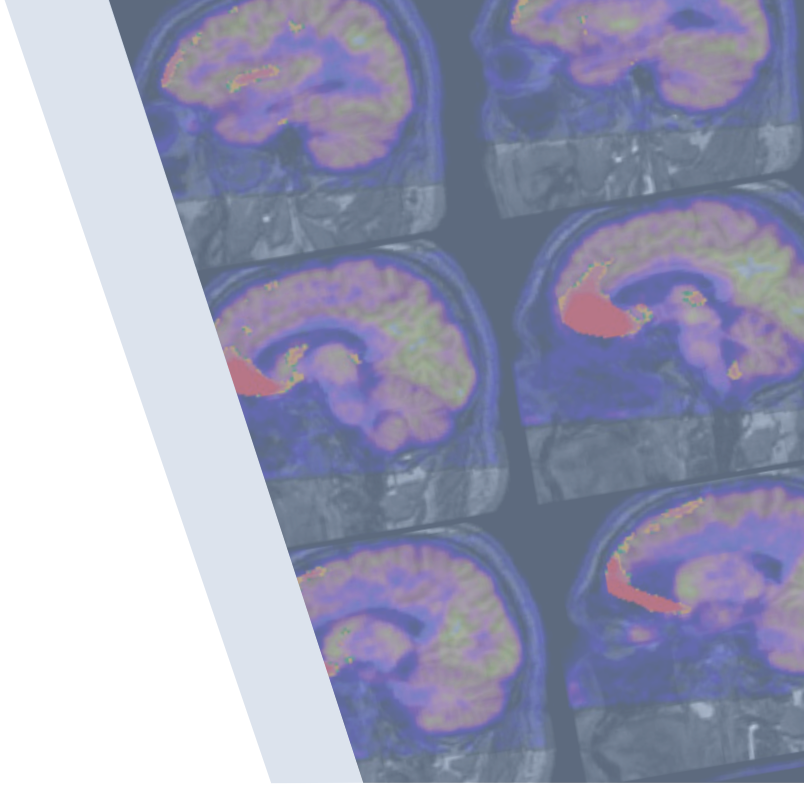
Neurocloud-PET

Your brain PET diagnostic assistant

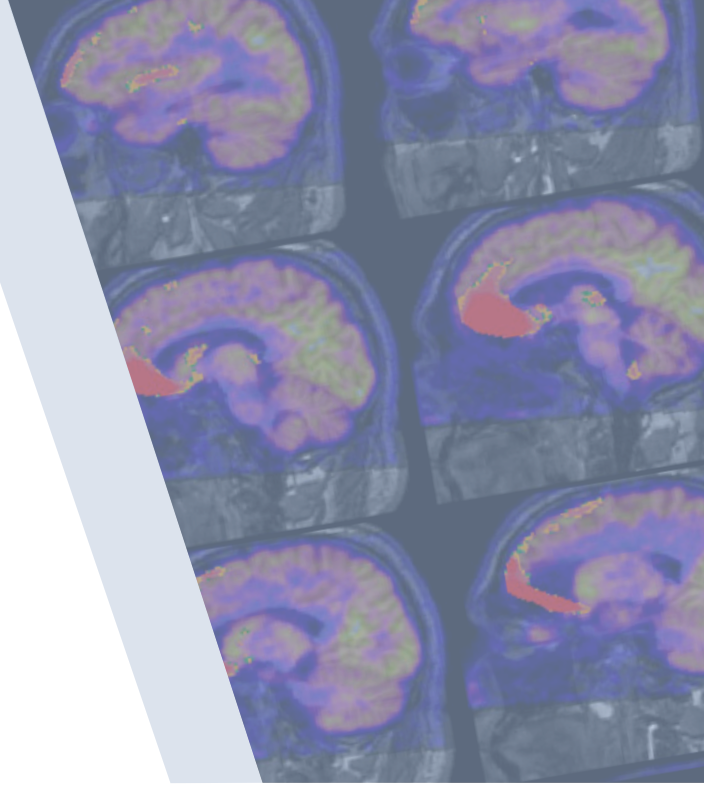
QUBIO tech



01 What is **Neurocloud-PET?**

Neurocloud PET is a CE marked software that provides a completely automatic approach to some essential processing and analysis methods for PET imaging quantification, supplying quantitative data of primary interest in the diagnosis and follow-up of different neuropathologies. Multimodal images (functional PET + structural MR or CT) are generated automatically, allowing the identification of abnormalities at first glance. These results can be reviewed in minutes using a web-based interface which permits the download of a customizable report of findings and all the relevant image, tabulated and graphical data provided by Neurocloud-PET in DICOM or NifTi format.

Neurocloud-PET is designed to assist the specialist in the diagnosis, monitoring and treatment planning of the patient by accelerating workflow and providing new information of clinical interest. The nuclear medicine physician can use the information provided by the software to validate his/her findings from the visual examination of the patient PET image and complement it with unbiased quantitative and less rater-dependent data for achieving a more robust evaluation and reducing the diagnostic errors rate.



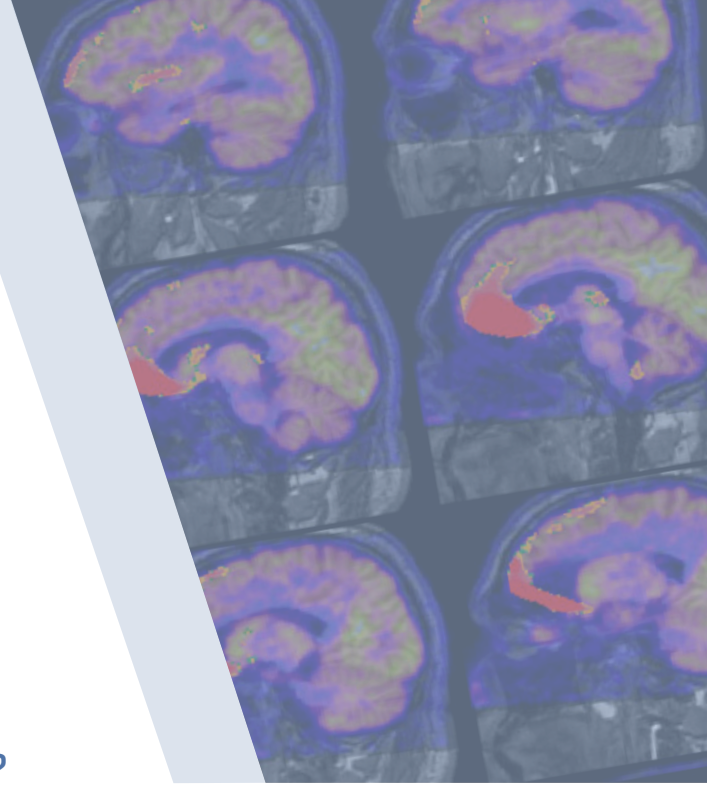
02 How **Neurocloud-PET** helps?

The inclusion of 18F-FDG Positron Emission Tomography (PET) as a biomarker in the diagnostic criteria of neurodegenerative diseases and its indication in the presurgical assessment for drug-resistant epilepsies allow to improve specificity, reproducibility and reducing the interrater reliability derived from visual analysis. For these reasons, the use of quantitative imaging methods is encouraged by Medical Societies such as Sociedad Española de Medicina Nuclear e Imagen Molecular and Sociedad Española de Neurología [1] or European Association of Nuclear Medicine and European Academy of Neurology [2].

Clinical application of 18FDG has been shown to be useful in different common cases such as:

- Differential diagnosis of dementias according to regional hypometabolism patterns,
- In Alzheimer Disease, hypometabolism can be an early signal before grey matter atrophy, and a symmetrical hypometabolism in the temporoparietal, posterior cingulate and medial temporal cortices is usually seen.
- In Parkinson disease, 18FDG can be also useful for identification of atypical parkinsonism.
- In refractory epilepsy 18FDG has proven to be a useful technique to localize the epileptogenic areas

Regarding amyloid PET imaging, Alzheimer's disease (AD) physiology has shown that amyloid-beta peptide fibrils increase its concentration in the course of the disease. Thus, Amyloid-PET imaging , as a biomarker of beta-amiloide, offers a unique opportunity to detect the presence of this protein in the human body during life. Therefore, automated and reliable PET-Amyloid imaging quantification, which is based on cortical-to-cerebellum standardized uptake value ratio (SUVR), provides the physician with valuable data for the early diagnosis of AD pathologies and the development and assessment of new treatment strategies [3].



03 How **Neurocloud-PET** works?

As a fully automatic cloud software, you can expect a plug and play solution ready to use from minute one. Neurocloud -PET just requires the upload of the PET imaging study of interest (DICOM or Nifti formats allowed) with no further operations by the user needed. After a secure upload to our cloud platform where a pseudo anonymization procedure removes any personal information stored in the images, our powerful cloud platform runs a pipeline of advanced image operations to identify abnormal brain areas in your patients brain in a few minutes.

1. Neurocloud-PET FDG analysis pipeline

The input PET image is spatially normalized to a standard space (MNI) and the resulting inverse transformation data are applied to the database of healthy controls and to the anatomical atlas of choice, allowing the generation of a normal uptake pattern and brain parcellations for each patient. The PET image is also normalized in intensity using our controls template as reference to remove global differences due, for instance, to differences in the injected dose. If a structural image is uploaded along with PET, both images are co-registered and a fusion image is provided (Fig. 1)

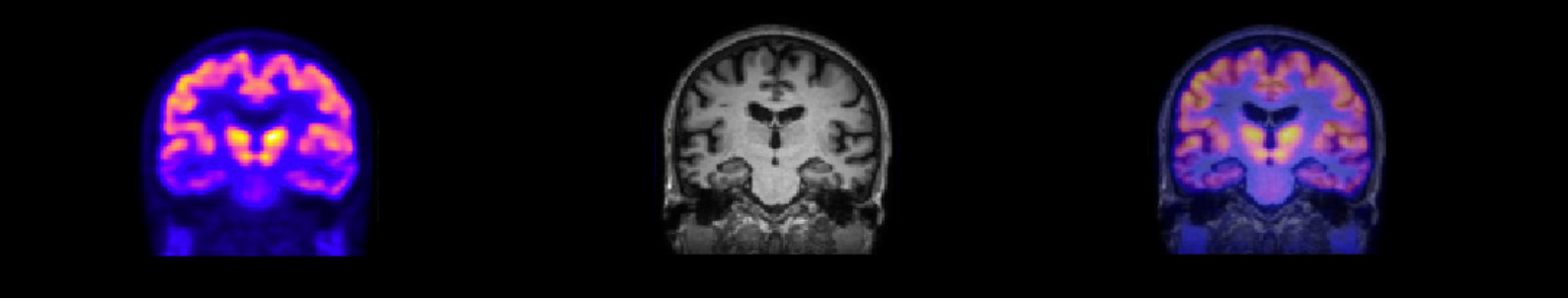


Figure 1: Coronal slices for PET-FDG (left), MRI-T1w (center) and the PET-MRI fusion image (right) that is automatically obtained with Neurocloud-PET.

Once the spatial and intensity normalization steps are completed, different statistical analyses are performed, which are described next:

- **Asymmetries analysis** Each ROI is compared with its contralateral pair to obtain the asymmetry indexes (AI). This value is then compared to the normal distribution delivered from our control database. The significance of each asymmetry index is characterized as the number of SDs it comprises. The results with a significance higher than 2SD are highlighted in the report.
- **ROI-based quantification:** The database of normal individuals is used to calculate the normal average uptake and standard deviation (SD) for each of the ROIs. The average uptake for each ROI in the patient's brain is compared with the mean average uptake in the healthy database, and this comparison is expressed by the number of Standard Deviation (SD).
- **Voxel-based analysis:** This is a voxel-wise comparison between the patient's PET image and the database of normal individuals. The result is an image showing clusters of voxels where Neurocloud-PET finds >= 2SD differences. This result complements the ROI-based analysis by detecting lesions that may not be detected in the calculation of asymmetries and ROI-based calculations (potentially because they are too small).

Controls database

All statistical results of Neurocloud PET are obtained through statistical comparison between the patient and an age stratified, controls database containing 75 subjects with normal neurological activity with ages between 19 and 85 years old, distributed in a uniform way among the different age ranges (6-10 patients in each 5-year interval).

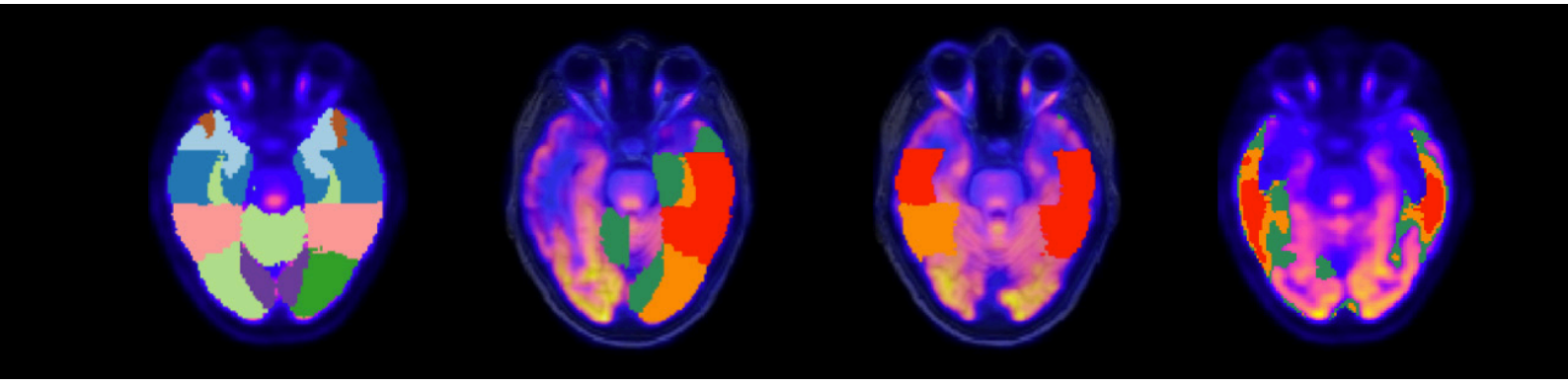


Figure 2: Axial slices for (left to right) the patient PET image co-registered with the Atlas, the results of asymmetries analysis, ROIs analysis and the voxel-wise analysis for hypometabolism on top of the functional FDG-PET image.

Frontal −

	ROI	Left Diff. [%]	Right Diff. [%]	Asymetry [%]	Deficit
	Superior frontal gyrus	-3.79	1.21	-4.84	Left
	Middle frontal gyrus	-13.66	-3.43	-11.29	Left
	Inferior frontal gyrus (Broca Area)	-5.44	1.96	-6.90	Left
	Subgenual anterior cingulate gyrus	-11.73	-10.60	3.43	

Figure 3. Neurocloud - PET results for PET-FDG hypometabolism analysis showing affected regions in the frontal lobe.

2. Neurocloud-PET Amyloid analysis pipeline

The pipeline for the Amyloid-PET imaging quantification starts with the co-registration of the PET and MR images and the spatial normalization of the structural image to obtain the set of transformations needed to register an amyloid analysis specific atlas in the patient space. Segmentation of gray matter and white matter from MRI is also performed in order to apply tissue dependent constraints for the specific regions where beta-amyloid uptake values are computed at, which include several cortical structures of consensus*****[4].

Using the whole Cerebellum as a non-specific reference region, the standard SUVR metric is finally obtained for the patient and compared with a threshold value of reference for positive/negative labelling. Extended quantitative data is provided tabulated for deeper examination together with image data that facilitates the review of the analysis results.

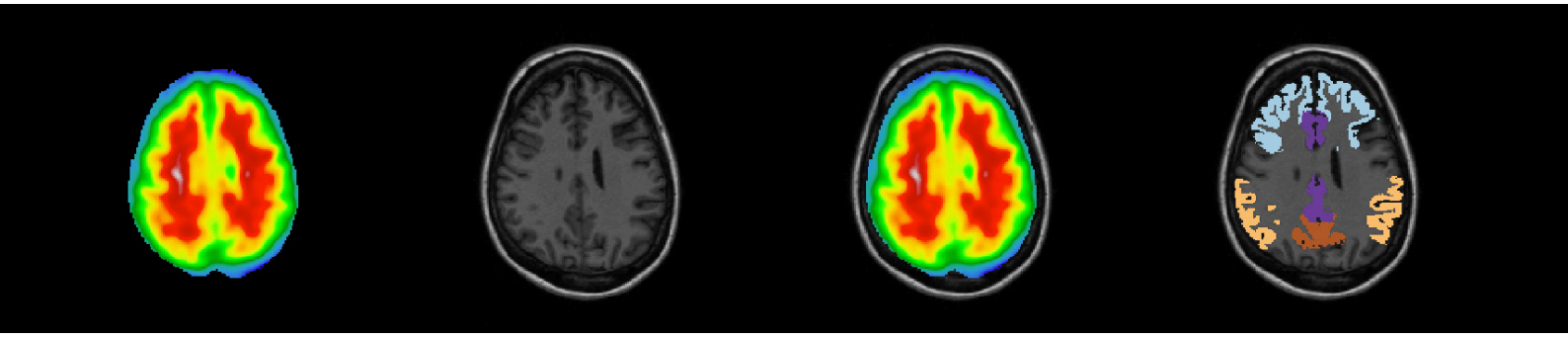


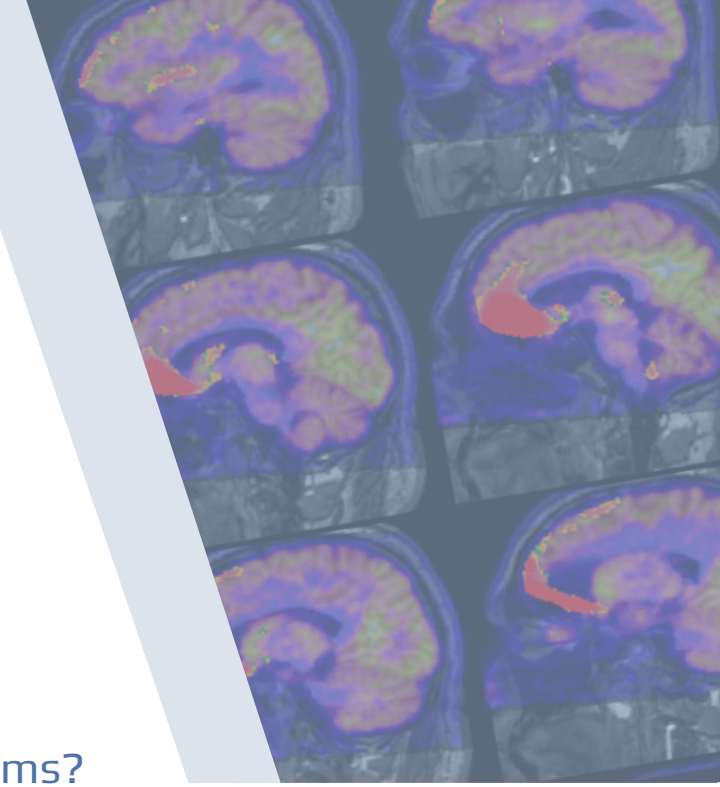
Figure 4. Axial slices (left to right) of the patient Amyloid-PET image, the patient MRI, the co-registration or PET/MRI fusion image and the segmentation of the specific regions for SUVR computation.

***** Prefrontal, Orbitofrontal, Parietal, Cingulate, Precuneus and Temporal regions.

Negative Positive Medium

Result			
SUVR	**Threshold**	**Tracer**	
1.01 +/- [0.04]	1.21	Flutemetamol	
Region	**Mean**	**Median**	**Total**
Prefrontal	0.95	0.99	0.84
Orbitofrontal	0.99	1.06	0.16
Parietal	0.99	1.03	0.31
Cingulate	0.95	1.03	0.17
Precuneus	0.91	0.95	0.3
Temporal	0.95	1.01	0.62

Figure 5. Neurocloud Amyloid results for the SURV quantification and quotients of the account values (mean, median and total number) in the ROIs of the cerebral cortex with respect to the reference region



04 How **Neurocloud-PET** performs?

Neurocloud-PET can provide research grade results thanks to its large database of controls and much improved quantification algorithms. A comparative study on 35 patients suspected of suffering dementia was carried out against neuroimaging research software standard (PALZ from PMOD Technologies) [5]. Results obtained with Neurocloud-PET and PALZ are almost equivalent, showing PALZ a better sensitivity score (92% versus 88%) but Neurocloud performed better on specificity (78% versus 73%).

In addition, Neurocloud-PET has been validated in clinical environments in 3 different spanish hospitals, carrying out different but complementary trials in order to quantify how much new information Neurocloud-PET can bring to the clinical routine:

- At Complexo Hospitalario Universitario de Santiago de Compostela (national reference epilepsy unit), a cohort of 88 patients previously diagnosed with refractory epilepsy were evaluated by using NeurocloudPET. Expert Nuclear Medicine Physicians were asked to compare the NeurocloudPET results with the previous report, achieved by the traditional visual analysis, using the software tool as a second opinion tool before emitting a diagnosis. Results showed that in 26,1% of evaluated cases, Neurocloud-PET quantification brought up previously unseen information relevant for the diagnostic.

- At Hospital San Pedro (La Rioja , Spain) nuclear designed a study on a cohort of 31 patients to evaluate the use of 18FDG-PET as a tool for improving Parkinson Disease diagnosis on especially difficult cases. The results show that Neurocloud improved visual diagnostic on 93% of the cases, while in 25% of the cases quantification provided by Neurocloud was the main source for making a diagnostic [6].

- In a study aimed to evaluate the use of 18FDG-PET image quantification on routine diagnosis of dementia patients, Dr. Carlos Torrijo (Hospital Casa de Salud, Valencia, Spain), used Neurocloud on a cohort of 50 patients. Results show that Neurocloud improved confidence in visual diagnosis in 38% of the cases, while in 10% of the cases information provided by Neurocloud made a better match with the neurologist clinical diagnostic that visual interpretation did.

Features

+ Sensitive. Identifying neurodegeneration in early stages of the disease thanks to one of the most extensive databases of PET-FDG (>120 subjects) of normal individuals on the market.
+ Specific.Integrating all the necessary resources for the diagnosis: results in images, and data tables and an interactive viewer.
+ Objective. Reducing inter-observer variability among specialists.
+ Quickly. Processing automatically the results in 5 minutes.

References

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Contact

qubiotech.com

+34 981 976 470

hello@qubiotech.com