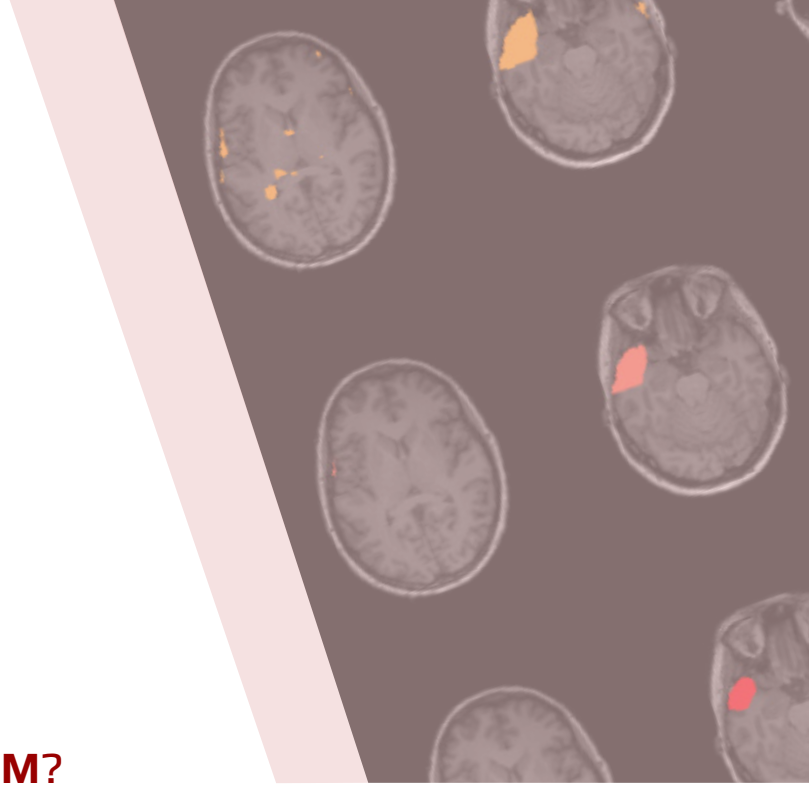
Neurocloud-SISCOM

your assistant in diagnosis with ICTAL SPECT quantification

QUBIO tech



01 What is **Neurocloud-SISCOM?**

Neurocloud-SISCOM is a CE marked software for the precise identification of the Epileptogenic focus following subtraction of, MRI co-registered, ictal and Interictal SPECT images. Through an easy-to-use web-based interface, the qualified user can upload neuroimages in the standard DICOM format and obtain valuable information with just one click of intervention. In a few minutes, the user can review the results in the specific analysis dashboard, showing both visual and quantitative data. The system also allows for downloading a customizable report of findings and navigating through different quantification overlays over the patient MRI and SPECT images with our 3D online viewer. All the relevant images and data provided by Neurocloud-SISCOM can be downloaded in DICOM format as well.

Neurocloud-SISCOM is a support tool for nuclear physicians and epileptologists that accompanies the specialist in the process of identifying the epileptogenic zone in patients with temporal lobe epilepsy and it has also been described as particularly useful in identifying the seizure-onset zone in focal dysplastic lesions. The SISCOM procedure provides a sensitivity greater than 80% and a specificity greater than 75% in the location of the epileptogenic focus [1]. To carry out this procedure requires the use of specific software for this purpose. Neurocloud-SISCOM enables its incorporation into the clinical routine through its automated, quick and ease of use and interpretation of results.

The physician can use the information provided by Neurocloud-SISCOM to validate his/her findings from the visual examination of SPECT images and MRI and complement them with unbiased quantitative and less rater-dependent data for achieving a more robust evaluation and reducing the diagnostic errors rate. This white paper aims to describe how Neurocloud-SISCOM can help in the clinic routine, how does the software works and the methodologies it uses, which information of interest provides and how reliable it is.

02 How **Neurocloud-SISCOM** helps?

Brain perfusion single-photon emisión computed tomography (SPECT) is a functional nuclear imaging technique performed in order to evaluate regional cerebral blood Flow (CBF). In SPECT, because CBF is closely linked to neuronal activity, the activity distribution is presumed to reflect neuronal activity levels in different areas of the brain. Brain SPECT imaging technique has many different applications such as the detection and evaluation of cerebrovascular disease, the differential diagnosis of suspected dementia or the detection of the seizure focus on patients with refractory epilepsy[2].

In the latter case, epilepsy surgery is highly effective in treating refractory epilepsy but, in order to evaluate its success chances, requires a very complex and accurate presurgical localization of the epileptogenic focus (EF)[3]. Briefly, localization of the region of seizure onset traditionally depends on seizure semiology, scalp electroencephalographic (EEG) recordings and correlation with anatomical imaging modalities such as Magnetic Resonance Imaging (MRI). In recent decades, the introduction of noninvasive functional neuroimaging methods, including SPECT and positron emission tomography (PET) has dramatically changed the method for presurgical epilepsy evaluation. These imaging modalities have become powerful tools for the investigation of brain function and are an essential part of the evaluation of epileptic patients.[4]

SPECT has the practical capacity to image blood flow functional changes that occur during seizures (ictal state) in the routine clinical setting, providing unique information on the seizure that cannot be accessible by any other means. Ictal SPECT has been shown to be effective, as it permits non-invasive disclosure of increased CBF in the areas affected by an epileptic discharge[5]. In addition, interictal SPECT can show, in contrast, decreased CBF in the same areas.

In order to appreciate the differences between the ictal and interictal SPECT studies, an image resulting from the subtraction of the interictal SPECT from the ictal is obtained. This image will identify the epileptogenic focus after applying an appropriate threshold.

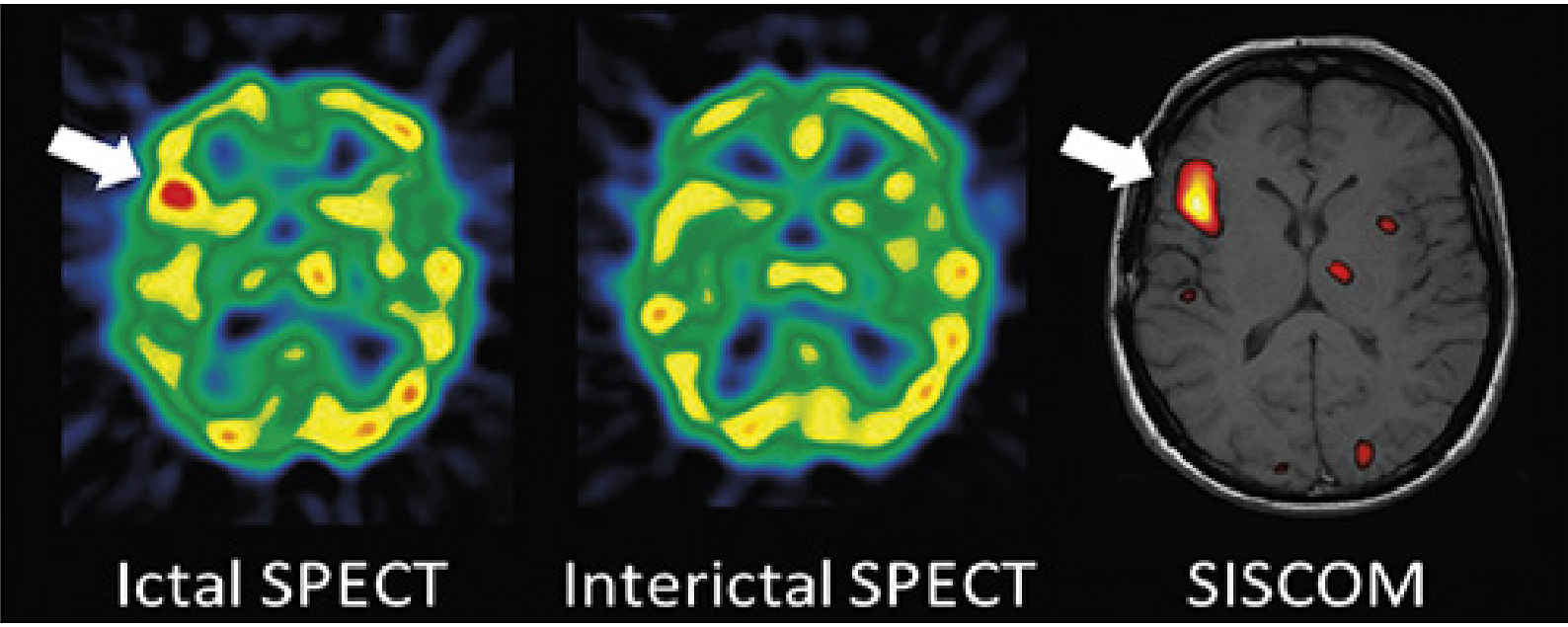


Figure 1. Example of the results of a SISCOM analysis. Images acquired during ictal (Left) and interictal (Centre) SPECT are shown. We can see also the subtraction result (Right).

Traditional side-by-side visual interpretation of SPECT ictal and interictal images is a tedious and challenging task to identify the epileptogenic focus. Epilepsy patients with frequent seizures that do not respond to medication should be evaluated for surgery. Neurocloud-SISCOM improves the location of surgical seizure focus,which translates into an improved surgery outcome by increasing the possibility of complete extraction of the focus.

Neurocloud SISCOM automatically processes the images in less than 5 minutes. The user can review the results in the Neurocloud platform, where the epileptogenic zone is visualized over the MRI, as well as the quantitative results of the analysis.

Below we can see a case of a patient diagnosed with epilepsy. The results of the software show the presence of an epileptogenic focus in the temporal lobe of the left hemisphere. Due to the fusion with the resonance image we can know with accuracy the location of the focus, which is very valuable information for the study of a possible surgical resection.

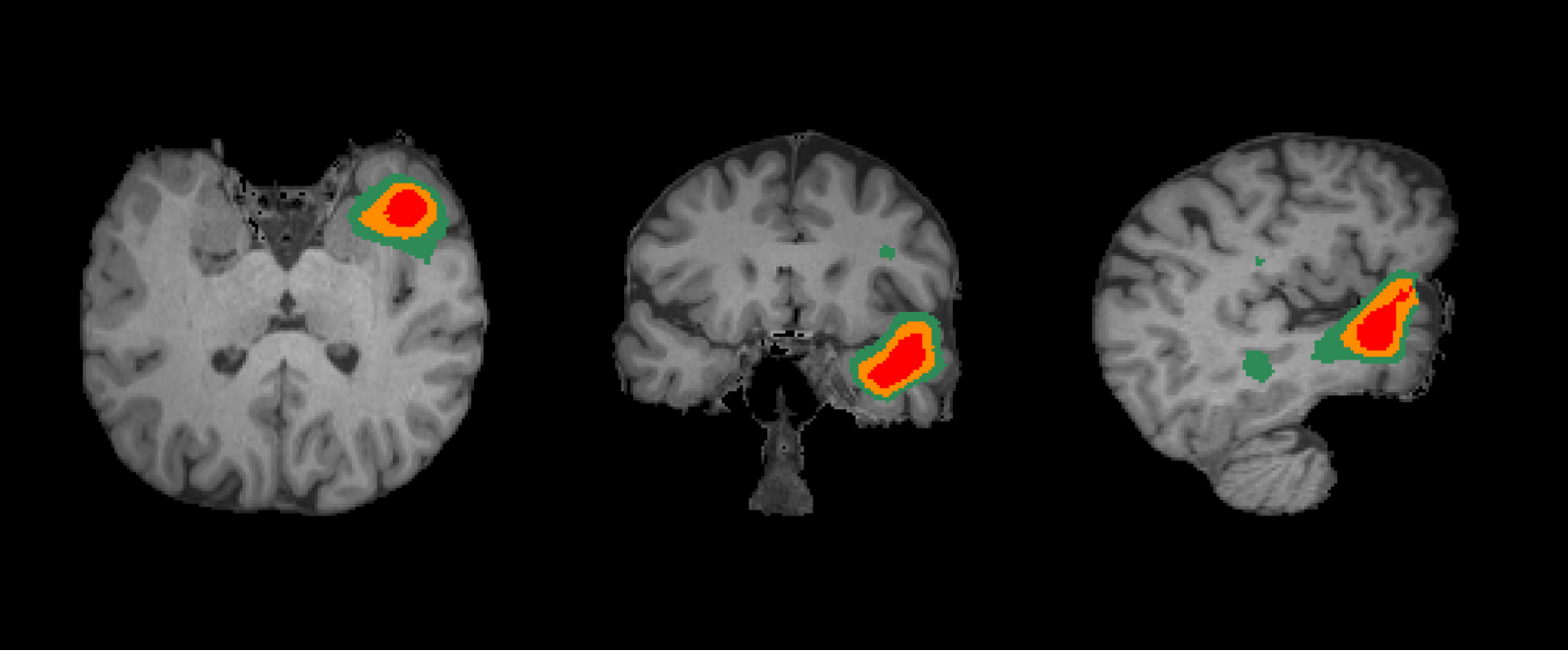


Figure 2. Epileptogenic focus identified by Neurocloud-SISCOM over the patient MRI.

In the data tables provided by Neurocloud-SISCOM presented in the figure below (Fig. 3), we can see that the focus extends over the anterior temporal lobe and the superior temporal gyrus. The physician can confirm the results by inspecting the images in the Neurocloud viewer (Fig. 4)

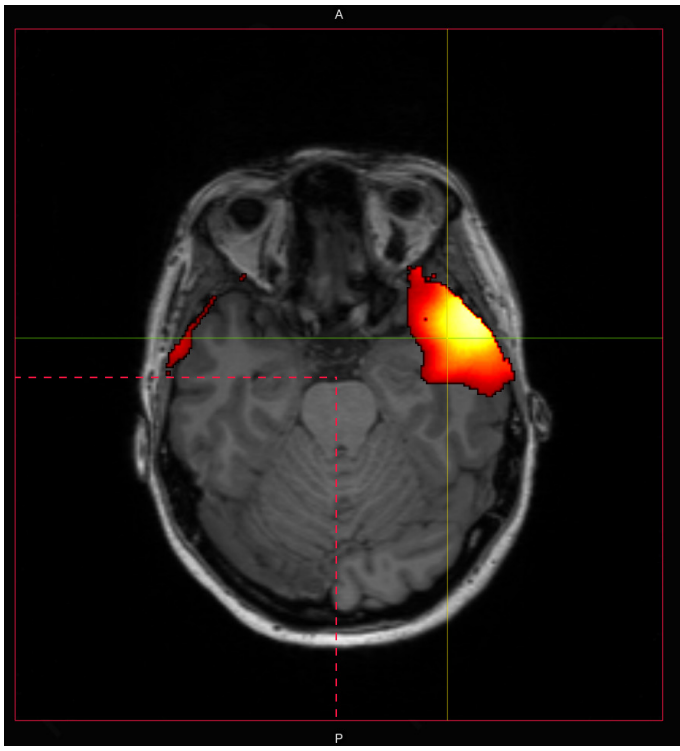
Temporal −

	ROI	Extension left [%]	Z-score left	Extension right [%]	Z-score right
	Anterior temporal lobe, medial part	34.28%	6.54	0.00%	0.00
	Anterior temporal lobe, lateral part	51.12%	7.75	0.25%	2.43
	Superior temporal gyrus, anterior part	77.42%	7.90	0.02%	2.28
	Superior temporal gyrus, posterior part	17.02%	5.62	0.02%	2.28
	Middle and inferior temporal gyrus	29.02%	6.08	0.00%	0.00

Figure 3. Caption of the Neurocloud SISCOM data table with the maximum significance values (Z score) as well as the percentage of overlap of the epileptogenic focus in the temporal lobe.

Figure 4. Epileptogenic focus localization in the patient MRI space. Axial view displayed using the Neurocloud-SISCOM online 3D-Viewer.

As we see in clinical cases as this, the use of a software tool is an essential support to reduce time and obtain high precision results. Neurocloud -SISCOM offers this service in a totally automatic and fast way, with a processing time of maximum 5 minutes, reducing considerably the working time and offering high precision results.



03 How **Neurocloud-SISCOM** works?

Neurocloud- SISCOM is a cloud based software designed to identify the epileptogenic zone by performing ictal and interictal subtraction and corregistering the result with the patient MRI. This section describes each of the steps conducted by the algorithm for the extraction of the epileptic focus from three input images: ictal SPECT, interictal SPECT and MRI. Moreover, it is explained how the data tables presented in the neurocloud- SISCOM results are obtained and how to interpret them.

SISCOM processing is commonly divided into four steps: SPECT-SPECT(S-S) registration, intensity normalization, subtraction and SPECT-MRI (S-M) registration. The processing core of the application is developed in C++ and it is based on robust open source libraries such as VTK, ITK, MITK, DCMTK, NETGEN and TETGEN among others.

1. SPECT- SPECT Registration

This process consists in the integration of both SPECT images, resulting in two relinged images in the same reference space. In order to improve the robustness of realignment Neurocloud-SISCOM first proceeded to mask the uploaded SPECT images to remove extracerebral regions with high radiotracer uptake and continues with the realignment of interictal study into ictal space. The realignment process is based on a rigid, voxel-based, matching technique[6].

2. Intensity normalization & SPECT subtraction

In order to appreciate the differences between the ictal and interictal SPECT studies, a parametric image resulting from the substracion of both realigned studies is obtained. To accomplish this, first it is performed an intensity normalization, to minimize total brain count differences between ictal and interictal realigned SPECT studies. Secondly, a subtraction image containing the relative difference between ictal and interictal image is obtained .

3. SPECT-MRI registration & Fusion of MRI and EF

The aim is to accurately locate the epileptogenic zone, which is why the MRI is used as an anatomical imaging modality by fusing it with the result of SISCOM analysis. This requires the previous step of co-registration of the MRI with the SPECT images.

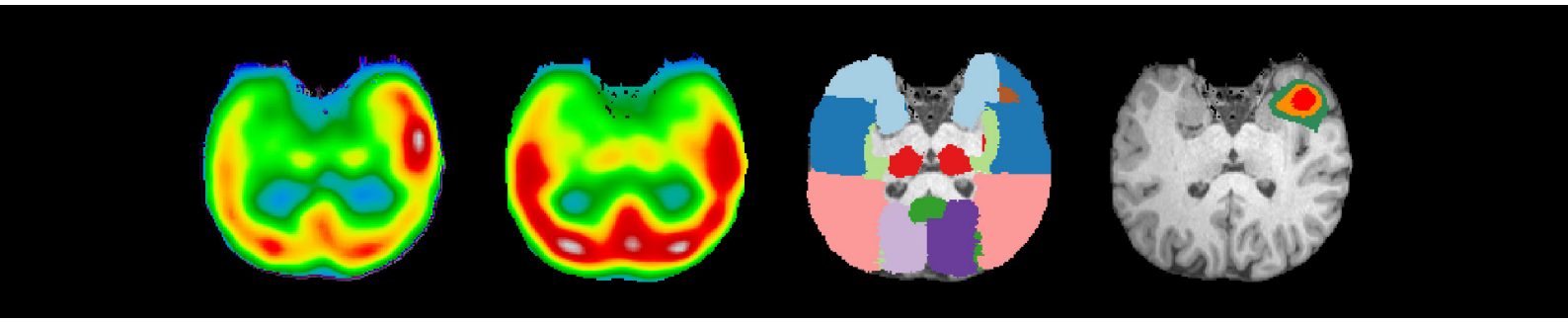
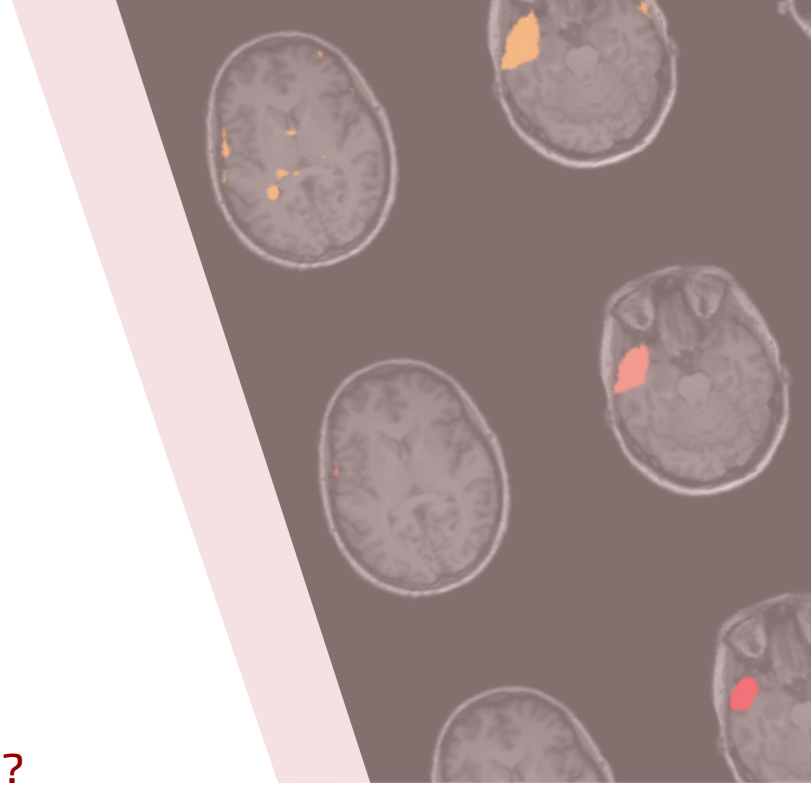


Figure 5. Ictal and Interictal image of the patient, Atlas coregistered with the patient's MRI and extraction of the epileptic focus shown on the MRI in axial view (from left to right).

Once the analysis has finished The results are accessible for the user in the cloud platform that consist of captions of the EF overlapped to the MRI along with quantitative information such as the ZScore value in each brain ROI.



04 What problems does **SISCOM** solve?

Based on solid evidence the European Association of Nuclear Medicine (EANM) included in its procedure (Kapucu et al, 2009)[7] guidelines for brain perfusión SPECT a recommendation to perform subtraction analysis techniques on SPECT imaging, namely SISCOM, in the study of epilepsy. Nevertheless, not all the hospitals have followed this recommendation, since SISCOM methodology is usually based on in-house algorithms, with multiple manual steps that make the whole process extremely complex and time-consuming.
In order to help physicians to include SISCOM procedure to identify EF, a team of researchers from several institutions (Universitat of Barcelona, Hospital Clinic and Universidad Politécnica de Madrid) grouped within CIBER-BBN (Centro de Investigación Biomédica en Red-Bioingeniería, Biomateriales y Nanomedicina) developed a SISCOM quantitation application named t-Sare. Qubiotech Health Intelligence signed (2017) a technology transfer contract in order to translate this algorithm in a commercial product named Neurocloud-SISCOM.

The resulting software developed by Qubiotech aims to provide a completely automatic approach for the SISCOM analysis on the clinical routine. Qubiotech offers a cloud-based platform so that the user can access with his credentials from any device. Its interface is designed to be intuitive and fast to use: in only two clicks and 5 minutes the user obtains the results of the uploaded study. The outcome of a Neurocloud-SISCOM analysis consists of a parametric map of the voxels identified as epileptogenic zone overlapped on the MRI, data tables with the maxim Z-Score for each región of interest (ROI) of the selected atlas (Hammers or AAL) as well as the percentage of focus overlap, the SPECT - MRI fusion image and quality parameters to verify the performance of the algorithm.
All the data can be reviewed on the analysis dashboard where it is presented in an easy to read structure. Imaging results can be displayed using the 3D online viewer and downloaded in DICOM (or NifTi) format. Moreover, a customizable report of findings can be obtained in PDF and DICOM formats.

05 How **Neurocloud-SISCOM** performs?

Since 2017, Neurocloud-SISCOM has been used in several hospitals, epilepsy units and other health centers in Spain and Portugal with satisfactory results.

Prior to launching the software as a quantification service for the physicians intensive validations were conducted in order to ensure the expected performance of the software.

Different analyses were simulated in order to mimic real cases where SISCOM analysis would be applied, using SimSET, a common software package for the Monte Carlo simulation of SPECT acquisitions. These same cases have been evaluated using the Neursocloud-SISCOM platform and compared with the original simulation. Neurocloud-SISCOM showed concordant results with the original analysis in 95% of the cases.

Features

- Sensitive. The SISCOM procedure provides a sensitivity above 80% in the location of the epileptogenic focus.
- Specific. With a specificity better than 90% in the location of the epileptogenic focus.
- Objective. Provides unbiased data reducing inter-observer variability among specialists.
- Quickly. Processing automatically the results in 5 minutes.

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