised and identified with the correct patient identification number before the files can be uploaded.** See the respective SOPs for Pseudonymisation provided b by the Study Centre in Hannover.

7.2 What is needed for secure FTP-Uploading of files?

The suggestion is to use the “FileZilla” client that is a free SFTP tool. Of course you can use any other efficient secure file transfer (sFTP) tool. In the following description you find information for downloading, installing, configuring and using the “FileZilla” tool.

Procedure

1.1. Download of FileZilla
Go to the following internet site and download the client setup file for the tool (note that an internet site might be available in your language of origin for your country):
https://filezilla-project.org/
Load down a current version. (We did it with FileZilla_3.9.0.3_win32-setup.exe)

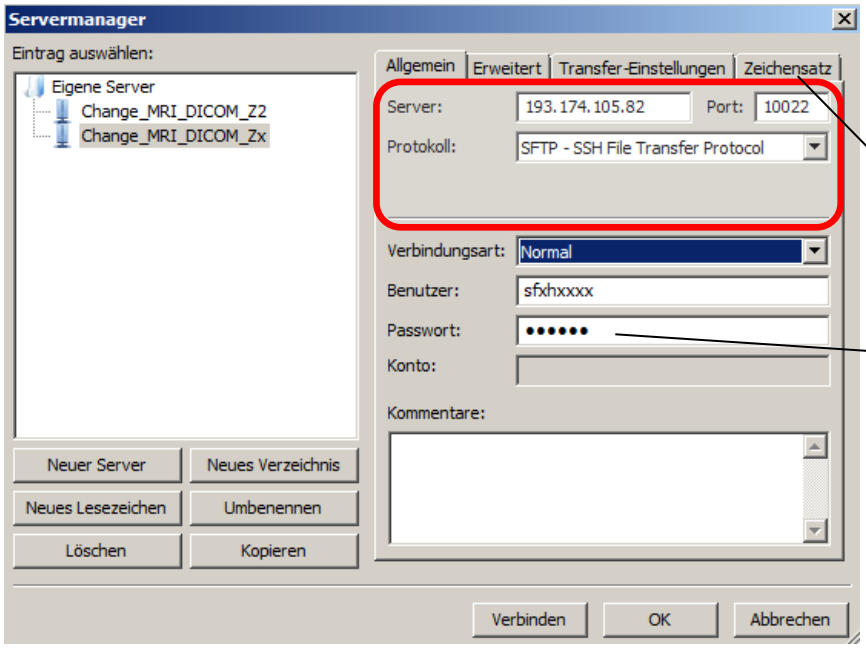
1.2. Installation
Administrative privileges are required. Double click the setup file and follow the install instructions.

1.3. Application for a user account at the FTP-Server for CHANGE-MRI
An application form is provided. After you received your account data you are able to configure the FileZilla tool

1.4. Configuration
After start of FileZilla got to File → Site Manager.

You will get the needed information by application data:

Customize according for New Site → , Host → , Port →, and User →



Customize the server connect with ….

Will be provided with your user application

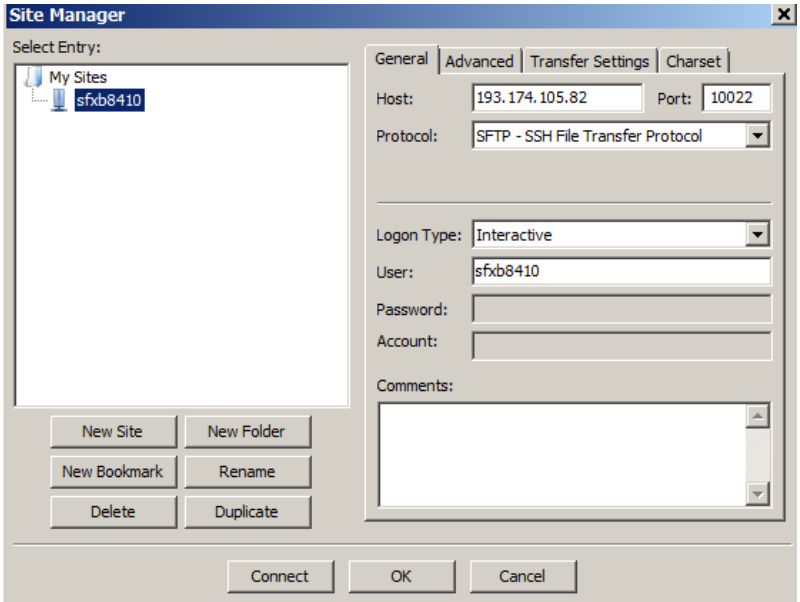
Save the customization with OK.

1.5. Use of FileZilla for file uploading

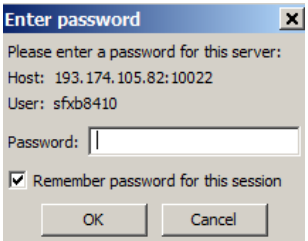
After successful customising start the session

File → Site Manger → select **your** site.

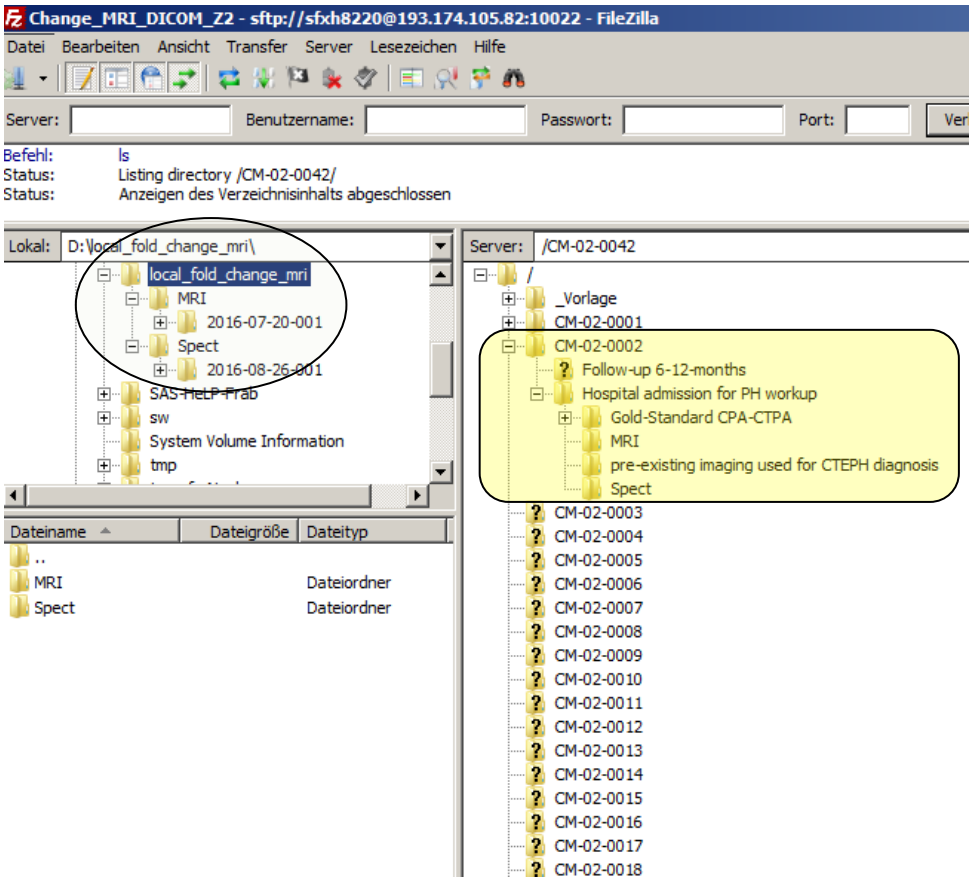
Here an example server connect is used



Connect and enter your password



Then you will find a similar situation (e.g. centre 2 here) as shown in the next picture.



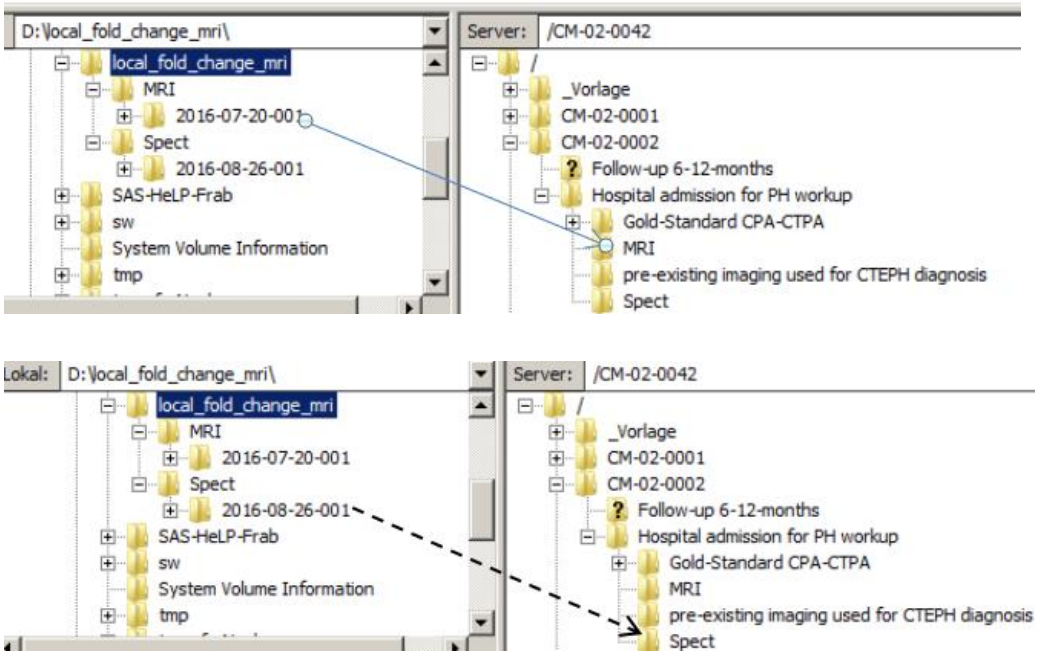
On the left-hand side you can find your local site with local and network drives.
Please create here a similar local directory structure as on the remote site already is prepared. See the arrow above

On the right-hand side you can see the Remote file system on the SFTP-Server in Hannover.
Each study site has on the SFTP-Server a directory tree similar to what is shown in the picture above on the right side. If you are a member of site 2 you only can access the site specific sFTp area for centre 2. If you want to upload files for patient CM-02-002 go the respective directory. There you will find a prepared directory structure with sub folders 'Follow-up 6-12-months', 'Hospital admission for PH workup' on the right side.

It is recommend creating a similar directory tree on your local computer where you can collect the files up to the next upload. You can copy the e.g. MRI scanning '2016-07-20-001' from MRI per drag and drop from your local MRI directory to the remote sftp area .

Please assure yourself, that **ALL FILES ARE ANONYMISED AND PROVIDED WITH THE CHANGE-MRI PATIENT-ID** (CM-Site-No-Patient-No: e. g. CM-02-045).
Just so the files are able to be linked to the associated patient!

Copy from local to Remote:



Mark the files in the left side of the browser, press the left mouse button and drag the files to the destination folder on the remote site.
In Append you can find the 'Application for a secure FTP-Account', at most two accounts in different sftp areas are available for one site. Only one account (one user & password combination) is available for one sftp area.

Version	Author(s)	Date	Changes	Approved by
1.0				
1.1				

Application for a secure FTP-Account

Hereby, the Change-MRI clinical centre ..... (short name of clinical centre) applies for a site-specific account to access the area of the file pooling secure FTP server to which image files (and ISFs,TIFs) within the Change-MRI project should be uploaded. **Single FTP-Account per modality (MRI/VQSpect) per site.**

The following person[1] will be responsible for this account and ensure clinical and account data security and confidentiality. **Data must be pseudonymised before uploading.**

Modality	First name	Last name	Profession	Email address	Signature
1 MRI					
2 VQSpect					

....

Date, place and signature of applicant 1 Date, place and signature of applicant 1

Please email the signed and scanned form to Change-MRI-DM@mh-hannover.de. You and the individuals will then be provided with login details and the required information.

[1]This must be a known person to the Change-MRI management