Cardiac T2*

Instruction Manual

Resonance Health
Be Better Informed

Thank you for choosing CardiacT2*!

CardiacT2* is a medical device that quantifies liver iron concentration from specially acquired magnetic resonance images. Use of CardiacT2*requires the user to acquire MRI images using a specific MRI data acquisition protocol and send those images to the CardiacT2*medical device for analysis. CardiacT2*is a software tool that analyses the acquired data in a single step to produce a heart iron concentration report.

If you have any questions about this product or its operation, please contact your local distributor or the manufacturer RESONANCE HEALTH ANALYSIS SERVICES PTY LTD.

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PATIENT SCANNING CHECKLIST

If you are having problems with any of these imaging parameters, please contact Resonance Health for assistance. Resonance Health cannot accept image data for Cardiac T2* analysis that does not comply with the requirements.

Patient with ECG setup is done properly.	☐
An 8 TE cardiac T2* sequence (either dark blood or bright blood method) has been setup as per requirements. A cardiac localizer and a volume shimming have been performed.	☐
Imaging Plane and Field of View (FOV) Short axis middle-ventricular imaging plane is selected and the in-plane FOV is adjusted/rotated to make the Phase Encoding Direction (PED) roughly perpendicular to the middle of inter-ventricular wall.	☐ ☐
DO NOT USE: CLEAR, SCIC, (Pre-Scan) normalize, Parallel imaging (such as, SENSE), Image filtering, etc…	☐
Acquisition Matrix is set at 256×96. Acquisition (Scan) Time is targeted < 15 s.	☐
Data acquisition is recommended within the diastolic phase.	☐
Repeat the scan at least THREE times with the same settings.	☐
The FAST electronic Patient Job Request Form is consistent with the patient information entered into the image header.	☐

INTRODUCTION TO CARDIAC T2*

Resonance Health provides a dual analysis service to customers who require a cardiac T2* analysis in addition to FerriScan. This is offered as a packaged service for both analyses. Alternatively, cardiac T2* analysis is also offered as a stand-alone service.

This manual provides information about the cardiac T2* imaging only. FerriScan imaging requirements are detailed in the FerriScan Instruction Manual.

MRI is an ideal medium for the assessment of iron overload as the iron produces disturbances in the magnetic field and the greater the iron load, the greater the signal decay rate. Figure 1 below shows a short axis mid-ventricular T2* image of the heart. Echo times from <3ms to >16ms are used to assess the signal intensities in the septum from which the cardiac T2* (R2*) can be calculated.

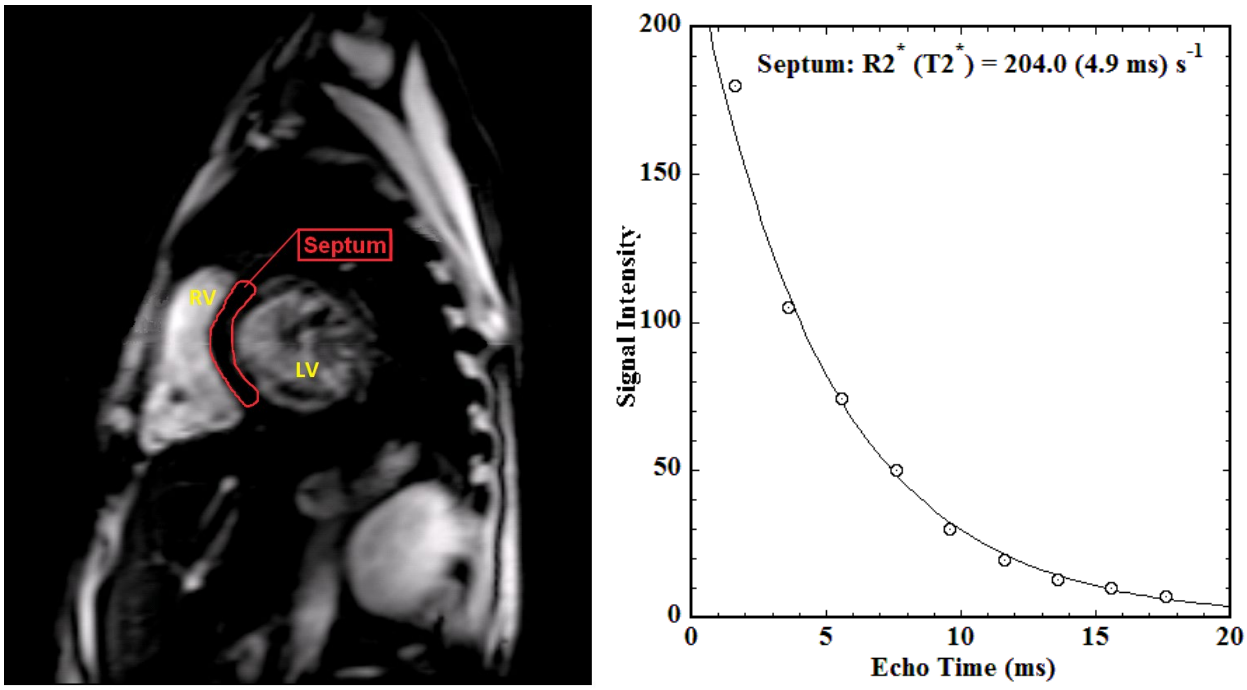


Figure 1. Note that the septum outline is for illustrative purposes only. Resonance Health endeavors to maximise the septum region. However, the area selected for analysis will vary depending on the level of artefac.

There are several published methods for acquiring data for cardiac T2* analysis which may vary across MRI scanners. They generally involve a breath-hold (usually 8-12 seconds) multi echo gradient echo pulse sequence to acquire a series of images at different echo times with either dark blood or bright blood method. An ECG-gated sequence is used to compensate for cardiac motion.

The cardiac T2* imaging protocol provided by your MRI scanner manufacturer should be used with modification defined in this protocol. Please contact your MRI manufacturer for the recommended cardiac T2* protocol for your scanner.

It is recommended to use a consistent set of image acquisition parameters for all patient scans to enable results to be compared over time.

The quality of the image data will affect the T2* result. The MRI Centre is responsible for providing Resonance Health with high quality images suitable for T2* analysis. If your staff are not sufficiently experienced in Cardiac T2* image acquisition, please consult your MRI manufacturer for additional training. Resonance Health provides several image acquisition recommendations aimed at increasing the reliability and quality of the acquired image data. Refer to steps 1 and 2.

STEP 1: DETERMINE SUITABILITY OF MRI SCANNER FOR PERFORMING CARDIAC T2*

An *MRI Centre Scanner Details* form will be sent to centres requesting this service. The purpose of this form is to capture information to enable Resonance Health to determine whether an MRI scanner will be suitable for performing FerriScan and cardiac T2* analyses.

THE TECHNICAL REQUIREMENTS FOR CENTRES ACQUIRING MR IMAGES FOR CARDIAC T2* ANALYSES ARE:

- MRI centre personnel with experience in acquiring cardiac MR images
- MRI scanner with a field strength of 1.5 Tesla with a cardiac MRI package that includes:
    - An RF coil suitable for acquiring cardiac images
    - An ECG facility
    - A single-breath-hold, multi-echo T2* sequence
    - Total of 8 echo times (TEs) or reduce/increase to 8 TEs if more/less TEs are in the default cardiac T2* sequence
        - Minimum TE < 3ms (the lower the better)
          The ability to achieve the minimum TE is dependent on the gradient performance of the scanner and other parameter settings. It may be necessary for sampling bandwidth to be adjusted to achieve the minimum TE.
        - Maximum TE > 16ms (ideally only **ONE** TE above 16ms)

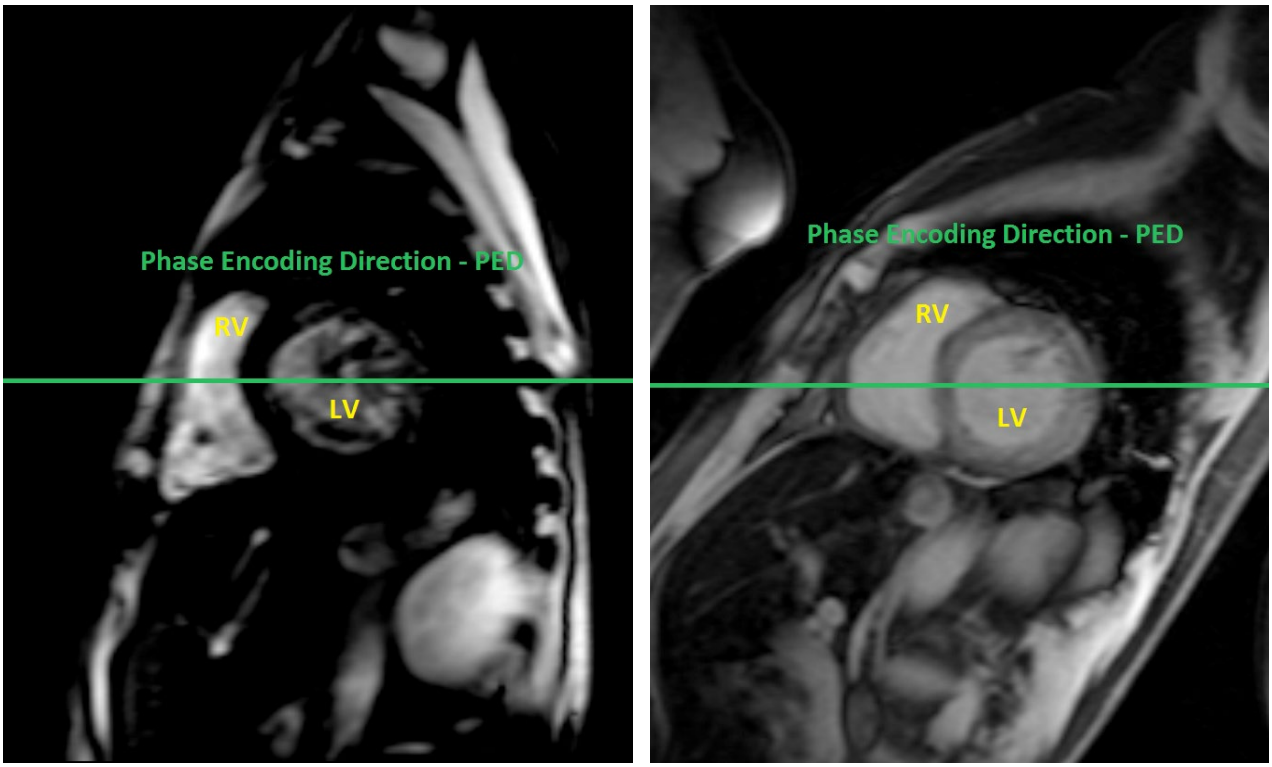
Contact Resonance Health for technical support if there are any issues.

STEP 2: ACQUIRE IMAGES FOR CARDIAC T2* ANALYSIS

Recommended data acquisition parameters for Resonance Health Cardiac T2* analysis.

A single, short axis mid-ventricular slice is to be acquired using a single-breath-hold, multi-echo T2* sequence (pre-set) on the MRI scanner. Refer to example acquisitions in Figure 2 (A and B).

It is requested that sites with limited Cardiac T2* experience initially scan a Test Patient and submit the data to Resonance Health to verify acceptable acquisition.



A **B**

Figure 2 Imaging position and FOV setting.

- Image data is to be acquired with 8 different echo times (TE); with the minimum TE < 3ms (the lower the better) and the maximum TE ≥ 16ms (ideally only one TE above 16ms).
- Refer to *Table 1* for recommended key acquisition parameter settings. All other acquisition parameters should be retained as per the default settings of the scanner for the pre-set single-breath-hold, multi-echo T2* sequence.
- Acquire the slice data at least three (3) times. If necessary (after reviewing the image quality of the acquisition data), additional scans may be needed. This is not mandatory, however will reduce the likelihood of a patient recall. Resonance Health will review the acquisitions and select the one with best overall image quality for analysis.

It is important to use the recommended image acquisition parameters from the table below in order to maintain the consistency and quality of the image data and consequently the quality of the analysis results.

Table 1. Summary of key acquisition recommendations and parameter settings

Recommendation/Parameter	Value	Comment
Perform a volume shimming before acquiring patient T2* data.	N/A	The aim is to improve image quality and reduce artefacts.
Use a single breath hold, multi gradient echo T2* sequence (*mandatory*), either dark blood or bright blood method.	N/A	The aim is to reduce artefacts and maintain a consistent septum position. A single gradient echo T2* sequence is **not** suitable for data acquisition.
Set the in-plane FOV position such that the Phase Encoding Direction is approx. perpendicular to the middle of the inter-ventricular septum.	N/A	The aim is to reduce motion artefact in the septum area for a more reliable analysis (refer to Figure 2 A and B). Use a rectangular FOV.
Acquire the same mid-ventricular slice at least 3 times.	N/A	Reduce the likelihood of patient recall. Use the same settings and imaging position.
Maintain consistent image acquisition parameter settings across patients and time.	N/A	The aim is to simplify the patient scanning process and maintain image and analysis quality. Only change settings if it is strictly required.
Echo-times	8 TE images - Min TE < 3 ms - Max TE > 16 ms	The lower the first TE the better. Ideally only one (1) TE greater than 16 ms.
FOV	300 x 400 mm	Use a rectangular FOV. Can be smaller to reduce scan time but ensure to maintain the voxel size at 1.56mm.
Freq. encoding matrix	256	To obtain a voxel size of 1.56mm.
Phase encoding matrix	≤ 96	To limit the scan time.
Slice thickness	10 mm	To maintain SNR.
Flip angle	20 – 30 degrees	To reduce T1 effect.
Scan Time	Targeting < 15 seconds	Related to heart rate and scan settings.
Data Acquisition Window	Recommended within diastolic phase	Setting linked to heart rate.

DO NOT USE: Spatially variable normalization	DO NOT USE: CLEAR, SCIC, (Pre-Scan) normalize, Parallel imaging, Image filtering, etc…	Turn off to avoid artificial signal intensity changes that may impact the T2* measurement.

For patients who are unable to hold their breath successfully, it is recommended to repeat the acquisition. Contact Resonance Health for other options if breath-holding continues to be an issue for a particular patient.

STEP 3: REGISTRATION IN FAST

FAST is a secure website that allows data transfer to Resonance Health. It can be accessed by selecting the **FAST Logon** link at www.resonancehealth.com. FAST also enables you to track the progress of jobs and receive results electronically from Resonance Health.

Detailed instructions on using FAST can be found in Step 6.

STEP 4: CARDIAC IMAGING SETUP – TEST SUBJECT

A test scan with a volunteer using the Cardiac T2* protocol is required as a part of the setup process. Resonance Health will review the received test scan image data to determine whether the setup is successful or further work is needed. A certification letter will be issued to site upon a successful test scan to inform the real patient scan may start.

STEP 5: SCANNING FOR CARDIAC T2*

In principle, the same Cardiac T2* sequence with individual data acquisition window adjustment can be used for all patients unless the FOV size becomes inappropriate. It is important to ask patients to hold their breath long enough allowing the image acquisition to finish promptly. The following tips may be helpful:

- Monitoring the scan time (as also heart rate dependent) to make sure it is short enough for patient to hold breath comfortably.
- Placing the data acquisition window at the diastolic phase tends to reduce artefacts level.
- Adjust the in-plane FOV to make sure the Phase Encoding Direction roughly perpendicular to the middle of the inter-septum wall (refer to Fig 2).
- Repeat the same acquisition at least three times as an insurance policy.
- Review the image quality to see whether furthermore scans are needed.

STEP 6: ELECTRONIC TRANSMISSION OF MRI IMAGE DATA TO RESONANCE HEALTH VIA FAST

Lodging a Cardiac T2* Job

1. Locate the folder containing the acquired Cardiac T2* DICOM images and compress the folder into a single .zip file.
2. Log on to FAST by selecting the **FAST Login** link at www.resonancehealth.com.
3. Select **New Patient Job** from the menu on the left and select the "**Cardiac T2*** (component of Dual Service)" option (refer to Figure 3).

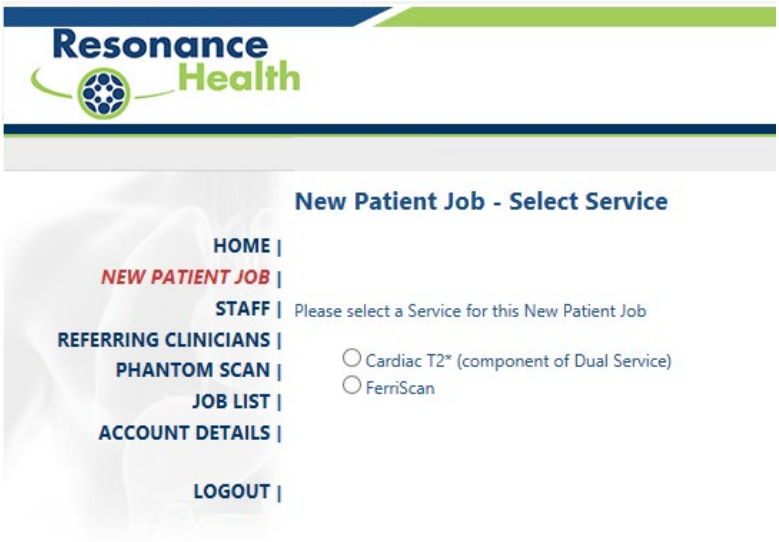


Figure 3 - Select Service

4. Upon selecting the required service, you are presented with the "**Submit image files**" screen. This continues to the upload screen.
5. Locate the .zip file using the "**Browse**" button and click on the **Submit files** link. This will begin the transfer process. When the transfer is finished, the Cardiac T2* Job Request Form will be displayed.
6. Select the "Cardiac T2* (component of Dual Service)" **Billing Category**.
7. Enter the Patient's **First Name** and **Surname**, EXACTLY AS ENTERED ON THE SCANNER PLATFORM. Enter **Test Patient** if applicable.

   Some of the fields may already be pre-populated with information retrieved from the DICOM image header.

Note: If the job is a part of a clinical trial that requires de-identification of patient information, please do so and provide only the trial-specific anonymised identifier for the patient.

8. Enter the Patient's **Date of birth** in the format of DD MMM YYYY (e.g. 01 Jan 2000).
9. Enter the **Patient ID**, EXACTLY AS ENTERED WHEN REGISTERING THE STUDY.
10. Select the appropriate **Scanner** from the drop-down menu.

11. Enter the **Referring Clinician**. If a referring clinician was entered when registering the study this is to be entered EXACTLY.
12. In the **Email Completion Notification to** field tick the checkbox for **Clinician** and enter the Referring Clinician's email address if you would like them to be notified that the results are available. Click on **Other Staff**. Tick the relevant staff member(s) to whom notification of result availability and other correspondence regarding the job is to be made. Once the selection is complete click on **Finish Selection**.

    Note: the email notifications that the result is available do not contain the patient results. It is the responsibility of the MRI Centre to retrieve the result from FAST and forward it to the clinician.
13. The **Comments** field is an optional field and may be used either for your reference or to provide notes to Resonance Health staff. If requested, these details may be produced on the Patient Report.
14. The **Customer Reference** field is an optional field and may be used for your reference. Details entered in this field will not be produced on the Patient Report.
15. Ensure that the Job Request Form is populated correctly and tick the "**I confirm the above information is correct**" declaration box.
16. Click on **Submit** link to complete job submission process.

Note: Upon submission a job will display in the Queued Jobs queue. Whilst in this queue the job details may be edited. Once processing of the job commences at Resonance Health the job will move to the Jobs in Progress queue and details can no longer be edited.

Resonance Health

HOME |
NEW PATIENT JOB |
STAFF |
REFERRING CLINICIANS |
PHANTOM SCAN |
JOB LIST |
ACCOUNT DETAILS |
LOGOUT |

New Cardiac T2* (component of Dual Service) Job Request Form

Please enter the details of the next job.

Please ensure that data entered into this form is accurate as some of the information is reproduced onto the Patient Report.

Billing Category: * ○ Cardiac T2* (component of Dual Service)

Subject:

First Name: * Joe

Surname: * Smith

Date of Birth: * 01 Jan 1950 (e.g. 28 May 2018)

Patient ID: * ABC123

Suspected Condition: *
- ☐ Haemochromatosis
- ☑ Thalassaemia
- ☐ Sickle Cell Anaemia
- ☐ Myelodysplastic Syndrome
- ☐ Other (please specify below)
- ☐ Don't Know

Scanner: * Siemens Magnetom Aera

Referring Clinician: * -- please select one --

Add New Referring Clinician

Email Completion Notification to: ☐ Clinician

Clinician Email:

Other Staff *(0 selected)*

Comments: Cardiac T2* component of the Dual Service with FerriScan 10025123

Customer Reference:

Confirm and Submit: * ☑ I confirm the above information is correct. Submit

* Denotes required items

Figure 4 – Cardiac T2* Job Request Form

STEP 7: RESONANCE HEALTH PROVIDES THE CARDIAC T2* REPORT

The Cardiac T2* report is provided via FAST. The MRI person with access to FAST must download the Report and provide it to the referring clinician as required. How to use FAST to access Cardiac T2* results is described in Appendix 1.

APPENDIX 1: THE FAST SYSTEM

The FAST system provides a convenient, secure and HIPAA-compliant mechanism for MRI Centres to submit Job Requests and transfer data to Resonance Health, as well as to receive results.

FAST LOGIN ID AND PASSWORD

1. A Login ID and temporary password will be emailed to the authorised MRI Centre contacts as part of the setup procedure. You will then be required to set a new password and set up your security credentials. The answer to your security question must be between 3 and 30 characters long and can contain numbers, letters and spaces. After the security question and answers have been successfully setup, the password MUST contain the following:

    - At least eight '8' characters
    - At least '1' upper-case, '1' lower-case character and '1' numeral
    - At least one of the following special characters (i.e.'! @#$%&_?-.)
    - No character may occur 4 or more consecutive times (i.e. Apple1111)
    - Password must not have been used in the past 12 months

2. Navigate to the secure FAST system by selecting the **FAST Logon** link at www.resonancehealth.com.
3. If you have forgotten your login ID, select the **FORGOT LOGIN ID** link, enter your email address and select **continue**. Follow the prompts.
4. If you have forgotten your password, select the **FORGOT PASSWORD** link, enter your login ID and select **continue**. Follow the prompts.
5. To change the password, first enter the **Login ID**, and then click on **CHANGE PASSWORD**. Enter the **Login ID, Current Password**, and then the new password in both the **New Password** and **Confirm New Password** fields. Click **SET PASSWORD** and then **CONTINUE**.
6. To change the security question, first enter the Login ID, and then click on change security question. Enter the Login ID, Current Password, and then select a new question and answer in the two required fields. Click change and then continue.
6. **It is your responsibility to keep your password secure and safe at all times.**

Figure 11: Login ID required for setup

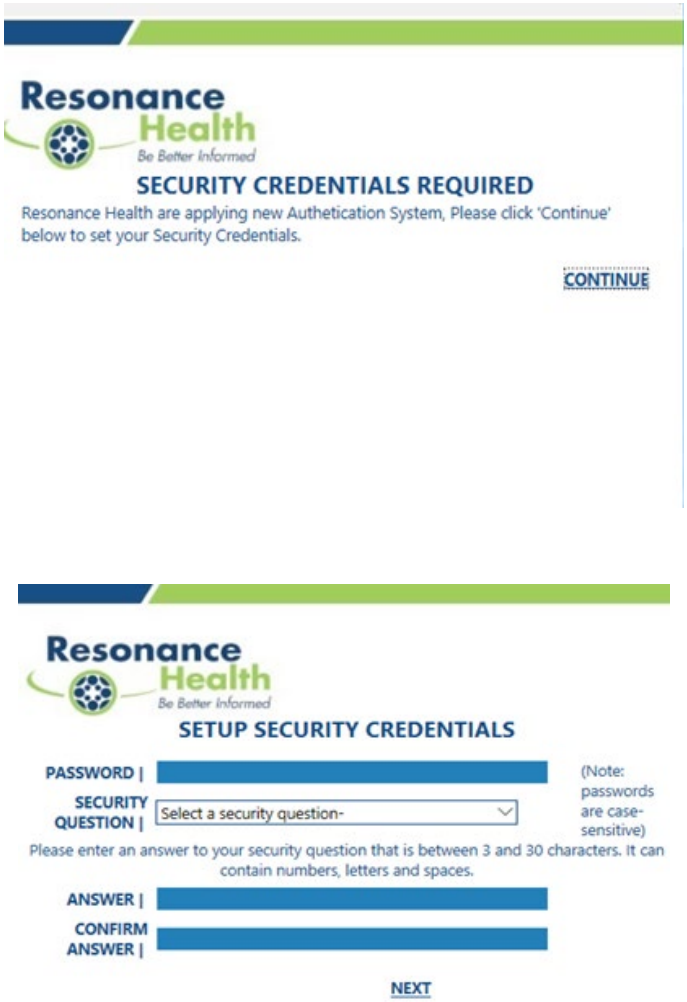
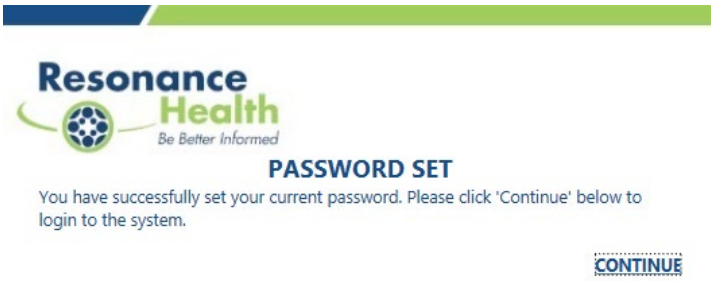


Figure 12: Security Credentials setup



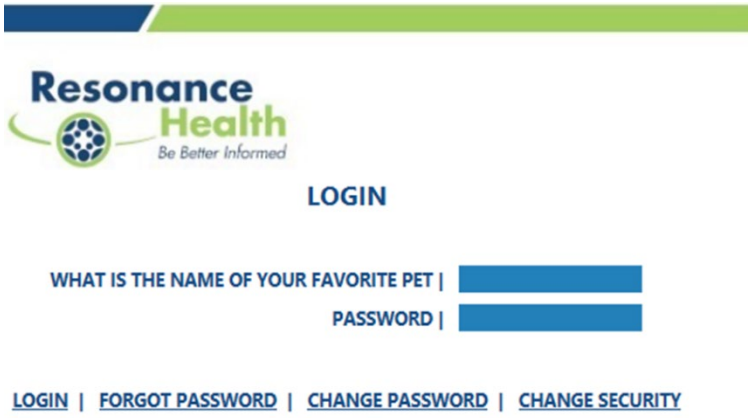


Figure 13: Password setup

VIEWING FAST JOB QUEUES AND JOB STATUS

1. Log on to the secure FAST system by selecting the **FAST Logon** link at www.resonancehealth.com. Enter the logon ID and password and click **login**.

2. Upon successful login, the **Home** page will appear containing your job queues. Every job submitted for Analysis will progress through a number of these queues. To view details of any job, click on the respective job link. The queues are as follows:

   Awaiting Response: Jobs are placed in this queue if Resonance Health is awaiting information before proceeding with the analysis. Please check your email for action to be taken before Resonance Health can proceed with analysis.

   Completed Jobs (last 30 days): Jobs that have been completed by Resonance Health within the past 30 days. To download a PDF version of the Cardiac T2*Report, click on the respective job link to view the job details and click on the image result file.

   Queued Jobs: Jobs that have been submitted to Resonance Health and are awaiting processing. The jobs can be removed from this queue by clicking on the **delete job** link.

   Jobs In Progress: Jobs that have been submitted to Resonance Health and are currently in the process of being analysed by Resonance Health.

   Unsuitable for Analysis: Jobs that Resonance Health have deemed unsuitable for analysis. A new Job Request with suitable data will need to be lodged in order to receive a result. Please check your email for action to be taken.

   Note: On the **Home** page only 5 jobs will be displayed for each queue, with the total number of jobs listed in brackets for each queue. To view all of the jobs for a particular queue, select the **more jobs....** link for that queue. Only jobs specific to that queue will be displayed. To return to the list of all queues select the **show all queues** link. The jobs within each queue will generally be displayed with the oldest at the top of the queue. In order to reverse the order of the jobs in the queues (so that the most recent job is at the top of the queue), click **Reverse Sorting**.

3. To refresh a webpage and update the latest data for the queues, click **refresh queues**.

SEARCHING FAST

1. Click on **Job List** on the main menu to search for a particular job or set of jobs in FAST.
2. Select **All Statuses** or select a specific status (e.g. Completed, In Progress).
3. Select **Service** to narrow the search to one or multiple services.
4. **Keywords** can be entered to locate a specific job(s). The following details are searchable: Patient First Name, Patient Surname, Patient ID, Job ID and Referring Clinician fields.

   Note: If multiple keywords are entered all jobs with ANY one (or more) of the keywords will be listed.
5. To search for jobs with known dates, select the **Date Filter** of interest from due date, completed date, scan date or subject DOB (patient date of birth). Either keep the current default date range or enter in the start and end date as required to narrow the list of jobs returned in the search.
6. Click on the **Search** link to return the search result.
7. Click on the **Extract** link to receive an email containing a spreadsheet of the search results.

APPENDIX 2: SCANNER VERIFICATION LETTER

02 Jan 2019

MRI Centre

Cardiac T2* Scanner Verification Acceptance Letter

Dear Doctor,

We are delighted to advise that your Phantom data (Job Number: 1000001]) scanned on 01 Jan 2019 on your Siemens 123456 scanner has been successfully completed and accepted for analysis. You may now commence patient or clinical trial scanning on this scanner.

Please note that it is a requirement that scanning parameters used to scan the Phantom data remain the same for all patient or clinical trial scanning. Please refer to your MRI Centre Manual for further instructions.

In addition, verification of the MRI scanner is required in the following circumstances:

1. If you purchase a new scanner,
2. If you are using Clinical Trial services, reverification is required on an annual basis or as stated in specific trial requirements,
3. Following any major software or hardware upgrades to an existing scanner. For further information regarding what constitutes a major upgrade please email support@resonancehealth.com.

MRI Centres will be notified by email when their scanner is due for reverification. A new Phantom Pack will be sent as required.

Should you or anyone else at your organisation have any questions about our service, please do not hesitate to contact us.

I would like to take this opportunity to sincerely thank you for your participation and we look forward to working with you in the future.

Kind Regards

Service Centre Manager
Resonance Health
support@resonancehealth.com

APPENDIX 3: SAMPLE CARDIAC T2* REPORT

Cardiac T2* Report

Report No:	10000001_S12	Scan Date:	12 Jul 2018
Birth Date:	10 Aug 2003	Analysis Date:	12 Jul 2018
Patient Name:	PATIENT, Patient		
Patient ID:	ABC-12345678		
Referrer:	Dr Doctor		
MRI Centre:	MRI Centre Name		

Cardiac T2* measurement: 10.0 ms

Cardiac R2* measurement: 100.1 /s

Authorised by: Service Centre Manager

The following may be used as a general guideline for interpreting cardiac T2* and R2* values:

T2* > 20 ms **R2* < 50 /s**	Cardiac iron deposition is not apparent
T2* 10 - 20 ms **R2* 50 - 100 /s**	Some cardiac iron deposition has occurred but there is little immediate risk of iron-induced cardiac decompensation
T2* < 10 ms **R2* > 100 /s**	Significantly increased risk of iron-induced cardiac decompensation

Adapted from Wood J.C. Magnetic resonance imaging measurement of iron overload, Current Opinion in Hematology 2007 14:183-190

Cardiac T2* decreases as tissue iron concentration increases. Cardiac T2* has an approximately inverse relationship with tissue iron concentration. Hence a change of 1 ms at low values of T2* corresponds to a larger change in iron concentration than a change of 1 ms at high values of T2*.

Cardiac R2* increases as tissue iron concentration increases. Cardiac R2* has an approximately linear relationship with tissue iron concentration. Hence a change of 1 /s corresponds to the same change in iron concentration at all values of R2*.

Resonance Health Analysis Services Pty Ltd www.resonancehealth.com

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APPENDIX 4: GLOSSARY

cm	Centimetre
DICOM	Digital Imaging and Communications in Medicine
DOB	Date of Birth
FAST	FerriScan Analysis Service Tracking system
FAQ	Frequently Asked Questions
FOV	Field of View
ID	Identification
mm	millimetre
MRI	Magnetic Resonance Image
ms	Millisecond
No.	Number
PACS	Picture Archiving and Communication System
PDF	Portable Document Format
Pty Ltd	Proprietary Limited
R_2^*	Effective Proton Transverse Relaxation Rate
RHAS	Resonance Health Analysis Services Pty Ltd
RF	Radio Frequency
RFOV	Rectangular Field of View
ROI	Region of Interest
T	Tesla
T_2^*	Effective Proton Transverse Relaxation Time Constant
TE	Echo Time
TR	Repetition Time

REVISION RECORD

Revision	Qualio	DCC#	Date	Description of Change
5		2721	18 Jun 18	Changed from a Form to an MRI Centre Manual. Inserted Appendix, Glossary, Table of Content, checklist and broke it down in to steps. Added information regarding FAST access. Updated screenshots and minor formatting changes.
6	2.0	2732	17 June 2019	Appendix1: changed criteria for password set up and 2 factor authentications for users. Added screenshots to aid in the setup of security credentials and password. Inserted new analysis report template and scanner verification letter.
	3.0	NA	26 May 2022	Layout changed with current branding.


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