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# User guide for Q Amyloid

An open access platform for A $\beta$  quantification

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# 1 Welcome to Q Amyloid

Welcome to the Q Amyloid user guide — your comprehensive resource for navigating the platform with confidence and clarity. Whether you're a researcher, clinician, or imaging specialist, this guide is designed to support your work in amyloid quantification from first login to analysis.

Before diving into the technical steps, let's take a moment to understand the purpose behind Q Amyloid and why it was developed. The deposition of amyloid-beta peptide ( $A\beta$ ) in the brain is one of the earliest neuropathological hallmarks of Alzheimer's disease (AD). This biomarker can be detected and measured *in vivo* using positron emission tomography (PET), with several radiotracers available for clinical and research use — including  $^{11}\text{C}$ -Pittsburgh Compound B (PiB),  $^{18}\text{F}$ -Flutemetamol (FTM),  $^{18}\text{F}$ -Florbetaben (FBB), and  $^{18}\text{F}$ -Florbetapir (FBP). Recently developed  $A\beta$  targeting therapies (ATTs) require a positive  $A\beta$  scan to initiate treatment, which made  $A\beta$  imaging essential for patient selection and monitoring. To meet this growing clinical and research need, we developed Q Amyloid: an open-access platform for automatic  $A\beta$  quantification. Designed to be agnostic to both tracer and scanning site, Q Amyloid offers a standardized, efficient, and accurate solution for localizing and quantifying brain  $A\beta$  burden using PET imaging.

Now that you know why Q Amyloid matters, let's get started !

## 2 Core functionalities

### 2.1 Implementation choices

#### Centiloid scale for amyloid quantification

The primary purpose of Q Amyloid is to quantify amyloid burden using PET imaging. To achieve this, Q Amyloid adopts the Centiloid (CL) scale [1] as its standard quantification method. The Centiloid framework offers a straightforward linear transformation that maps the results of any amyloid PET analysis technique onto a standardized 0–100 scale. This approach assumes that, with proper calibration, consistent and comparable results can be obtained across different tracers, acquisition sites and processing pipelines. As defined by the Centiloid methodology itself, both amyloid-PET and T1w-MRI magnetic resonance imaging (T1w-MRI) images are required.

#### Centiloid cut-off to discriminate positive and negative cases

Following a review of the literature on various approaches for determining the Centiloid cut-off, we adopted the method based on reliable worsening method [2]. This approach defines a threshold baseline value beyond which the rate of change in the biomarker shows a consistent and clinically meaningful deterioration over time. According to this criterion, a Centiloid value of 19 is used as the cut-off to distinguish between amyloid-negative and amyloid-positive cases.

#### Supported amyloid tracers

Q Amyloid supports the Centiloid quantification only for the actual tracers used in clinical and research settings:  $^{11}\text{C}$ -PiB,  $^{18}\text{F}$ -FTM,  $^{18}\text{F}$ -FBB, and  $^{18}\text{F}$ -FBP. These tracers are calibrated using reference datasets available on the GAAIN website [3]. However, users may choose to analyze PET images acquired with other tracers by selecting the "Other" option (see Section 2.2 — front-end). In such cases, the platform calculates only the Standardized Uptake Value ratio (SUVr), without computing Centiloid units, and a **warning** message will be displayed: "*The pipeline was not calibrated for this radiotracer. Centiloid quantification will not be available in the final report. Are you sure you want to start the analysis anyway?*".

#### T1w-MRI-PET data within 90 days

As previously mentioned, the Centiloid scale relies on both PET and T1w-MRI images. To ensure reliable quantification, Q Amyloid requires that these scans be acquired within a 90-day window. This constraint is based on clinical and technical considerations, and the development team guarantees result validity only when this condition

is met. If the uploaded images do not satisfy this requirement, the platform will display a pop-up **warning** message: "*PET/T1w-MRI Timepoint distance is too long: possible coregistration error due to PET/T1w-MRI mismatch. Are you sure you want to start the analysis anyway?*" .

### FDA-EMA acquisition protocol compliance

Q Amyloid adheres to the acquisition protocols recommended by the FDA and EMA. The corresponding values are reported in Table 2.1. For each radiotracer, Q Amyloid defines predefined tolerance ranges (see Table 2.2), which can be managed only by users with administrator privileges. If the input values fall outside these ranges, the platform triggers a **warning** message: "*The pipeline was not calibrated with this experimental design. Are you sure you want to start the analysis anyway?*"

Radiotracer	Uptake time	PET acquisition duration (min)
<sup>11</sup> C-Pittsburgh Compound B	[40; 50]	[20; 30]
<sup>18</sup> F-Florbetaben (Neuraceq)	[80; 90]	[20]
<sup>18</sup> F-Florbetapir (Amyvid)	[30; 50]	[10]
<sup>18</sup> F-Flutemetamol (Vizamyl)	[80; 90]	[20; 30]

Table 2.1: Acquisition protocols approved by FDA and EMA for amyloid radiotracers supported by Q Amyloid.

Radiotracer	Uptake time	PET acquisition duration (min)
<sup>11</sup> C-Pittsburgh Compound B	[35; 55]	[15; 35]
<sup>18</sup> F-Florbetaben (Neuraceq)	[85; 95]	[15; 25]
<sup>18</sup> F-Florbetapir (Amyvid)	[25; 55]	[5; 15]
<sup>18</sup> F-Flutemetamol (Vizamyl)	[75; 95]	[15; 35]

Table 2.2: Tolerance values defined within Q Amyloid's processing pipeline.

**Note** → For a clearer understanding of the warning messages, refer to the next chapter on Q Amyloid infrastructure.

## 2.2 Q Amyloid infrastructure

Like any modern tool, Q Amyloid is structured into two main layers: the **back-end** and the **front-end**. Generally speaking, the back-end refers to the part of a software system that operates behind the scenes — it handles data processing, logic, and communication with databases and external services, ensuring that everything runs smoothly for the user. Otherwise, the front-end is the part of a software system that users interact with directly. It includes everything visible on the screen — such as buttons, menus, forms, and visualizations — and is responsible for displaying information and capturing user input.

In Q Amyloid, both level can results in one of the following outcomes:

- **Successful:** the level is completed successfully with no generated warnings;
- **Warning:** the level is completed, but some issues have been detected. There are two types of warnings:
  - **Warnings generated during the upload of input data** — in such cases, when a warning is triggered and the user clicks “Save and submit”, a pop-up window appears displaying the relevant message. At this point, the user has two options:
    - \* proceed with the pipeline execution, acknowledging the warning. In that case, the warning will be also reported in the final report.
    - \* modify the entered data to address the warning, and restart the pipeline only after updating and resubmitting the data.

That scenario includes the following warnings:

- \* Time between PET and T1w-MRI timepoints exceeds 90 days: "*PET/T1w-MRI timepoint distance is too long: possible coregistration error due to PET/T1w-MRI mismatch. Are you sure you want to start the analysis anyway?*"
- \* Tracer set to 'Other': "*The pipeline was not calibrated for this radiotracer. Centiloid quantification will not be available in the final report. Are you sure you want to start the analysis anyway?*"
- \* PET uptake time or acquisition duration outside the tolerance ranges of calibration protocols (see Table 2): "*The pipeline was not calibrated with this experimental design. Are you sure you want to start the analysis anyway?*"
- **Warnings triggered during pipeline execution** — reported only in the final output and no pop-up notifications are shown in the front-end. These may include:
  - \* "*Missing qform and sform information: image orientation may be undefined*";
  - \* Abnormal SUVr values in cortical target regions: "*Cortical target region SUVr results outside the expected range*";
  - \* Centiloid values outside the expected range: "*Centiloid results outside the expected range.*";
  - \* Radiotracer not supported by the calibration pipeline: "*The selected radiotracer ('Other') is not included in the pipeline calibration: Centiloid calculation was not performed*";
  - \* Suboptimal coregistration performance: "*Coregistration performance below expected threshold: processing results may be suboptimal*";
  - \* T1w-MRI with abnormal intensity values: "*T1w-MRI with abnormally negative intensity values*".
- **Fatal error:** a critical issue prevents the level from completing correctly; the process is halted, and a fatal error message is generated. Two cases:
  - when user try to initiate the analysis without a pair of T1w-MRI and PET images. In that case, the front-end does not allow the user to continue, therefore no analysis can start
  - when the user loads a pair of T1w-MRI and PET images, if either image is 4D instead of 3D, the issue is detected directly by the integrated pipeline, as no automatic quality control module is currently implemented in the loading procedure. In such cases, the pipeline halts execution and generates a final report without performing quantification. The report includes a fatal error message: "*4-dimensional PET image. The pipeline only works with 3D image data*".

## Back-end

In the case of Q Amyloid, the back-end is built as a cloud-based infrastructure hosted on Amazon Web Services (AWS), leveraging certified environments that comply with international standards such as ISO/IEC 27001, ISO/IEC 27017, ISO/IEC 27018, ISO/IEC 9001, for information security and cloud data protection. The main function of the back-end is to run a robust analysis pipeline for the automated amyloid quantification (Figure 2.1) that:

- Receives and pre-process T1w-MRI and PET imaging data;
- Extracts standardized uptake value ratio (SUVRs) using the same cortical target region (CTX VOI) defined in [1], which includes brain areas typically affected by high amyloid burden in Alzheimer's disease — the frontal, temporal, and parietal cortices, as well as the precuneus. The target region also encompasses the anterior striatum and insular cortex. The whole cerebellum is used as the reference region.(Figure 2.1);
- Convert this value into CL;
- Generate a report in .pdf format which contains:
  - A summary schedule of subject information and input data. These informations are required by the front-end (see front-end for more details);
  - Potential warnings/fatal error generated during the run of the analysis;
  - Pipeline results (back-end):
    - \* SUVr value calculated over the CTX VOI;

- \* CL value, if a pre-calibrated radiotracer was selected (see Implementation choices — supported amyloid radiotracers);
- \* A $\beta$  positivity status, based on the selected threshold (threshold = 19);
- \* Color bar, indicating the position of the CL value along the scale;
- Three representative slices (at coordinates 35, 45, and 55) are extracted from both T1w-MRI and PET images, in axial and sagittal orientations.

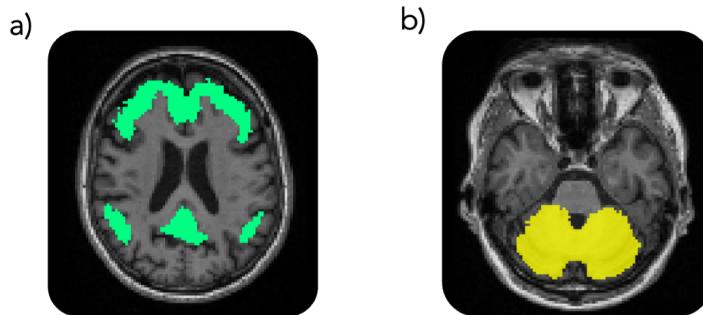


Figure 2.1: reference and target regions used for the computation of the standardized uptake value ratio. a) target CTX region, b) reference region — whole cerebellum

**Note:** This entire pipeline was designed to be remain dynamic, enabling continuous updates in response to emerging A $\beta$  quantification methods.

## Front-end

In Q Amyloid, the front-end provides a user-friendly interface that guides users through the data input process. To start a new analysis, users must follow two main steps:

1. **Add a new subject** → by entering basic demographic information. Mandatory fields are marked with an asterisk (\*), while optional fields can be left blank. If any required information is missing, the system will prevent you from proceeding. Below is the list of required and optional input fields:

- Subject ID \*
- Sex at birth (M/F) \*
- Year of birth \*
- Day of birth (defaults to the first day of the month if not provided)
- Month of birth (defaults to January if not provided)

2. **Add a new timepoint** → each timepoint can be associated with T1w-MRI and/or PET scans. For the analysis to run, both T1w-MRI and PET images must be uploaded. However, they do not need to belong to the same timepoint. What matters is that the time gap between the T1w-MRI and PET scans does not exceed 90 days (otherwise a warning will be generated when user try to initiate the analysis). As with subject entry, some fields are mandatory (\*) and must be completed to continue:

- 3D T1w-MRI image in NifTI format (.nii or .nii.gz file) \* ;
- T1w-MRI sidecar meta information in *json* format (.json file) ;
- T1w-MRI Timepoint additional information:
  - Age on scan day (years)
  - BMI (kg/m<sup>2</sup>)
  - Manufacturer: Siemens - GE - Philips - Canon - Other
  - Manufacturer's Model Name: depends on the manufactures selected above. Some examples: Magneton - Signa MRI - Ingegnia - Vantage
  - Software

- Magnetic Field Strength: 1.5 T - 3 T - 7 T -11.7 T
- 3D PET image in NifTI format (.nii or .nii.gz file) \* ;
- PET radiotracer \*:
  - <sup>11</sup>C-Pittsburgh Compound B;
  - <sup>18</sup>F-Florbetapir (Amyvid<sup>®</sup>);
  - <sup>18</sup>F-Flutemetamol (Vizamyel<sup>®</sup>);
  - <sup>18</sup>F-Florbetaben (Neuraceq<sup>®</sup>)
  - Other
- PET Timepoint additional information \*;
  - Uptake time (minutes)
  - PET Acquisition duration (minuntes)
- PET Timepoint additional information;
  - Age on scan day (years)
  - BMI (kg/m<sup>2</sup>)
  - Manufacturer: Siemens - GE - Philips - Canon&Toshiba – United Imaging - Other
  - Manufacturer's Model Name: depends on the manufactures selected above. Some examples: Discovery - Biographical - Vereos Digital -Celesteion.
  - Software
  - Reconstruction method

3. Once that the timepoint is added, users can ask for a **new analysis**. Each analysis is divided into three steps:

- (a) Analysis in progress: 1/3 Data Preparation;
- (b) Analysis in progress: 2/3 Data Analysis;
- (c) Analysis ready: show result. At this stage users, can visualize and download the final report.

## 3 Getting started

If this is your first time using the platform, welcome aboard! To get started, you'll need to follow these instructions and log-in.

### 3.1 Data & Use terms

Before starting the registration process and accessing the Q Amyloid platform, users are required to complete a brief Data & Use Terms form. This step ensures compliance with data usage policies and helps define the intended scope of use. During this phase, users have to provide the name of the Principal Investigator (PI) and specify the purpose for which the platform will be used.

### 3.2 Required configuration details

During this preparation phase, Q Amyloid team needs to collect some information to configure access to the platform. Specifically, users are asked to provide:

- The **operating system** they intend to use
- Whether a **single account** is sufficient or if a **main account with multiple sub-accounts** is needed for different team members
- The **username** (email address) associated with the account(s), depending on the chosen setup
- The name of the **center** or institution that will be using the platform

This information helps ensure that the platform is set up correctly and securely for each user or research group.

### 3.3 Installing a .p12 Certificate for Website Access

Once all the required information has been provided to the Q Amyloid contact, the team will proceed with the registration. After completion, users will receive a temporary password along with an access certificate. The instructions for installing a *.p12* certificate for website access vary depending on the operating system in use.

#### 3.3.1 Windows operating system

On Windows, user can install the certificate via Internet options:

1. Open *Control Panel* → *Network and Internet* → *Internet Options* (or search *Internet Options* from the Start menu);
2. Select the Content tab;
3. Under Certificates, click *Certificates*;
4. In the Certificates window, open the *Personal tab* → click *Import*;
5. The Certificate Import Wizard opens:
  - Click **Next**
  - Click Browser, select your *.p12* (or *.pfx*) file, then **Next**
6. Enter the password for the file when prompted, then click **Next**;
7. Choose Automatically select the certificate store based on the type of certificate, then click **Next** → **Finish**.
8. You should see the message: *The import was successful*.

#### Browser usage

- Microsoft Edge and Google Chrome use the Windows certificate store automatically.
- Firefox maintains its own store — see the Linux/Firefox section below for steps.

#### 3.3.2 Linux operating system

On Linux systems, certificates are imported directly into each browser, as there is no unified system-wide certificate store for personal certificates. Here the steps to follow:

- **Firefox**
  1. Open Firefox;
  2. Go to *Settings* → *Privacy & Security*.
  3. Scroll down to Certificates → *View Certificates*;
  4. In the Your Certificates tab, click **Import**;
  5. Select your *.p12* file and enter its password;
  6. After import, the certificate will appear under **Your Certificates**.

Firefox will automatically present the certificate when a secure website requests it.

- **Chrome**
  - Open Chrome;
  - Navigate to *Settings* → *Privacy and security* → *Security* → *Manage certificates*;
  - Under Your Certificates, click **Import**.
  - Select your *.p12* file, enter the password, and confirm.

Chrome will then use this certificate when required by a secure site.

### 3.3.3 MacOS operating system

On macOS, personal certificates are managed through Keychain Access. Because the certificate is self-signed, you must explicitly mark it as trusted. Here the steps to follow:

1. Double-click the *.p12* file (or open Keychain Access manually from *Applications → Utilities*);
2. When prompted, choose the login keychain and enter the *.p12* password;
3. After import, locate the certificate under **My Certificates**;
4. Double-click the certificate entry to open its details;
5. Expand the Trust section;
6. From the dropdown When using this certificate, select: **Always Trust**;
7. Close the window — macOS will request your administrator password to confirm the trust setting.

Once this is done, the certificate is installed and fully trusted. Both Safari and Google Chrome (on macOS) will automatically use it when a website requests client authentication.

## 3.4 First log-in

When the certificate is correctly installed, user may proceede with log-in. Open the browser, go to Q Amyloid website - link, click log-in and insert the provided credential (username and temporary password).

After receiving your temporary credentials, change the latter with a your personal password. Once your password has been successfully updated, return to the login page and access the platform using your new credentials. If you've forgotten your password, select *Forgot Password* and follow the on-screen instructions to reset it.

## 4 Q Amyloid home page

Once logged in, users will be directed to the Q Amyloid home page (4.1):

- In the top right corner, highlighted by a violet rectangle (a), users can access their personal account. To log out, click the downward arrow next to your username and select *Logout*.
- The green rectangle (b) displays all subjects currently registered in the system. Users can update subject's demographic information by clicking the edit button. To remove a subject, click the red bin icon. Please note that if an analysis is pending or in progress for that subject, clicking the bin will also delete the associated analysis. The analysis status is shown next to the corresponding subject entry;
- The button *Add Subject* within the light blue rectangle (c) allows users to add a new subject

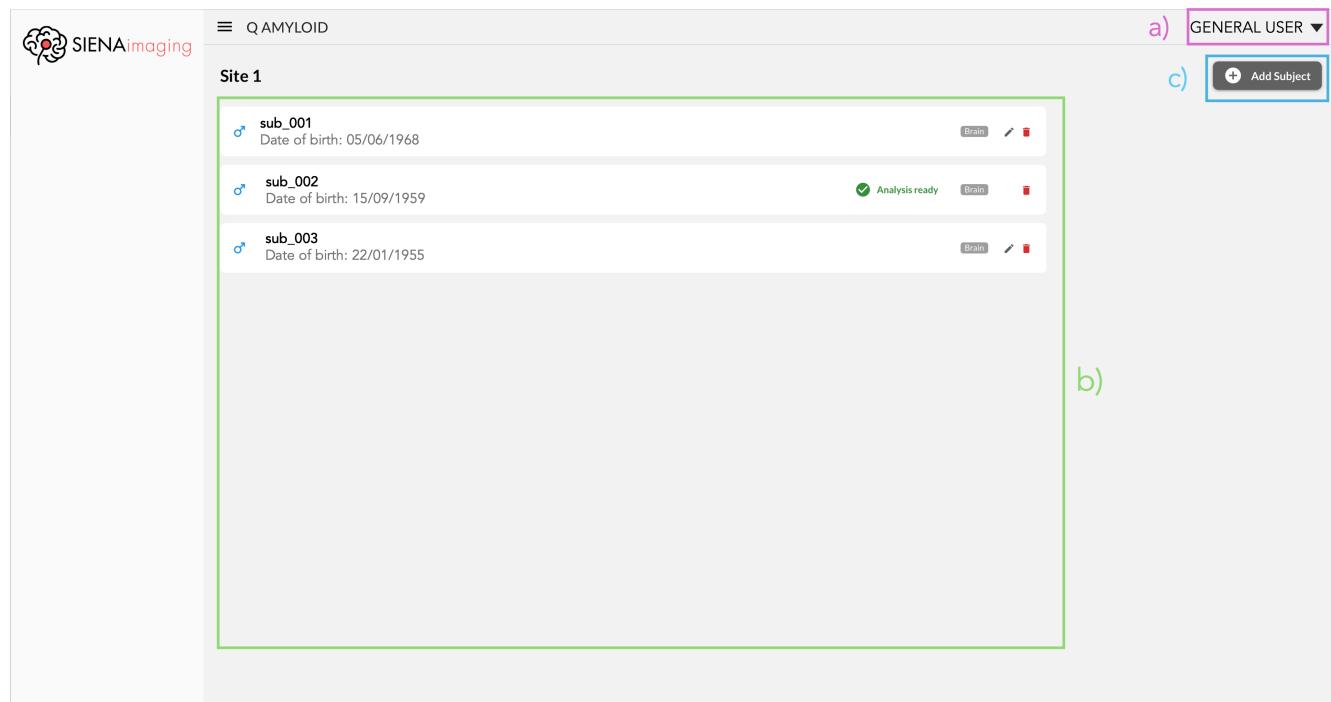


Figure 4.1: Q Amyloid home page

# 5 Amyloid quantification simulation

This chapter is intended to simulate a step-by-step amyloid quantification analysis.

## 5.1 Add a new subject

To start a new analysis, users must first add a new subject. Click the *Add Subject* button (Figure 4.1) to open a form with multiple fields (Figure 5.1). As explained in Section 2.2 — Front-end, some fields are mandatory. These fields are marked with a red asterisk. Once all the required and available information has been entered, click *Save* to register the subject. Once saved, the new subject will appear on the home page (green rectangle — Figure 5.2).

The screenshot shows the 'New Subject' dialog box. It has sections for 'Subject Information' (Subject ID: test-subject, Sex at Birth: Female, Age at Diagnosis: Not available), 'Date of Birth' (Day: 12, Month: 4, Year: 1960), and 'Disease Information' (Diagnosis if any: Brain). A 'Save' button is at the bottom.

Figure 5.1: Fields marked with a red asterisk are mandatory. If any required field is left incomplete, the Save button will remain disabled and cannot be clicked.

The screenshot shows the Q Amyloid home page. It lists subjects under 'Site 1': sub\_001 (Date of birth: 05/06/1968), sub\_002 (Date of birth: 15/09/1959), sub\_003 (Date of birth: 22/01/1955), and test-subject (Date of birth: 12/04/1960). The 'test-subject' entry is highlighted with a green border. A 'GENERAL USER ▾' dropdown and an 'Add Subject' button are visible.

Figure 5.2: Subject added in the home page

## 5.2 Add a new T1w-MRI — PET timepoint

After adding a subject, users can proceed to upload T1w-MRI and/or PET scans. When an image or pair of T1w-MRI/PET images are uploaded they are associated at a timepoint. Although Q Amyloid requires both T1w-MRI and PET scans to perform the analysis, these scans do not need to be uploaded within the same timepoint. As explained in Section 2.2 — Front-end, users may, for example, upload a new PET scan and link it to a previously uploaded T1w-MRI image from a different timepoint. The critical requirement is that the two scans used in the analysis must have been acquired within a 90-day interval.

To add a timepoint, users must click on the subject's name from the main page. If no timepoints have been added yet, the timepoint register will appear empty, as shown in Figure 5.3.

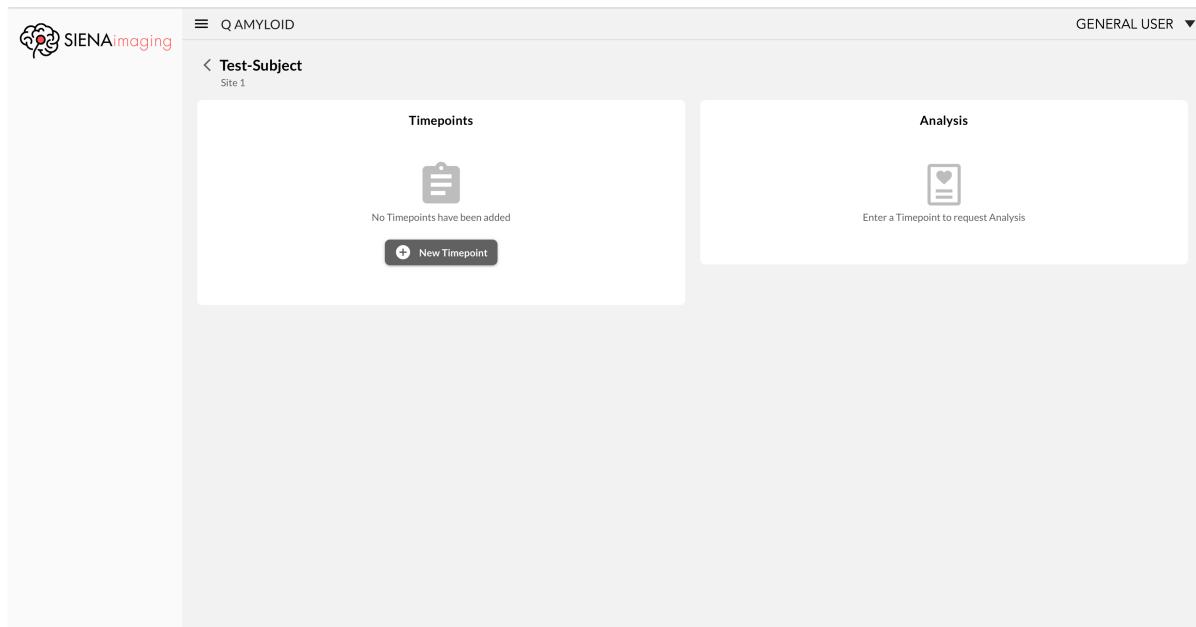


Figure 5.3: The subject *Test-Subject* has been registered. At this stage, no timepoints or analyses are available.

By clicking on *New Timepoint*, a dedicated page will open. This page initially displays a section related to the T1w-MRI scan (Figure 5.4). Users must complete all mandatory fields and click *Save* to confirm the MRI data. Once saved, the section for the PET scan will automatically appear (Figure 5.5). In the top-left corner users can set the Timepoint Date, which typically corresponds to the scan acquisition date. This date will automatically apply to both T1w-MRI and PET scans. However, if the scans were acquired on different dates, users can manually adjust the MRI-PET date in its designated field. To upload an MRI or PET file, users have to click *SELECT FILES* files and choose the appropriate scan. It is also possible to upload the corresponding *json* file. After selecting the file, users have to click Additional Information (Figures 5.4, 5.5) and complete the required fields, as detailed in Section 2.2 — Front-end. Once the upload is complete, users can click *Save* to confirm. This procedure must be performed twice: once for the MRI scan and once for the PET scan. One that T1w-MRI and PET scans are uploaded correctly, both timepoints will appear in the subject's timepoint register (Figure 5.6). Also here, by clicking on the red bin, users can delete the timepoint.

Figure 5.4: T1w-MRI timepoint. Fields marked with red asterisk are mandatory.

Figure 5.5: T1w-MRI and PET timepoints. Fields marked with red asterisk are mandatory.

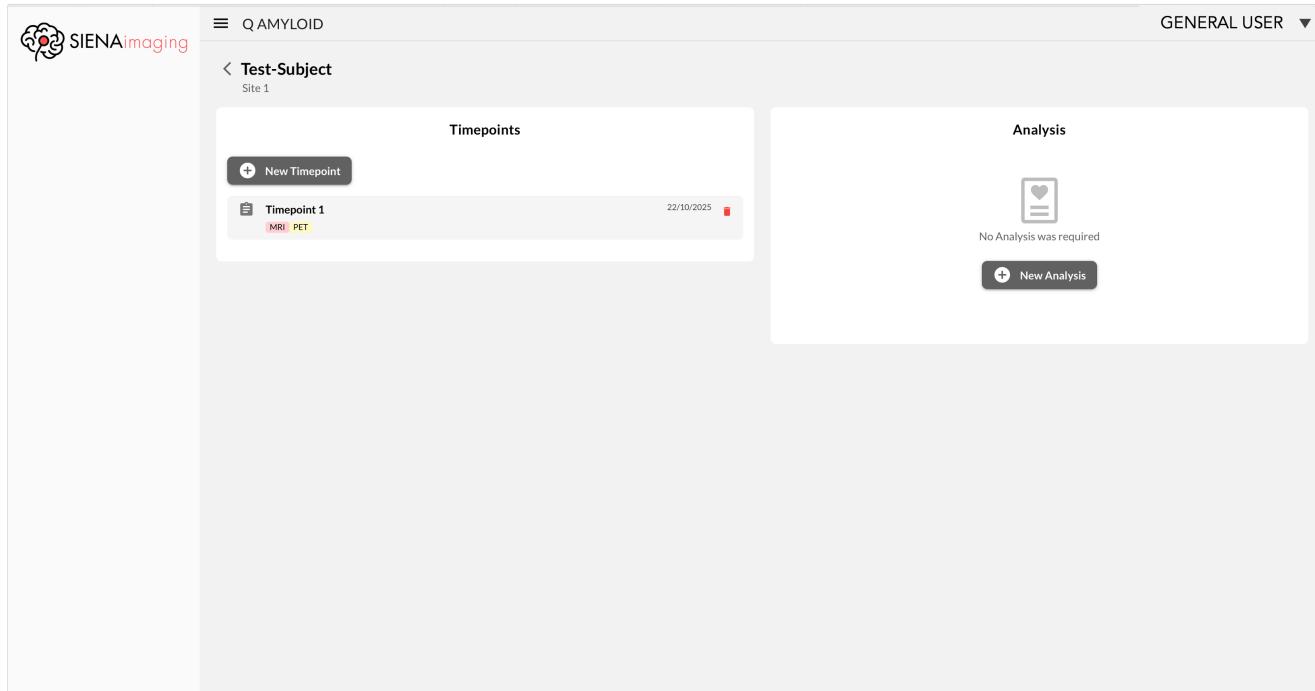


Figure 5.6: T1w-MRI and PET timepoint added.

### 5.3 Run a new analysis

When at least one pair of T1w-MRI—PET images is available for the subject to be analyzed, users can initiate a new analysis by clicking the *New Analysis* button (Figure 5.6). A new window will open (Figure 5.7); click on the menu and select the only available option: *AMYLOID QUANTIFICATION (CENTILOID)*, then click on *Add Analysis*.



Figure 5.7: Initiate a new amyloid quantification analysis

Next, another menu will appear. In the left panel, select again *AMYLOID QUANTIFICATION (CENTILOID)*. On the right side, two fields will be displayed: PET Timepoint and T1w-MRI Timepoint (Figure ??). Select the PET-T1w-MRI pair you wish to analyze. The only constraint at this stage is the presence of both images, regardless of the timepoint. However, it is recommended that the scans be acquired within a 90-day window. If this condition is not met, a **warning** pop-up will be triggered and users are asked to modify data or continue (see Section 2.2). Once that the timepoints are added, the button *Save and request analysis* button is available (Figure 5.9). Clicking on that, now a new analysis compare at the analysis register of the subject (Figure 5.10). As the analysis progresses, its status is updated and displayed in the front-end interface (Figure 5.11). When the analysis is complete, users can view and download the final report directly from the platform (Figures 5.12 - 5.14).

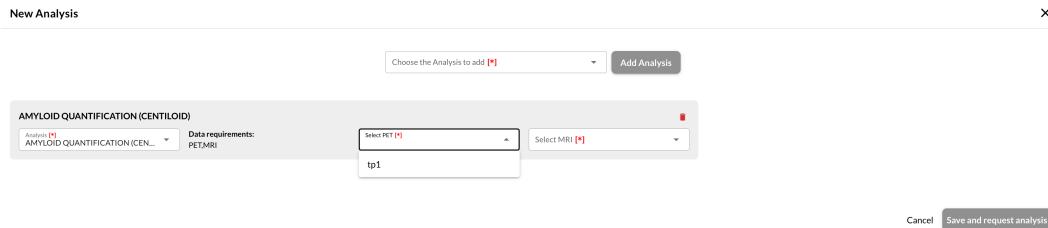


Figure 5.8: Timepoint selection

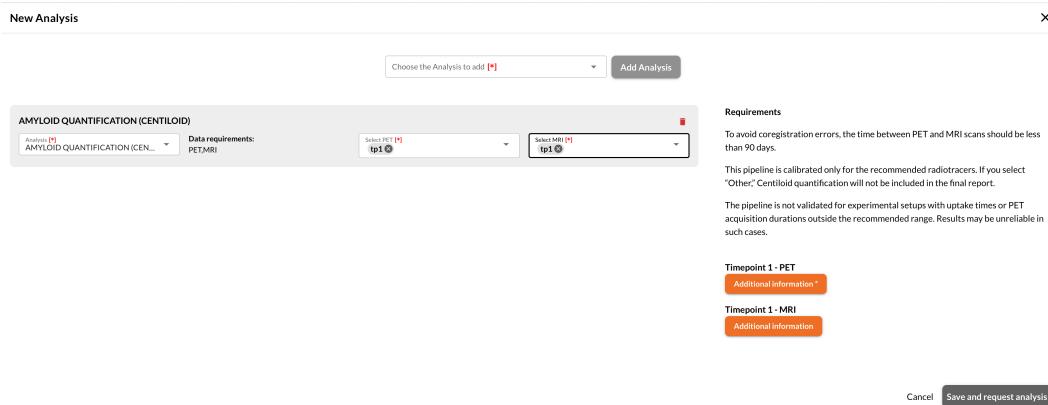


Figure 5.9: Timepoint added, users can ask for a new analysis

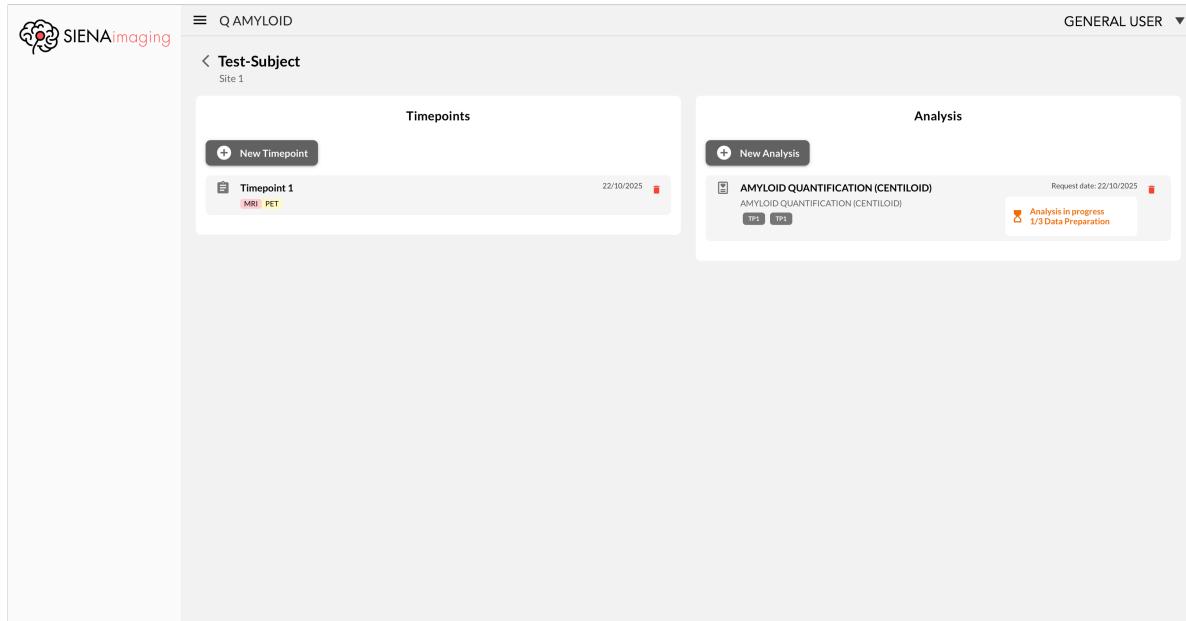


Figure 5.10: Analysis status 1/3: data preparation

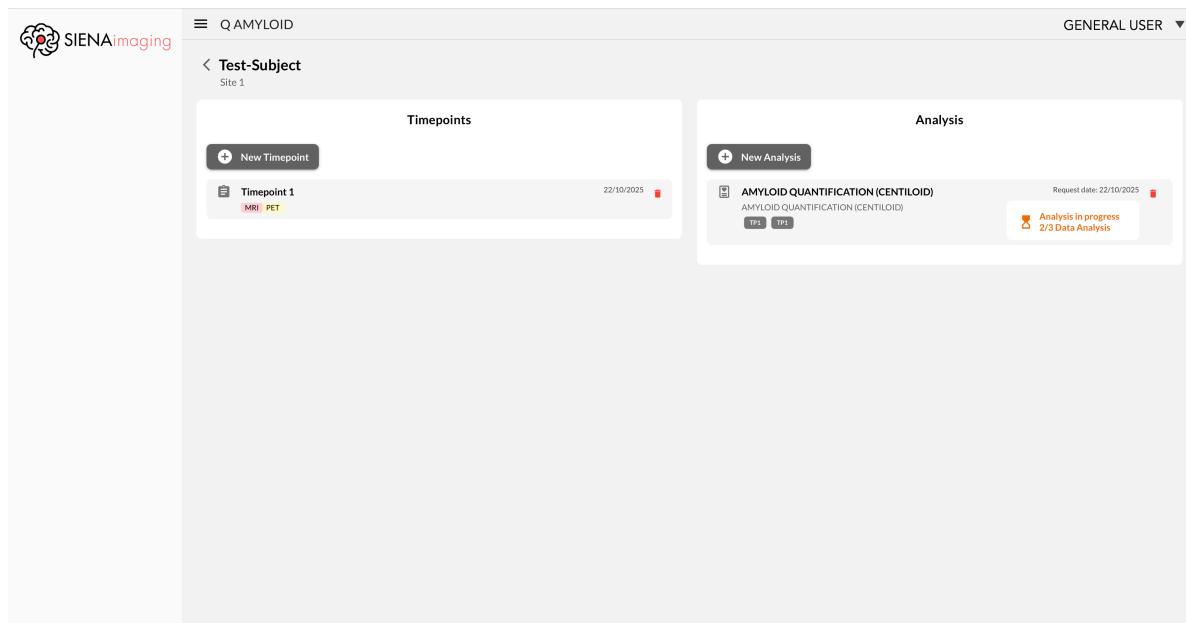


Figure 5.11: Analysis status 2/3: data analysis

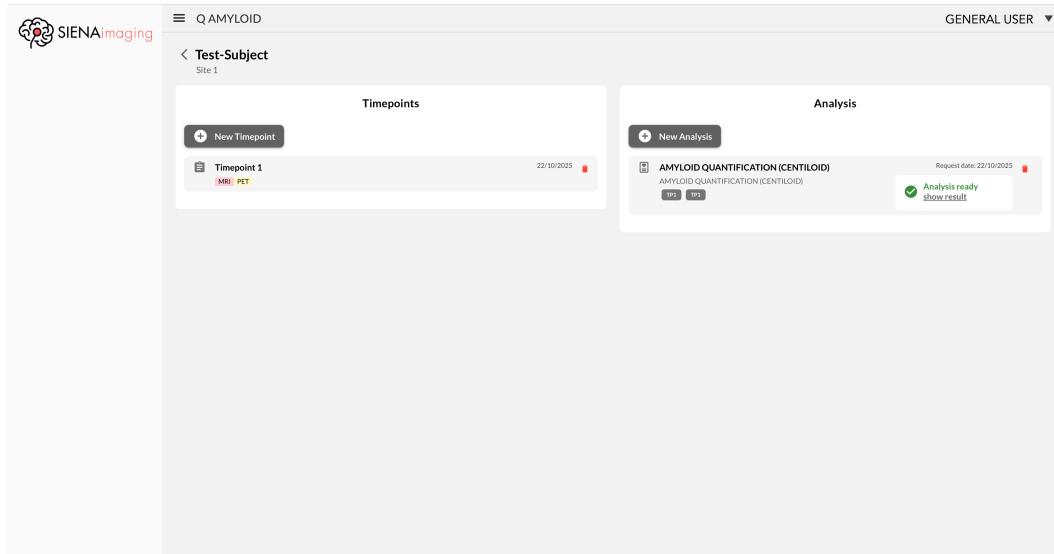


Figure 5.12: Analysis status 3/3: report is ready to download

**Q AMYLOID**  
powered by SIENA imaging

**Amyloid quantification report**  
Report Date: 22/10/2025

**Subject Information**

Subject ID: Test-Subject    Sex at birth: F    Date of Birth: 12/04/1960

**Analysis status**

Successfully completed

**Input Data**

MRI		PET	
Scan day	22/10/2025	Scan day	22/10/2025
Age on scan day	65	Age on scan day	65
BMI	Not Available	BMI	Not Available
Manufacturer	Siemens	Radiotracer	PIB
Manufacturer's Model Name	Not Available	Uptake Time	50
Software	Not Available	Acquisition Duration	20
Magnetic Field Strength	3T	Administered Dose	Not Available
		Manufacturer	Siemens
		Manufacturer's Model Name	Not Available
		Software	Not Available
		Reconstruction Method	Not Available

**Results**

**Amyloid load quantification**

SUVr	1190049
Centiloid	16
Amyloid status	Negative

The Standardized Uptake Value Ratio (SUVr) is calculated as the ratio between the tracer uptake within a cortical target region and the tracer uptake in the whole cerebellum (reference region).

**Centiloid scale**

The Centiloid (C1) scale provides a standardized measure of amyloid accumulation. Scores near 0 reflect the absence of amyloid, while scores approaching 100 are associated to the presence of amyloid accumulation as reported by patients with Alzheimer's disease. A biomarker-based cutoff value of 19 was used to distinguish between amyloid-negative and amyloid-positive individuals.

Project supported by the cascading grant "Q Amyloid - Quantitative Amyloid Imaging" of the Department of Information Engineering University of Padova under PRIN & PON projects, and funded by the European Commission through the NextGeneration EU programme

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Figure 5.13: Q Amyloid report: page 1

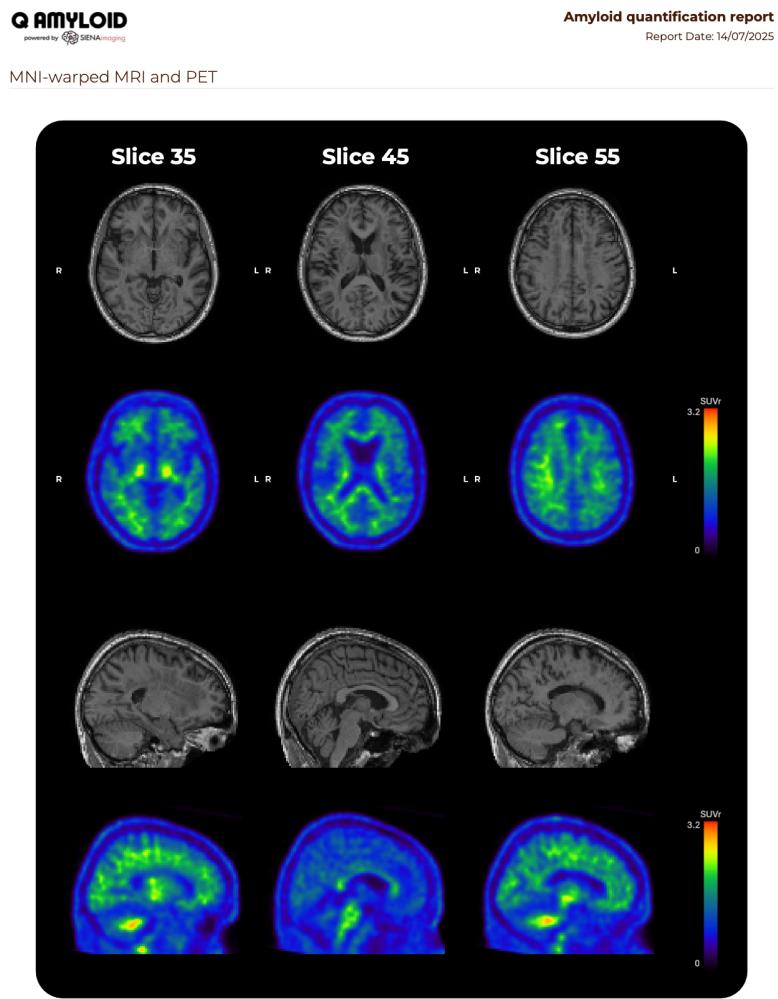


Figure 5.14: Q Amyloid report: page 2

## 6 Contact & Support

Support & Assistance: qamyloid@dei.unipd.it

## 7 Acknowledgments

This project is supported by the cascading grant "Q Amyloid – Quantitative Amyloid Imaging", under PNRR ECS00000017 "THE-Tuscany Health Ecosystem," Spoke 6: "Precision Medicine & Personalized Healthcare", funded by the European Commission through the NextGeneration EU programme.

The development of the Q Amyloid platform was made possible thanks to the dedicated work of three engineers: Francesco Piva, Benedetta Marin, and Chiara Da Villa, under the supervision of Prof. Mattia Veronese, who acted as Principal Investigator (PI). We also gratefully acknowledge the valuable support provided by Siena Imaging and Plurimedia, whose collaboration played a key role in the design and implementation of the platform's back-end/front-end infrastructure.

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