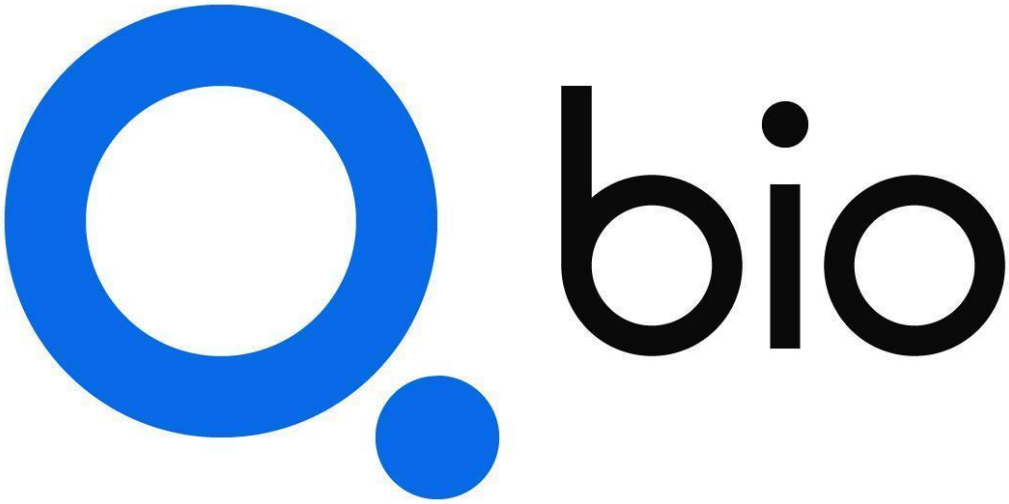


Constellation v1.5 User Manual

Revision A.0

Rx Only

Table of Contents

1. Introduction

Welcome to the User Manual for Constellation, a Command Line Interface (CLI) software tool developed for the analysis of MR image datasets. This document provides essential information on how to safely and effectively use the software to achieve the intended purposes. Please read this document carefully before using the software tool.

1.1. Device Information

Q Bio

1411 Industrial Road

San Carlos, California 94070

Device Name: Constellation™

Contact Email: support@q.bio

Model Number: CON-001

1.2. Indications for Use

Constellation is intended for non-invasive labeling and calculation of quantitative measurements for anatomical regions. Constellation utilizes DICOM MR images gathered on a GE MR450W that encompass the whole-body. It is intended to be used for healthy adult patients. Clinicians may use Constellation as a clinical decision support tool, but it is not to be used in triage events, emergency medicine, or critical care. A clinician retains the ultimate responsibility for making the pertinent diagnosis based on their standard practices.

1.3. Intended Users, Uses, and Use Environment

Constellation is a software application that stitches together MR images, automatically labels, and calculates quantitative measurements for anatomical regions. The device outputs are designed to be used by clinicians as a clinical decision support tool and are not to be used in triage events, emergency medicine, or critical care. It is not intended to be a sole source of medical diagnosis. A clinician retains the ultimate responsibility for making the pertinent diagnosis based on their standard practices.

Constellation is an Rx Only device that is not intended to be used by patients or untrained individuals. Constellation is intended to be used for a healthy, adult patient population.

Constellation software users are expected to be Q Bio company employees that execute a Constellation workflow. Employees are expected to be familiar with operating a computer and using the command line functions on a computer. Constellation supports an additional option for initiating processing via a cloud-based service. Constellation outputs users are expected to be clinicians. Before operating Constellation or using any of its outputs—including PDF report and machine-readable formats—both software and clinician users are required to read and understand the information contained in this User Manual. Clinicians are expected to use their best clinical judgment to make pertinent diagnoses when using Constellation outputs.

Constellation is classified as a Software as a Medical Device (SaMD) and is developed by Q Bio. The PDF report output of Constellation is intended for viewing on devices supporting PDF v1.3 file format. Alternatively, Clinicians can also access the same data in machine-readable formats (e.g. JSON and NIfTI files).

2. Warnings, Contraindications, and Prec⚠tions

2.1. Warnings

- Constellation outputs do not provide a sole diagnosis or diagnostic recommendations. Radiologists and other relevant clinicians may use Constellation in conjunction with other clinical findings as a part of a wider clinical assessment process.
- Patient management decisions should not be made based solely on the results from Constellation.
- Constellation outputs should only be reviewed and interpreted by trained radiologists and clinicians who have appropriate anatomical knowledge and are trained to read radiological images.
- Using an incorrect MR scan protocol may affect results.
- MRI artifacts due to noise, motion, or other causes may affect results.
- Reports that show missing relevant anatomical region data should not be considered as a valid output for interpretation.

2.2. Contraindications

- Do NOT use the Constellation with any datasets that do not meet the required clinical quality standards. Images cannot include image artifacts, severe motion blurring, or incomplete anatomy.

- Constellation CANNOT be used for populations that are outside the intended healthy population, or patients that exhibit:
    - Pregnancy
    - Surgery of uncertain type

  If Constellation is used for a population outside that of the intended use, results may not be accurate and should not be used to make clinical decisions.
- Constellation is NOT intended for analysis of data from patients under 22 or over 80 years of age. Inaccuracies may occur in results of patients outside of this age range.
- Constellation is NOT intended for analysis of data from patients who have participated in vigorous activity immediately before being scanned. Inaccuracies may occur in results of patients who participate in vigorous activity immediately prior to the MR scan.
- Constellation is NOT intended for analysis of patients with surgical resections, lesions, and/or anatomical tumors.
- Constellation is NOT intended for analysis of patients with implanted metal clips or wires that may concentrate radiofrequency fields. Examples include:
    - Aneurysm clip
    - Implanted neurostimulator
    - Implanted cardiac pacemaker or auto defibrillator
    - Cochlear implant
    - Ocular foreign body (e.g., metal shavings)
    - Any implanted device (pumps, infusion devices, etc.)
    - Shrapnel injuries
    - Metal implants or objects of unknown identity or composition
- Constellation is NOT intended for analysis of people who cannot undergo MRI imaging e.g., patients that demonstrate hemidiaphragm, morbid obesity, claustrophobia, uncontrollable shaking and/or cannot lie still on their back for two hours, etc. Consult a physician before undergoing MRI imaging to confirm MRI imaging can be completed.

- Constellation is NOT intended for use on images acquired post-contrast.

2.3. Precautions

- Constellation is intended to be used in a professional medical technology setting.
- Constellation is intended to be installed on a Q Bio computer terminal by trained personnel of Q Bio. Installation by the clinical end user is not approved or recommended.
- All Constellation users should read the user manual in its entirety prior to device use.
- Caution: Federal law restricts this device to sell by or on the order of a physician.

2.4. Important Notes

- This software tool is not a replacement for clinical judgment. The results generated by the tool should be interpreted by qualified medical professionals.
- Always comply with applicable laws, regulations, and standards when using the software tool in a medical context.

3. Installation

3.1. System Requirements

Constellation must be used on a computer terminal with access to a command line program. The computer terminal must also have access to the Q Bio Virtual Private Network (VPN) and Virtual Private Cloud (VPC). The computer terminal must meet the following system requirements:

- 8GB of RAM
- Intel Core i5 processor (an equivalent processor is acceptable)
- MacOS® 13.15.1+ operating system
- A PDF viewer compatible with PDF v1.3

3.2. DICOM Requirements

All DICOM images must be obtained from a GE MR450W scanner. Constellation requires all input images to use the DICOM format. The files cannot be compressed and a full series of images that cover the whole body must be available.

3.3. Network Requirements

The Constellation software must be installed and accessed on a Q Bio network computer that can communicate using the TCP/IP protocol with other devices on the network.

3.4. Installation Package

Q Bio provides an installation package in the form of a zipped folder containing the Constellation binary files and the user manual file. The installation package contains the following set of files:

- `Constellation - Intel` – binary file for Mac computers with an Intel chip.
- `Constellation - Mx` – binary file for Mac computers with an Mx chip.
- `User Manual - Constellation.pdf` - PDF file of this user manual.

3.5. Downloading Constellation

Q Bio provides the installation package described in Section 3.4, “Installation Package” through a secure portal. Users should follow these instructions to ensure the secure and authorized acquisition of version-identifiable manufacturer-approved version of the Constellation software.

1. Navigate to the designated download portal provided by Q Bio. Ensure that the portal is securely hosted and accessible via encrypted connections (HTTPS).
2. Sign-in to the download portal with valid credentials or other access mechanisms.
3. Navigate to the location of the downloadable files and carefully review and verify the version details of the software or firmware you intend to download, ensuring it aligns with your requirements and is not deprecated by Q Bio.
4. Select the latest version of the software or firmware and initialize the download.

5. After downloading, users should follow the instructions for installation in Section 3.6, “Installing Constellation”.

Avoid downloading software from unsecured or unauthorized sources to mitigate the risk of malware or counterfeit software. Users must comply with licensing agreements, usage terms, and any applicable regulations governing the use of Constellation.

3.6. Installing Constellation

Follow these steps to install the Constellation:

1. Navigate to the Apple Menu icon in the top left corner of the Desktop and select “About this Mac”.
2. Under “Processor”, determine which processor is present in the computer and make a note of whether it is an Intel or Apple (“M”) processor.
3. Download the installation package and select the appropriate binary file based on the processor type.
4. Copy the binary file to the desired file location.
5. Right-click the file and select “Rename”. Rename the file to “constellation”.
6. Open a terminal window by pressing Cmd + Space. Enter “Terminal”, and open the Terminal application.
7. Use the cd command to move into the directory that contains the Constellation binary file.
8. Run the following command: `chmod +x ./constellation.`
9. Press Cmd + Space, enter “Finder” and open a Finder window or open a new Finder window by pressing Cmd + N. Navigate to the directory that contains the Constellation binary file.
10. Right-click the binary and select “Open” and confirm the opening of the application on the dialogue screens.
11. Let the program run until the text window displays “Process completed” and exit the terminal window.
12. Congratulations, Constellation is now ready to run. See Section 4.3 for instructions to run Constellation.

4. Operating Constellation

4.1. User Interface Overview

Constellation operates through a CLI. Users interact with the tool by typing a command and providing different arguments. Typing the command results in designated actions based on the status of the algorithm computation.

command: `constellation`
Input QRI:
`1.X.XXX.XXXXXX.X.XXX.XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX`
Output directory: `/example/outputdirectory`
Public API key: `AKIAIOSFODNN7EXAMPLE`
Private API key: `wJalrXUtnFEMI/K7MDENG/bPxRfiCYEXAMPLEKEY`
SSO session token:
`IQoJb3JpZ2luX2IQoJb3JpZ2luX2IQoJb3JpZ2luX2IQoJb3JpZ2luX2IQoJb3JpZVERYLONGSTRINGEXAMPLE`
Retrigger flag: `--retrigger`

Full command line argument:
`./constellation <YOUR_QRI> /example/outputdirectory $AWS_ACCESS_KEY_ID $AWS_SECRET_ACCESS_KEY $AWS_SESSION_TOKEN`

4.2. Command Arguments

The following commands are used to operate Constellation. There are no additional configurations or inputs for Constellation outside of these commands.

- **Command**

The command to access and run Constellation is the constellation pathname. Use the cd command to move into the directory that contains the constellation binary file to shorten this section of the command to "`./constellation`".

- **INPUT_QRI**

The Input QRI is the name of the image dataset that should be processed by Constellation. Input QRIs are numerical strings assigned to datasets by Q Bio's internal processing. Users should not edit the names of these datasets.

- **OUTPUT_DIRECTORY**

The output directory is a pathname for the designated output file location on the local computer.

- **PUBLIC_API_KEY**

The public API key is autogenerated by Amazon Web Services (AWS). It is an alphanumeric string. This key can be found in the AWS access portal, labeled `aws_access_key_id`. The AWS access portal can be accessed through Jumpcloud. Follow the instructions in Section 4.2.1 “Accessing Jumpcloud for AWS Credentials”.

- **PRIVATE_API_KEY**

The private API key is autogenerated by AWS. It is an alphanumeric string that may contain special characters. This key can be found in the AWS access portal, labeled `aws_secret_access_key`.The AWS access portal can be accessed through Jumpcloud. Follow the instructions in Section 4.2.1 “Accessing Jumpcloud for AWS Credentials”.

- **SSO session token**

The SSO session token is autogenerated by AWS. Each session remains open for 12 hours. After 12 hours, the session must be re-authenticated and re-opened. Each token is an alphanumeric string. This key can be found in the AWS access portal, labeled `aws_session_token`.The AWS access portal can be accessed through Jumpcloud. Follow the instructions in Section 4.2.1 “Accessing AWS Credentials Through Jumpcloud”.

- **--retrigger (Optional)**

The retrigger flag is an optional flag that can be added to the end of the command to signal a reset of the pipeline run. A conditions table to describe the use case of a retrigger flag is included below.

Table 1: Retrigger Conditions

Condition	Outcome	Action
Input QRI has never been run	Running will kick-off the processing of the data. Processing of the input QRI will either succeed or fail.	Wait until the pipeline has completed running.
Input QRI has been run and the processing of the data succeeded	Successful outputs generation	None, successful outputs generation
Input QRI has been run and the processing of the data failed	Error, no outputs generated	Re-run with retrigger flag
Input QRI has been run and	Possible success. No errors	Wait until the pipeline has

Condition	Outcome	Action
the pipeline is currently running	encountered yet.	completed running.

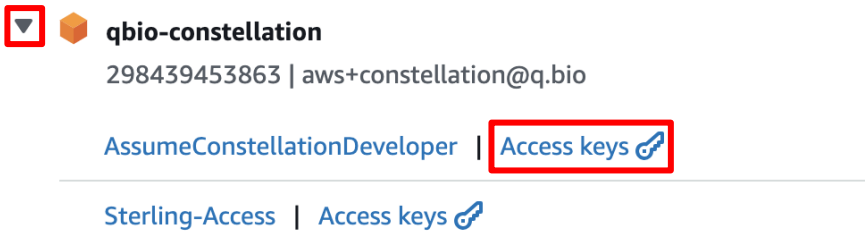
4.2.1. Accessing AWS Credentials Through Jumpcloud

Follow these steps to use the Jumpcloud portal to access AWS credentials used to run Constellation.

1. Navigate to jumpcloud.com and login with valid credentials.
2. Navigate to the “Applications” homepage and click on the “AWS SSO New Org” icon.

3. A new AWS tab will open in the browser and direct to the account homepage. Click on the “AWS Account” tile.

4. Select “qbio-constellation” from the drop-down menu and select the drop down arrow on the left. Select “Access keys”



5. Scroll down to “Option 3: Use individual values in your AWS service client (Short-term credentials)" and copy and paste the AWS credentials. An example set of credentials is shown below:

```
aws_access_key_id = AKIAIOSFODNN7EXAMPLE
aws_secret_access_key = wJalrXUtnFEMI/K7MDENG/bPxRfiCYEXAMPLEKEY
aws_session_token = IQoJb3JpZ2luX2IQoJb3JpZ2luX2IQoJb3JpZ2luX2IQoJb3JpZ2luX2IQoJb3JpZVERYLONGSTRINGEXAMPLE
```

4.2.2. Accessing AWS Credentials through Granted

The AWS credentials can be accessed and stored via Granted to allow for Terminal access. Once profiles are created within Granted, they are accessible through the CLI. Reach out to a Q Bio Administrator for more information on setup and use of the Granted profiles and credentials.

If this is setup, the AWS credentials can be referenced in the Terminal with:

- $AWS_ACCESS_KEY_ID
- $AWS_SECRET_ACCESS_KEY
- $AWS_SESSION_TOKEN

4.3. Running Constellation

To use Constellation, follow these steps:

1. Connect to Q Bio’s VPN via Perimeter 81.
2. Open the Constellation Input Data Log and start a new entry. Input and save the PatientID and any other required information.
    - Take note of the generated Constellation QRI as this shall be communicated back to the QA team and clinician for cross-referencing purposes.
3. Create or locate the output directory where the Constellation outputs will be saved.
4. Open a terminal window by pressing Cmd + Space, enter “Terminal”, and open the Terminal application.
5. Use the cd command to move into the directory that contains the Constellation binary file.

6. Open a browser window to access a set of valid AWS credentials (see Section 4.2.1) or use the “assume” command to select a profile to access the AWS credentials via the CLI.

7. Run the command in the Terminal window with the required parameters. Each parameter must have a space between arguments to separate the inputs.

   Required parameters are:

   - constellation binary file pathname (`./constellation`)
   - INPUT_QRI
   - OUTPUT_DIRECTORY
   - PUBLIC_API_KEY (AWS Access Key ID, $AWS_ACCESS_KEY_ID)
   - PRIVATE_API_KEY (AWS Secret Access Key, $AWS_SECRET_ACCESS_KEY)
   - SSO Session Token (AWS Session Token, $AWS_SESSION_TOKEN)

8. Outputs will automatically download to the output directory once the pipeline has completed running.

9. If the pipeline does not complete a run, it will present an error message in the CLI to the user.

10. The user must provide the Constellation outputs and the Constellation QRI to the QA team for review. Outputs are not acceptable for clinical reads or associated diagnosis until they have completed a QA check from the QA team.

11. The QA team will review the PDF report and release it to the clinician user by placing the report in a designated location on a HIPAA compliant data sharing platform. Clinicians will receive an

email notification from the QA team when a new report is uploaded to the platform.

Example CLI command:

```
./constellation
1.X.XXX.XXXXXX.X.XXX.XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
/example/outputdirectory AKIAIOSFODNN7EXAMPLE
wJalrXUtnFEMI/K7MDENG/bPxRfiCYEXAMPLEKEY
IQoJb3JpZ2luX2IQoJb3JpZ2luX2IQoJb3JpZ2luX2IQoJb3JpZ2luX2IQoJb
```

Notes:

- Constellation will fail to run and will present an error message if any of the following conditions are met:
  - Invalid public or private API keys are provided
  - Invalid SSO session token is provided
  - Invalid output directory is provided
  - Images do not pass quality standards
- The command line will display a message indicating the running, success, or error status of the program when a command with required parameters is issued through the CLI.
- If Constellation outputs or error logs already exist for an existing scan in the output directory location, files will be overwritten.

4.4. Input Data Management

4.4.1. Input Data Transfer and Storage

DICOM images that are generated by a MR scanner are presented as inputs to Constellation. All images are either passed directly from the scanner to an AWS s3 bucket where they are held for processing by Constellation or placed in the appropriate s3 bucket by a Q Bio Administrator. No additional processing is required for images to be placed in the s3 bucket and no further data processing is applied to the images while they are stored in the s3 bucket. Please reach out to a Q Bio Administrator for additional information regarding the image transfer process.

Authorized users may upload DICOM files directly to the AWS s3 bucket. Please reach out to a Q Bio Administrator for additional information about this functionality.

Before data can be run through Constellation, the Constellation user must do the following:

1. Implement a manual check process for DICOM information by cross-referencing the patient data with the corresponding DICOM files stored in the S3 bucket.
2. Register the patient in the Constellation Input Data Log (See Section 4.3 “Running Constellation”).
3. Populate the required information for the new entry, which includes an anonymized PatientID and no PHI.
4. Communicate the auto-generated Constellation QRI from the Constellation Input Data Log back to the QA team and clinician for cross-referencing purposes. Proper registration of the required data into the Constellation Input Data Log is necessary to ensure data provenance requirements are met.

All DICOM files uploaded through this process must also meet the following protocol requirements in Section 4.4.2 “Compatible Protocols” and all other image quality parameters described in Section 4.7 “Operational Range”.

4.4.2. Compatible Protocols

All DICOM images that are generated using the following list of protocols are acceptable inputs to Constellation. If you are unsure if a specific protocol or sequence is compatible with Constellation, please reach out to a Q Bio Administrator.

- AMRA head and neck: FAT
- AMRA head and neck: InPhase
- AMRA head and neck: OutPhase
- AMRA head and neck: WATER
- 3D Sagittal T1 BRAVO - NQ
- 2-point DIXON AMRA 1,2 - BH: FAT
- 2-point DIXON AMRA 1,2 - BH: InPhase
- 2-point DIXON AMRA 5 Thigh: FAT
- 2-point DIXON AMRA 5 Thigh: InPhase
- 2-point DIXON AMRA 5 Thigh: OutPhase
- 2-point DIXON AMRA 5 Thigh: WATER
- 2-point DIXON AMRA 6 Thigh: FAT
- 2-point DIXON AMRA 6 Thigh: InPhase
- 2-point DIXON AMRA 6 Thigh: OutPhase

- 2-point DIXON AMRA 1,2 - BH: OutPhase
- 2-point DIXON AMRA 1,2 - BH: WATER
- 2-point DIXON AMRA 2,3 - BH: FAT
- 2-point DIXON AMRA 2,3 - BH: InPhase
- 2-point DIXON AMRA 2,3 - BH: OutPhase
- 2-point DIXON AMRA 2,3 - BH: WATER
- 2-point DIXON AMRA 4 Thigh: FAT
- 2-point DIXON AMRA 4 Thigh: InPhase
- 2-point DIXON AMRA 4 Thigh: OutPhase
- 2-point DIXON AMRA 4 Thigh: WATER
- 2-point DIXON AMRA 6 Thigh: WATER
- 2-point DIXON AMRA 7 Calf: FAT
- 2-point DIXON AMRA 7 Calf: InPhase
- 2-point DIXON AMRA 7 Calf: OutPhase
- 2-point DIXON AMRA 7 Calf: WATER
- Liver 6 Point DIXON AMRA: FAT
- Liver 6 Point DIXON AMRA: FatFrac
- Liver 6 Point DIXON AMRA: InPhase
- Liver 6 Point DIXON AMRA: OutPhase

4.4.3. Fat/Water Images

Fat/Water images need to be acquired using the following configurations:

- With a 3D two-point Dixon sequence (dual echo).
- All images must be acquired in the axial/transverse plane. The in-plane resolution should be 2-3 mm and the slice thickness 4-5 mm.
- The field-of-view (FOV) will depend on the scanner capabilities: 400 minimum and 500 mm maximum.
- To minimize image degradation in the Z direction due to B0 inhomogeneity while maximizing for coverage, each station's length/thickness in the Z direction needs to be between 280 to 340 mm (larger volumes will increase artifacts).
- Breath-holds are required for stations covering the torso and pelvic area.
- All image interpolation options for image reconstruction must be turned off (e.g. zero padding off).
- Parallel image acceleration can be used only when using surface coils for acquisition.

- The parallel image acceleration factor cannot exceed 2x2 in any station.
- All images need to be provided: in-phase, out-phase, fat, and water.

4.4.4. T2-W & STIR Images

T2-W & STIR images must be acquired using the following configurations:

- With the same geometric prescription in each scan (resolution and station location).
- 2D or 3D sequences options can be used during acquisition. However, if the 2D option is used, there should be “zero” gap between slices.
- All images must be acquired in the coronal plane with an in-plane resolution of 1.6 to 2.6 mm and slice thickness of 6 mm.
- Breath-holds or free-breathing options are required for images covering the torso and pelvis to reduce motion artifacts.
- The number of slices per station needs to be sufficient to cover all vital organs: typically, 36 to 46 slices.
- The FOV needs to cover all vital organs (400 mm minimum).
- Image reconstruction should not exceed double prescribed (matrix size) resolution.
- Parallel imaging can only be used when using surface coils and should not exceed 2x2 acceleration factor.

4.5. Uninstalling Constellation

To uninstall Constellation, follow these steps:

1. Open a Finder window
    a. Press Cmd + Space, enter “Finder”, and open the Finder application
    b. Press Cmd + N while in the Desktop.
2. Navigate to the file location of the Constellation binary file.
3. Delete the binary file by right clicking it and selecting “Delete” or “Move to Trash”.

4.6. Updates

Users shall be able to verify they have the latest version of Constellation by navigating to the download portal provided by Q Bio for Constellation software files. Q Bio will also notify users via email or other messaging systems to provide alerts that there is an updated version of Constellation available for use. No device configurations are available to end users.

To update Constellation, follow these steps:

1. Uninstall Constellation by following the instructions above in Section 4.5 “Uninstalling Constellation”.
2. Download the new Constellation file.
3. Follow the installation instructions above in Section 3.5 “Installing Constellation”.

Only authorized users should apply updates to Constellation.

4.7. Operational Range

This section provides an overview of the operational requirements essential for maintaining Constellation performance and reliability. Understanding and adhering to these operational guidelines are critical for ensuring consistent and accurate performance of the Constellation system in clinical and research settings. These requirements are grouped into two main categories:

Patient Factors: Patients should be among the healthy populations, with an age range spanning from 22 to 80 years old. For further details, please refer to Section 2.2.

Imaging Parameters: The operational range for the shared imaging parameters for the series is listed below. The table summarizes the imaging parameters that are specific to each series.

- Manufacturer: GE MEDICAL SYSTEMS
- Model: Optima MR450w (1.5T)
- Echo Number: 1
- Sagittal T1 BRAVO specific parameter: Inversion Recovery Time (TI) = 500ms
- STIR specific parameter: Inversion Recovery Time (TI) = 180ms

Series Description	MR Acquisition Type	Flip Angle (degrees)	Pixel Spacing ([mm,mm])	Slice Thickness (mm)	Spacing Between Slices (mm)	Repetition Time (ms)	Echo Time (ms)	Echo Train Length	Percent Sampling
2-point DIXON AMRA 1,2 - BH	3D	10	[1.9531, 1.9531]	5	5	5.788	2.084-4.168	1	70
2-point DIXON AMRA 2,3 - BH	3D	10	[1.9531, 1.9531]	5	5	5.788	2.084-4.168	1	70
2-point DIXON AMRA 4 Thigh	3D	10	[1.9531, 1.9531]	4	4	6.028	2.084-4.168	1	68.5714
2-point DIXON AMRA 5 Thigh	3D	10	[1.9531, 1.9531]	4	4	6.028	2.084-4.168	1	68.5714
2-point DIXON AMRA 6 Thigh	3D	10	[1.9531, 1.9531]	4	4	6.028	2.084-4.168	1	68.5714
2-point DIXON AMRA 7 Calf	3D	10	[1.9531, 1.9531]	4	4	5.964–6.028	2.084-4.168	1	68.5714
3D Sagittal T1 BRAVO - NQ	3D	10	[0.9766–1.0547, 0.9766–1.0547]	1.2	1.2	9.94–10.232	3.904-4.036	1	100
AMRA head and neck	3D	10	[1.9531, 1.9531]	5	5	5.784	2.084 - 4.168	1	69.4444
Cor STIR station 2 - BH	2D	160	[0.9766, 0.9766]	6	6	2000.0–14161.0	31.456-32.512	15	58.3333
Cor STIR station 3	2D	160	[0.9766, 0.9766]	6	6	3169.0–5841.0	26.848-33.2	15	58.3333
Cor T2 station 2 - BH	2D	90	[0.9766, 0.9766]	6	6	1000	68.16-71.936	1	57.1429
Cor T2 station 3	2D	90	[0.9766, 0.9766]	6	6	1000	68.16-71.936	1	57.1429
Liver 6 Point DIXON AMRA	3D	5–7	[1.5625–1.6406, 1.5625–1.6406]	10	5	11.259–11.999	4.474-4.732	6	71.625-72.4359

5. Clinician Users & Constellation Outputs

Clinician users must review the following section for information on Constellation's outputs and best practices for using them.

The PDF report output from Constellation presents Constellation results as color-coded volumetric segmentations with individual and overview metrics. The report must be displayed using a program that supports the viewing of PDF files. Clinicians are encouraged to use Constellation in conjunction with typical clinical practices to provide relevant clinical diagnosis to patients.

Furthermore, clinicians can also access the same data provided in the PDF report in machine-readable formats (e.g. JSON and NIfTI files) which are the source for PDF generation. These machine readable outputs provide additional interoperability with external visualization tools.

There are no intermediate inputs or output values available to users. Clinicians are not expected to interface with Constellation through the CLI and are not granted access to device configuration settings for Constellation. Clinicians are given access to the Constellation outputs once they are released by the QA team. When outputs are released, they are uploaded to HIPAA compliant data sharing platforms. Outputs for each patient are identified by a unique QRI number.

If you are unsure if the provided DICOM images are compatible with Constellation, refer to Section 4.4.2 for a list of compatible protocols or contact a Q Bio Administrator.

5.1. Constellation PDF Report

The Constellation PDF report includes the following sections:

- **Preamble**

  The preamble of the report contains the patient information.

- **Brain**

  Brain volumetric measurements are reported in cubic centimeters (cm^3) in a table along with the segmentation images. The segmentation legend correlates a unique color with a specific brain structure present in the brain images.

- **Whole Body**

  Organ and body composition volumetric measurements are reported in liters (L) in a table along with the segmentation images. The segmentation legend correlates a unique color with a specific

organ or body composition structure present in the whole body images.

- **Fat Fraction**

  Fat fraction percentages (%) for bone marrow and the liver are reported on the report in their respective tables. The liver fat fraction section also includes VOI images.

- **Definitions**

  A list of definitions is included on each report. The defined terms are specific to the report and the anatomical structures and values presented in the report.

5.1.1. Preamble

The Preamble section incorporates information including

- Patient name
- Patient ID
- Sex
- Date of Birth
- Weight
- Scan Date
- Report Generation Date
- Accession Number
- Constellation Version Number

5.1.2. Brain

Whole brain volumetric measurements, reported in cubic centimeters (cm^3) for bilateral structures, brain lobes, and aggregate structures.

5.1.2.1. Bilateral Structures

5.1.2.1.1. Measurements

Volumetric measurements in cubic centimeters (cm^3) are reported for both the left and right hemispheres of the following structures:

- Lateral Ventricles
- Cerebellum

- Caudate
- Putamen
- Thalamus
- Hippocampus
- Amygdala

5.1.2.1.2. Segmentation Figure

Three images showing the original DICOM series overlaid with Q Bio's segmentation results are shown in this section. The segmentation legend is described in the Bilateral Structures table and corresponds to the 'Key' entry.

5.1.2.2. Brain Lobes

5.1.2.2.1. Measurements

Volumetric measurements in cubic centimeters (cm^3) are reported for both the left and right hemispheres of the following structures:

- Frontal Lobe
- Parietal Lobe
- Occipital Lobe
- Temporal Lobe

5.1.2.2.2. Segmentation Figure

Three images showing the original DICOM series overlaid with Q Bio's segmentation results are shown in this section. The segmentation legend is described in the Brain Lobes table and

corresponds to the 'Key' entry.

5.1.2.3. Aggregate Structures

Volumetric measurements in cubic centimeters (cm^3) are reported for both the left and right hemispheres of the following structures:

- Hemispheric Cortical Volume
- Cerebral White Matter Volume

Volumetric measurements in cubic centimeters (cm^3) are reported for the following structures:

- Total Cortical Volume
- Total Cerebral White Matter Volume
- Total Gray Matter Volume

- Brain Segmentation Volume (Non Ventricular)
- Total Intracranial Volume

5.1.3. Whole Body

5.1.3.1. Thoracic Organs

Volumetric measurements in liters (L) are reported for the left and right lungs.

5.1.3.2. Abdominal Organs

Volumetric measurements in liters (L) are reported for the following structures:

- Spleen
- Left Kidney
- Right Kidney
- Liver

5.1.3.3. Body Composition

Volumetric measurements in liters (L) are reported for the following structures:

- Abdominal Visceral Fat
- Subcutaneous Fat

Volumetric measurements in liters (L) and fat infiltration measurements in percentages (%) are reported for the following structures:

- Left Posterior Thigh
- Right Posterior Thigh
- Left Anterior Thigh
- Right Anterior Thigh
- Left Lower Leg
- Right Lower Leg

5.1.3.4. Segmentation Figure

A coronal whole-body water image and a coronal whole-body fat image showing the original DICOM series overlaid with Q Bio's segmentation results are shown in this section. The segmentation legend is described in the Thoracic Organs, Abdominal Organs, and Body Composition tables and corresponds to the 'Key' entry.

5.1.3.5. Bone Marrow Fat Fraction

5.1.3.5.1. Measurements

Bone marrow fat fraction measurements in percentages (%) are reported for the following structures:

- Left Femur
- Right Femur

5.1.4. Liver Fat Fraction

5.1.4.1. Measurement

Fat fraction measurements in percentages (%) are reported for the following structures:

- Liver

5.1.4.2. VOI Figure

Two images showing the original DICOM series overlaid with Q Bio's Volume of Interest (VOI) results are shown in this section. The VOI legend is described in the table and

corresponds to the 'Key' entry.

5.1.5. Definitions

5.1.5.1. Terms

The following terms are defined in this section:

- Left and Right Lateral Ventricles
- Left and Right Cerebellum
- Left and Right Caudate
- Left and Right Putamen
- Left and Right Thalamus
- Left and Right Hippocampus
- Left and Right Amygdala
- Left and Right Frontal Lobe
- Left and Right Parietal Lobe
- Left and Right Occipital Lobe
- Left and Right Temporal Lobe

- Left and Right Hemispheric Cortical Volume
- Left and Right Cerebral White Matter Volume
- Total Gray Matter Volume
- Brain Segmentation Volume (Non-Ventricular)
- Total Intracranial Volume
- Left and Right Lung Volume
- Spleen Volume
- Liver Volume
- Left and Right Kidney Volume
- Abdominal Visceral Fat
- Subcutaneous Fat
- Left and Right Posterior Thigh Muscle Group
- Left and Right Anterior Thigh Muscle Group
- Left and Right Lower Leg Muscle Group
- Muscle Fat Infiltration
- Muscle Volume
- Fat-Free Muscle Volume
- Lean Muscle Volume
- Left and Right Femur
- Bone Marrow Fat Fraction
- Liver Fat

5.2. Constellation Machine-Readable Outputs

Constellation machine-readable outputs include files in NIfTI and JSON formats, as detailed in the subsequent subsection.

5.2.1. Image files in NIfTI format

Converted DICOM image series, including stitched whole-body series, in NIfTI format:

- *stitched_cor_stir_stn.nii.gz*
- *stitched_cor_t2_stn.nii.gz*
- *stitched_visualization_f.nii.gz*
- *stitched_visualization_w.nii.gz*
- *stitched_water_amra_bcp.nii.gz*
- *stitched_outphase_amra_bcp.nii.gz*
- *stitched_inphase_amra_bcp.nii.gz*
- *stitched_fat_amra_bcp.nii.gz*
- *fat_amra_liver.nii.gz*
- *fatfrac_amra_liver.nii.gz*
- *inphase_amra_liver.nii.gz*
- *outphase_amra_liver.nii.gz*
- *r2_amra_liver.nii.gz*
- *water_amra_liver.nii.gz*
- *brain_t1_label_compatible.nii.gz*

5.2.2. Segmentation Label Maps in NIfTI format

NIfTI-formatted maps for anatomical segmentations

- *stitched_water_amra_bcp_label.nii.gz*: Segmentation label map for the body
- *t1_label.nii.gz*: Segmentation label map for the brain
- *liver_vois.nii.gz*: Segmentation label map containing two Volume of Interests (VOIs) in the liver

5.2.3. Measurements JSON file

The *measurements.json* file contains all computed quantitative measurements from the segmented anatomical regions. All volumetric measurements with units of cm^3, L, and % are expected to have 1, 2, and 0 decimal places respectively.

5.2.4. Manifest JSON file

The *manifest.json* file categorizes outputs, and provides metadata to facilitate visualization of the NIfTI images; also it contains the following patient and exam information:

- first_name: Patient's first name

- last_name: Patient's last name
- middle_name: Patient's middle name
- sex: Patient's sex
- dob: Patient's date of Birth
- weight: Patient's weight
- patient_qri: Patient's ID
- study_date: Exam date

Table 5-1, 5-2, and 5-3 summarize the segmentation labels and associated measurement fields included in the Constellation machine-readable outputs for body, brain, and liver VOIs regions, respectively. The segmentation labels are derived from the *stitched_water_amra_bcp_label.nii.gz* file for body regions, the *t1_label.nii.gz* file for brain regions, and *liver_vois.nii.gz* file for liver VOIs. The corresponding measurement fields are sourced from *measurements.json*.

Table 5-1. Segmentation labels and measurement fields in Constellation machine-readable outputs for body regions.

Region	Field Name in "manifest.json" file	Segmentation Label Value in "stitched_water_amra_bcp_label.nii.gz" file	Measurement Field Name in "measurements.json" File
Left Lung	left_lung	128	left_lung_volume
Right Lung	right_lung	127	right_lung_volume
Left Kidney	left_kidney_native_dixon	121	left_kidney_native_dixon_volume
Right Kidney	right_kidney_native_dixon	120	right_kidney_native_dixon_volume
Spleen	spleen_native_dixon	122	spleen_native_dixon_volume
Liver	liver	123	Liver_volume
Visceral Adipose Tissue (VAT)	vat_synth_seg	306	vat_ fat_volume
Subcutaneous Adipose Tissue (SAT)	sat	305	sat_fat_volume
Left Femur	left_femur	299	left_femur_bone_marrow_fat_fraction

Right Femur	right_femur	300	right_femur_bone_marrow_fat_fraction
Right Anterior Thigh Muscle	right_anterior_thigh_muscles	301	right_anterior_thigh_muscles_volume right_anterior_thigh_muscles_muscle_fat_fraction right_anterior_thigh_muscles_fat_free_volume right_anterior_thigh_muscles_lean_volume
Right Posterior Thigh Muscle	right_posterior_thigh_muscles	303	right_posterior_thigh_muscles_volume right_posterior_thigh_muscles_muscle_fat_fraction right_posterior_thigh_muscles_fat_free_volume right_posterior_thigh_muscles_lean_volume
Left Anterior Thigh Muscle	left_anterior_thigh_muscles	304	left_anterior_thigh_muscles_volume left_anterior_thigh_muscles_muscle_fat_fraction left_anterior_thigh_muscles_fat_free_volume left_anterior_thigh_muscles_lean_volume
Left Posterior Thigh Muscle	left_posterior_thigh_muscles	302	left_posterior_thigh_muscles_volume left_posterior_thigh_muscles_muscle_fat_fraction left_posterior_thigh_muscles_fat_free_volume left_posterior_thigh_muscles_lean_volume
Left Lower Leg Muscle	left_lower_leg_muscles	307	left_lower_leg_muscles_volume left_lower_leg_muscles_muscle_fat_fraction left_lower_leg_muscles_fat_free_volume left_lower_leg_muscles_lean_volume
Right Lower Leg Muscle	right_lower_leg_muscles	308	right_lower_leg_muscles_volume right_lower_leg_muscles_muscle_fat_fraction right_lower_leg_muscles_fat_free_volume right_lower_leg_muscles_lean_volume

Table 5-2. Segmentation labels and measurement fields in Constellation machine-readable outputs for brain regions.

Region	**Field Name in *manifest.json* file**	**Segmentation Label Value in *t1_label.nii.gz* file**	**Measurement Field Name in *measurements.json* File**
Left Thalamus Proper	left-thalamus-proper*	10	subcortical_volumes_Left-Thalamus
Left Caudate	left-caudate	11	subcortical_volumes_Left-Caudate
Left Putamen	left-putamen	12	subcortical_volumes_Left-Putamen
Left Hippocampus	left-hippocampus	17	subcortical_volumes_Left-Hippocampus
Left Amygdala	left-amygdala	18	subcortical_volumes_Left-Amygdala

Region	Field Name in *manifest.json* file	Segmentation Label Value in *t1_label.nii.gz* file	Measurement Field Name in *measurements.json* File
Right Thalamus Proper	right-thalamus-proper	49	subcortical_volumes_Right-Thalamus
Right Caudate	right-caudate	50	subcortical_volumes_Right-Caudate
Right Putamen	right-putamen	51	subcortical_volumes_Right-Putamen
Right Hippocampus	right-hippocampus	53	subcortical_volumes_Right-Hippocampus
Right Amygdala	right-amygdala	54	subcortical_volumes_Right-Amygdala
Left Temporal Lobe	left_temporal_lobe	3001	left_temporal_lobe_volume
Left Parietal Lobe	left_parietal_lobe	3002	left_parietal_lobe_volume
Left Occipital Lobe	left_occipital_lobe	3003	left_occipital_lobe_volume
Left Frontal Lobe	left_frontal_lobe	3004	left_frontal_lobe_volume
Left Cerebellum Lobe	left_cerebellum_lobe	3005	left_cerebellum_lobe_volume
Left Lateral Ventricles	left_lateral_ventricles	3006	Left_lateral_ventricles_volume subcortical_volumes_Left-Lateral-Ventricle
Right Temporal Lobe	right_temporal_lobe	4001	right_temporal_lobe_volume
Right Parietal Lobe	right_parietal_lobe	4002	right_parietal_lobe_volume
Right Occipital Lobe	right_occipital_lobe	4003	right_occipital_lobe_volume
Right Frontal Lobe	right_frontal_lobe	4004	right_frontal_lobe_volume
Right Cerebellum Lobe	right_cerebellum_lobe	4005	right_cerebellum_lobe_volume
Right Lateral Ventricles	right_lateral_ventricles	4006	right_lateral_ventricles_volume subcortical_volumes_Right-Lateral-Ventricle
Total Brain	-	-	subcortical_volumes_BrainSegVol subcortical_volumes_lhCortexVol subcortical_volumes_rhCortexVol subcortical_volumes_CortexVol subcortical_volumes_lhCerebralWhiteMatterVol subcortical_volumes_rhCerebralWhiteMatterVol subcortical_volumes_CerebralWhiteMatterVol subcortical_volumes_TotalGrayVol subcortical_volumes_EstimatedTotalIntraCraniaIVol

Table 5-3. Segmentation label and measurement field in Constellation machine-readable related to VOI in the liver regions.

Region	Field Name in "manifest.json" file	Segmentation Label Value in "liver_vois.nii.gz" file	Measurement Field Name in "measurements.json" File
Liver VOIs	liver_vois	800	liver_vois_liver_fatfrac

6. Quality Assurance and Performance Specifications

6.1. Quality Assurance Process

Constellation PDF reports must undergo review by a qualified, trained QA reviewer prior to release of the outputs to a clinician. Each member of the QA team must be qualified and trained to review final PDF reports. If a PDF report is rejected by the QA team, a clinician will not be provided with final outputs.

6.2. Performance Specifications

Accuracy and repeatability information for the output measurements of Constellation are detailed below.

For brain measurements, accuracy is validated using the mean Percent Absolute Difference (PAD) and Pearson's Correlation Coefficient (CC). PAD represents the absolute value of the difference between measurements as a percentage of their mean value. Pearson's Correlation Coefficient is a unitless measure of linear correlation between two sets of measurements. Aggregate cortical and subcortical volumes, as well as total cerebral white matter volume, are derived from validated inputs and are not independently validated for accuracy.

For non-brain measurements, accuracy is validated using the Dice Similarity Score (DSC), which compares Constellation's structure segmentation to the ground truth, and the mean Percent Absolute Difference (PAD) between volumetric measurements derived from each segmentation. The DSC is a unitless metric indicating the overlap portion of two segmentations. Lean muscle volumes and muscle fat infiltration measurements are derived from segmentations of the relevant muscles and their accuracies are indicated by DSC of the relevant label maps.

Inter-examination repeatability, abbreviated as repeatability, refers to the consistency of results obtained across different examinations and is validated by analyzing results from the same patient using the same scanner. It is validated using the mean Percent Absolute Difference (PAD) and Pearson's Correlation Coefficient (CC) by comparing the outputs of two consecutive exams performed on the same subject.

The femur bone marrow fat fraction, liver fat fraction, and thigh muscle volume measurements are derived from FDA-approved GE product sequences. Specifically, femur bone marrow and thigh measurements use 3D LAVA; 2-point DIXON and liver fat fraction uses 3D IDEAL IQ. These derived measurements are not independently validated for accuracy or repeatability. For additional information, refer to the GE MR450w manual.

6.2.1. Brain Performance Specifications

6.2.1.1. Bilateral Structures

Measurement	Accuracy		Repeatability	
	PAD	CC	PAD	CC
Left Lateral Ventricles Volume (cm³)	12.6	1.00	1.7	1.00
Right Lateral Ventricles Volume (cm³)	13.6	1.00	1.6	1.00
Left Cerebellum Volume (cm³)	3.2	0.98	0.9	0.99
Right Cerebellum Volume (cm³)	3.2	0.97	1.0	0.99
Left Caudate Volume (cm³)	3.6	0.95	2.8	0.96
Right Caudate Volume (cm³)	3.3	0.94	2.7	0.97
Left Putamen Volume (cm³)	9.2	0.85	5.5	0.88
Right Putamen Volume (cm³)	5.2	0.92	3.9	0.94
Left Thalamus Volume (cm³)	15.4	0.89	4.3	0.92
Right Thalamus Volume (cm³)	15.6	0.88	4.4	0.92
Left Hippocampus Volume (cm³)	8.1	0.78	2.8	0.94
Right Hippocampus Volume (cm³)	7.5	0.86	2.8	0.89
Left Amygdala Volume (cm³)	15.6	0.71	6.6	0.84
Right Amygdala Volume (cm³)	12.0	0.71	6.5	0.82
Abbreviations: PAD = Percent Absolute Difference; CC = Pearson's Correlation Coefficient				

6.2.1.2. Brain Lobes

Measurement	Accuracy		Repeatability	
	PAD	CC	PAD	CC
Left Frontal Lobe Volume (cm³)	2.2	0.96	2.2	0.94
Right Frontal Lobe Volume (cm³)	2.1	0.98	1.9	0.97
Left Parietal Lobe Volume (cm³)	2.9	0.92	2.3	0.93
Right Parietal Lobe Volume (cm³)	2.7	0.96	2.1	0.97
Left Occipital Lobe Volume (cm³)	1.8	0.98	2.0	0.97
Right Occipital Lobe Volume (cm³)	2.2	0.97	2.3	0.97
Left Temporal Lobe Volume (cm³)	4.3	0.99	2.6	0.92
Right Temporal Lobe Volume (cm³)	4.1	0.98	2.8	0.93
Abbreviations: PAD = Percent Absolute Difference; CC = Pearson's Correlation Coefficient				

6.2.1.3. Aggregate Structures

Measurement	Accuracy		Repeatability	
	PAD	CC	PAD	CC
Left Hemispheric Cortical Volume (cm³)	N/A*	N/A*	1.7	0.96
Right Hemispheric Cortical Volume (cm³)	N/A*	N/A*	1.8	0.97
Total Cortical Volume (cm³)	N/A*	N/A*	1.7	0.96
Left Cerebral White Matter Volume (cm³)	2.1	0.99	2.0	0.96
Right Cerebral White Matter Volume (cm³)	2.6	0.99	2.0	0.97
Total Cerebral White Matter Volume (cm³)	N/A*	N/A*	1.9	0.97
Total Gray Matter Volume (cm³)	7.4	0.95	1.3	0.98
Brain Segmentation Volume (Non-Ventricular) (cm³)	5.0	0.98	1.3	0.97

Total Intracranial Volume (cm³)	3.6	0.91	0.5	1.00
Abbreviations: PAD = Percent Absolute Difference; CC = Pearson's Correlation Coefficient				
*Note: Aggregate measurements derived from validated input data were not independently validated for accuracy.				

6.2.2. Whole Body Performance Specifications

Structure	Measurement	Accuracy		Repeatability	
		DSC	PAD	PAD	CC
Left Lung	Volume (L)	0.94	3.3	11.3	0.90
Right Lung	Volume (L)	0.95	3.3	11.9	0.86
Abbreviations: DSC = Dice Similarity Coefficient; PAD = Percent Absolute Difference; CC = Pearson's Correlation Coefficient					

6.2.2.1. Thoracic Organs

6.2.2.2. Abdominal Organs

Structure	Measurement	Accuracy		Repeatability	
		DSC	PAD	PAD	CC
Spleen	Volume (L)	0.89	12.5	13.5	0.93
Left Kidney	Volume (L)	0.94	10.0	4.4	0.96
Right Kidney	Volume (L)	0.93	11.3	3.8	0.97
Liver	Volume (L)	0.96	2.8	8.9	0.89
Abbreviations: DSC = Dice Similarity Coefficient; PAD = Percent Absolute Difference; CC = Pearson's Correlation Coefficient					

6.2.2.3. Body Composition

Structure	Measurement	Accuracy		Repeatability	
		DSC	PAD	PAD	CC
Abdominal Visceral Fat	Volume (L)	0.95	3.5	1.9	1.0
Subcutaneous Fat	Volume (L)	0.90	5.8	1.2	1.0
Abbreviations: DSC = Dice Similarity Coefficient; PAD = Percent Absolute Difference; CC = Pearson's Correlation Coefficient					
*Note: Measurements derived from validated input data were not independently validated for accuracy or repeatability.					
Left Posterior Thigh	Volume (L)	0.92	N/A*	1.0	1.0
	Fat-Free Volume (L)		4.7	N/A*	N/A*
Right Posterior Thigh	Volume (L)	0.92	N/A*	1.2	1.0
	Fat-Free Volume (L)		5.7	N/A*	N/A*
Left Anterior Thigh	Volume (L)	0.93	N/A*	1.6	1.0
	Fat-Free Volume (L)		4.8	N/A*	N/A*
Right Anterior Thigh	Volume (L)	0.93	N/A*	1.6	1.0
	Fat-Free Volume (L)		4.7	N/A*	N/A*
Abbreviations: DSC = Dice Similarity Coefficient; PAD = Percent Absolute Difference; CC = Pearson's Correlation Coefficient					
*Note: Measurements derived from validated input data were not independently validated for accuracy or repeatability.					

7. Cybersecurity

7.1. Network Interfaces

Constellation can be installed and run on any Q Bio network computer that can communicate using the TCP/IP protocol with other devices on the network. Constellation requires connection to the Virtual Private Network (VPN). There are no physical ports that need to be exposed to the device. If physical data ports are present on the computer, they must be secured. See Section 3.3 for minimum network requirements.

If a user is not connected to the Q Bio VPN, Constellation will not run. An error message will be provided to the user that indicates that Constellation could not be run.

7.2. Digital Interfaces

Constellation is operated through a CLI. The command prompts and arguments are passed through Constellation through the user's inputs to Terminal or another command line interface program.

7.3. PHI

Constellation as a device does not contain PHI at rest. All PHI is masked to the Constellation user during operation and all cases are de-identified at the point of use. The DICOM input data and theConstellation outputs contain PHI. This PHI is secured and protected by security policies in place at Q Bio, the AWS Business Associate Addendum (BAA). This BAA is an agreement between Q Bio and AWS that ensures the use of HIPAA Eligible Services in connection with PHI and encryption of all PHI in-transit and at-rest. All data is encrypted by AES which is approved in the guidance provided by the US Secretary of HHS "Guidance to Render Unsecured Protected Health Information Unusable, Unreadable, or Indecipherable to Unauthorized Individuals".

7.4. Access Keys and Session Token

Two API keys are required to operate Constellation. The public key is also known as the AWS Access Key ID. The private key is also known as the AWS Secret Access Key. The SSO session token is also known as the AWS Session Token. Each of these values is issued by AWS and accessible through the AWS website or CLI. The SSO session token expires 12 hours after validation. Constellation will become inoperable upon token expiration. Users must generate a new token to continue operating Constellation.

If an invalid key or token is used to initialize Constellation, an error message will be displayed to the user. Continued attempts to use invalid credentials will continue to result in repeated error messages.

7.5. Security Events and Changes

Constellation users will be notified of any security events or security changes via email, message, or other notification by a Q Bio Administrator.

Constellation users are encouraged to contact a Q Bio Administrator if they encounter cybersecurity vulnerabilities or incidents while using Constellation. The report should include comprehensive details regarding the nature of the vulnerability or incident, its potential impact, and any relevant contextual information. Users should refrain from attempting to mitigate or address the issue independently, to ensure a coordinated and effective response strategy. Timely and accurate reporting is crucial for mitigating risks and safeguarding the Q Bio's digital assets and infrastructure.

7.6. Known Security Vulnerabilities

Software OTS Analysis, REC026, lists the Off-The-Shelf (OTS) software used as part of Constellation.

Software Bill of Materials, REC017, lists the software component vulnerabilities, risk controls, support level, and end of life dates. All identified vulnerabilities are not applicable to the software.

Cybersecurity Risk Analysis, MTX016 is the list of known vulnerabilities as of the release of this document. There are no vulnerabilities that are rated as High or Critical severity. Therefore there are no further mitigation efforts required.

7.7. Backup and Restoration

Restoration of Constellation can be accomplished through the uninstallation and subsequent re-installation of Constellation. Users are responsible for installing and using the most up-to-date version of Constellation available. Users may confirm the latest version of Constellation by contacting a Q Bio Administrator. There are no authenticated device configurations to restore within a restored version of Constellation.

7.8. Sensitive Data Protection

Sensitive data is protected with the following:

- The device will not operate with corrupt DICOM files.
- The device will not operate without valid public or private API keys.
- The device will not operate without a valid SSO session token.
- The SSO session token expires after 12 hours.
- The device has been analyzed for vulnerabilities and does not have any known, unmitigated security vulnerabilities.

For any sensitive data change requests or questions regarding data access, data purging, or other related topics, please contact a Q Bio Administrator.

7.9. User Controls

Q Bio implements the following digital security best practices to keep data and infrastructure safe:

- Unique identification and authorization are required for all Constellation users.
- Unique identification and authorization are required for VPN access to access Constellation resources.
- Data and device access are restricted to authorized users.
- Outside network access is restricted to validated activities.
- Regular security checks are performed on computation infrastructure.
- No PHI is stored within the device.

7.10. Software Lifetime

After Constellation's end of life date, Q Bio will cease providing software updates, ensuring continued support for our products within the stated lifecycle. We recommend transitioning to supported versions to maintain optimal performance, security, and compatibility. If Constellation remains in service past the lifetime of the software, the cybersecurity risks for users may increase over time.

8. Troubleshooting

If troubleshooting reveals a patient health problem rather than a device problem, please reach out to a health care professional for emergency assistance.

8.1. General Troubleshooting Tips

Problem	Resolution
PDF Report and machine-readable outputs are not available	Check if the pipeline is still running by inspecting the Terminal window. If there is an initialization message that confirms Constellation was triggered ("[QRI] has not been previously run. Trigger is being sent" and/or "Trigger Sent"), submit the same command with a retrigger flag. If the trigger has been run, the message will read "[QRI] has been previously called and is actively running".

Problem	Resolution
	An error report will not be generated for any QRIs that contain image files that cannot be processed by the pipeline. Error messages that indicate this status include: “DAG for [QRI] has been previously called and failed. Downloading error logs to {output_directory}” See Section 8.2 below for more detail. If the command has been sent with the retrigger flag and the returned error message reads, “No error logs downloaded. Please contact Q Bio Support”, an error report will not be generated. See Section 8.2 below for more detail.
Constellation continues to run	If Constellation has been initialized correctly, the CLI window will present a “Trigger Sent” message. Continue to wait for the pipeline to finish running. If a PDF report and the corresponding machine-readable outputs are not available after 24 hours of run time, submit the same command with a retrigger flag.
The following message is displayed in the CLI: “DAG for [QRI] has been previously called and failed. Downloading error logs to {output_directory}”	The image files cannot be processed by the pipeline. Check the image files of the specified QRI for corrupt images or incorrect image file types. Check the error logs for information on the pipeline failure.
Error messages appear	See error messages table below.

8.2. Configuration Troubleshooting

Error Message	Definition	Solution
Invalid access keys. Combination of aws_access_key_id = XXX, aws_secret_access_key = XXX and	One or more of the three access keys provided with the command are not valid.	- Use a valid set of credentials consisting of a public API key, private API key, and SSO session token. All three must be valid. - Ensure user permissions used to generate the credentials include access

Error Message	Definition	Solution
aws_session_token = XXX is not valid		to Constellation. Contact Q Bio Support if this is believed to be an error.
XXX is not a valid input QRI	The QRI number is not available in the input files s3 bucket or the bucket is inaccessible.	- Ensure there is a stable connection to the VPN - Use a valid input QRI with valid image files - Ensure user permissions include access to the correct Constellation resources. - Contact Q Bio Support if this is believed to be an error.
The following arguments are required: aws_access_key_id, aws_secret_access_key, aws_session_token	Constellation is unable to correctly read the set of three credentials.	- Check the number of lines entered between arguments on the command line. Only include spaces in between arguments. - Use a valid set of credentials consisting of a public API key, private API key, and SSO session token
Command not found	The system is unable to find the location of the binary file to run Constellation.	- Check the spelling of “constellation” - Use the correct file pathname - Change to the correct constellation file directory location and retry - Include “./” before “constellation” if launching Constellation from the home directory.
The following arguments are required: aws_session_token	Constellation is unable to correctly distinguish the aws_session_token in the command.	- Include the correct number of arguments. - Include the correct number of spaces or lines separating arguments. Check if there is a space between the aws_secret_access_key and aws_session_token values.

Error Message	Definition	Solution
The following arguments are required: qri, output_dir, aws_access_key_id, aws_secret_access_key, aws_session_token	Constellation is unable to correctly distinguish the set of arguments in the command.	- Include a valid set of arguments. Use valid QRI, output directory path, and valid set of credentials. - Include the correct number of spaces or lines separating arguments. Check if there is a space between each of the argument values.
No error logs downloaded. Please contact Q Bio Support	Constellation is unable to process the DAG.	Contact Q Bio Support.
“DAG for [QRI] has been previously called and failed. Downloading error logs to {output_directory}"	Constellation is unable to process the input data.	Error logs are downloaded in the designated output directory. If you need further support contact Q Bio Support

9. Failure Modes and Mechanisms

9.1. Constellation Failure Modes

9.1.1. Constellation Software Fails to Produce Report

Constellation may occasionally be unable to generate a final PDF report. Typical causes include invalid or incomplete input sequences, atypical or distorted anatomy that falls outside supported assumptions, and software defects that interrupt processing.

9.1.2. Report Conditionally Pass Quality Control

In some cases, Constellation produces segmentations or measurements that are clinically irrelevant or insufficiently reliable. The QA process can exclude these elements and issue a conditional pass; a final report containing only the clinically acceptable results, with excluded components clearly flagged and the reason for exclusion stated. If issues affect the overall integrity of the report, QA will reject it and route it for correction and re-review.

Representative Constellation error that will result in conditional pass:

- Metal Artifact
- Region partially outside field of view

- Misaligned stations
- Non-overlapping stations
- Fat/water swap
- Motion artifact
- Bilateral measurement imbalance
- Pathological Conditions
- Constellation software error

9.2. Constellation Failure Causes

9.2.1. Scan Issues

Various factors significantly impact MRI scan processing, potentially leading to a Constellation failure. These factors can be categorized as:

- **Patient Factors:** Physiological variations such as movement artifacts or breath-hold artifacts introduce distortions that obscure anatomical details.
- **Operator Factors:** Variations in technique, experience level, or training can affect the quality and consistency of MRI scans.
- **Deviations from Standardized MRI Acquisition Protocols:** Non-adherence to recommended protocols outlined in Section 4.4.2 can compromise the accuracy and reliability of results.
- **Presence of Abnormalities or Anatomical Distortions:** Conditions like anatomical abnormalities or distortions can impact the interpretation and fidelity of MR images.
- **Instrument (Scanner) Errors:** Issues such as calibration drift, coil malfunction, or inadequate maintenance contribute to poor MR data quality and imaging noise.
- **Environmental Factors:** Fluctuations in temperature, humidity, or electromagnetic interference can introduce variability in MRI scan quality.

Addressing these factors is critical for minimizing errors and enhancing the reliability of MRI-based assessments in clinical and research settings. Additionally, limitations imposed by physical principles, such as spatial resolution constraints and biological variability, impact the accuracy of measurements in MRI.

9.2.2. Constellation Traditional Image Processing Deficiencies

Traditional image processing methods for MRI segmentation often face several challenges that can impact their effectiveness. Common deficiencies include:

- **Limited Adaptability**: Traditional methods may struggle to adapt to diverse MRI protocols and varying anatomical structures, leading to inconsistent results across different imaging settings.

- **Sensitivity to Noise and Artifacts**: These methods can be highly sensitive to noise and artifacts in MRI images, which can adversely affect segmentation accuracy and result in unreliable outputs.

9.2.3. Constellation Deep Learning Algorithm Deficiencies

Neural network-based approaches for MRI segmentation offer significant advancements in medical imaging, but they are not without their challenges. Understanding and addressing these common failures is crucial to ensure the reliability and accuracy of segmented results. Below are some of the common issues encountered in neural network-based MRI segmentation and how they are handled by Constellation's algorithms:

- **Overfitting:** Neural networks can become highly specialized to the training data, performing well on seen examples but poorly on new, unseen MRI scans. This is particularly problematic when the training set is not representative of the diverse patient population.
- **Class Imbalance:** MRI datasets often have an unequal distribution of different tissue types or pathologies. Neural networks can become biased toward more prevalent tissue classes, leading to poor segmentation performance for underrepresented tissues.
- **Noise Sensitivity:** MRI images can contain noise and artifacts. AI-based approaches might struggle to distinguish between actual tissue boundaries and noise, resulting in inaccurate segmentations.
- **Generalization to Different MRI Protocols:** Variation in MRI acquisition protocols, including differences in scanners and imaging parameters can affect the performance of neural networks trained on a specific protocol. This can lead to inconsistent segmentation results across different clinical settings.

9.2.4. Addressing Deficiencies

To address the common failures discussed in Sections 9.2.2 and 9.2.3, the following strategies have been taken:

- **Robust Data Preparation, Augmentation, and Validation to Avoid Overfitting:** A temporal data split was used to separate the training and performance validation datasets to establish the data insulation. During model development, intensive data augmentation, including MRI intensity normalization, random region of interest crop, random intensity and contrast augmentation, and random elastic deformation, are applied to the training data to make it as diverse and representative as possible. Once the model is trained, it is validated on different sources and sites of MRI images, ensuring that the neural network's performance is consistent across diverse and independent datasets. The sample population used in the training and validation was aimed to mirror the general human adult population distribution of the U.S. These steps help mitigate overfitting and improve the algorithm's generalizability.

- **Balanced Training Datasets:** Class imbalance is mitigated by training models specifically for different anatomic organs. This targeted approach ensures balanced and accurate segmentation across all organ classes. Additionally, the Dice Similarity Coefficient (DSC) is adopted as a penalty loss function, which intrinsically handles class imbalance.
- **Improved Noise Robustness:** The neural networks are trained with augmented data that includes various types of additive noises to improve algorithm performance.
- **Protocol Standardization:** Constellation is designed to work with a standardized set of MRI scanning protocol and imaging parameters (See Section 4.7). Enforcing these input data requirements significantly reduces the risk of variability in scanning protocol affecting segmentation performance.

More importantly, the QA team meticulously reviews the final PDF report, including the segmentation outputs, to detect any anomalies. In V1.5, when poor-quality segmentations or measurements are identified, they can be excluded from the final output using the updated exclusion tool. This careful QA process ensures that only accurate and clinically accepted data are included, maintaining the reliability and accuracy of the outputs and prevents the dissemination of potentially misleading or incorrect information.

If the QA review results in a Conditional Pass, a final report will still be generated. In this case, all accurate components will be included, and any excluded components will be clearly marked in the report along with a note explaining the reason for their exclusion. This ensures that clinicians have full transparency regarding the completeness and limitations of the report while preserving access to the valid results.

10. Frequently Asked Questions

Is Constellation compatible with my computer system?

Constellation is compatible with computer systems that meet the following minimum technical specifications:

- 8GB of RAM
- Intel Core i5 processor or Apple M1 (an equivalent processor is acceptable)
- MacOS® 13.15.1+ operating system

Please see the System Requirements section above for more information.

What protocols is Constellation compatible with?

Constellation is compatible with the protocols listed in the Compatible Protocols section of this User Manual. All images must be gathered on a GE Optima MR450w scanner.

What are the final outputs from Constellation?

Constellation will output a PDF report along with the machine-readable outputs as described in the Constellation Outputs section of this User Manual. If the pipeline does not complete and results in an error, error logs as described in the Troubleshooting section of this User Manual will be output.

How long does it take to receive results?

Constellation is designed to complete a pipeline run in 24 hours. If the pipeline computation takes longer than 24 hours, refer to the actions outlined in the Troubleshooting section of this User Manual.

How are DICOM images stored and protected?

DICOM images are stored in HIPAA compliant AWS storage buckets (s3) and the images are secured and protected by security policies in place at Q Bio. No DICOM images are accessible without three different access keys (public API, private API, and SSO session token) and access to the Q Bio VPN. Q Bio does not retain or collect any Patient Health Information (PHI) that is not present in a DICOM image file. Please refer to the Cybersecurity section of the User Manual for more information.

How are incidental findings handled?

Q Bio is not responsible for the clinical diagnosis and review and determination of incidental findings discovered as a result of using Constellation.

Who do I contact if I have a technical question?

Technical questions can be directed to support@q.bio.

11. Adverse Events Reporting

If you experience any adverse events or unexpected outcomes while using the Constellation, please report them to Q Bio by sending an email to support@q.bio.

If noticeable inaccuracies (e.g. non-anatomically possible measurement values, labels presented outside the body) are present in Constellation outputs, stop the use of Constellation and contact Q Bio.

12. Contact Information

For technical support or questions related to the Constellation, please contact a Q Bio Administrator by email at support@q.bio or by phone at (415) 967-7622.

If you are a clinician using the Constellation outputs and have questions related to the Quality Assurance (QA) process, please contact a Q Bio Administrator and request to be connected to a Q Bio QA Team member. The QA team will be able to address Quality Assurance related inquiries related to the outputs.

13. Device Labeling

The Constellation is labeled in accordance with “21 CFR Part 801 - Labeling”.

14. Disclaimer

This User Manual is provided as a guide for using the Constellation. Q Bio assumes no liability for any errors, omissions, or misinterpretations arising from the use of this document or the software tool. Use of Constellation and subsequent interpretation of the Constellation results are subject to a trained user and clinician’s best judgment for use. Users should thoroughly read and understand the User Manual before using the software to ensure the safe and effective use of the tool. If Constellation presents an error or a report is rejected through the QA process, no final report will be available. If the report receives a Conditional Pass, a final report will be generated with the accurate components included, and any excluded components will be clearly documented for the reviewing clinician.

15. Image Glossary

Indicates that the current situation needs operator awareness or operator action in order to avoid undesirable consequences.