



neuropacs™

neuropacs™ Instructions for Use

DHF-IFU-05XX

Rev. 1.6

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neuropacs™
Version 1.1



neuropacs™

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1 Instructions for Clinical Use

1.1 Device Description

neuropacs™ is a fully automated, generalizable software that differentiates three Parkinsonian syndromes: Parkinson's disease (PD), multiple system atrophy parkinsonian variant (MSAp), and progressive supranuclear palsy (PSP). It uses AI to analyze diffusion Magnetic Resonance Imaging (dMRI) measurements from pathologically relevant brain regions of a patient who experiences symptoms consistent with PD, MSAp or PSP. The differentiation report generated from neuropacs™ can assist healthcare providers in accurately diagnosing people with these three types of Parkinsonism.

1.2 Indications for Use

The neuropacs™ system is a software application intended to receive and analyze diffusion MRI data from patients aged 40 years and older presenting with Parkinson's Disease (PD) symptoms. The neuropacs™ system provides a report to aid neuroradiologists and/or neurologists in identifying patients with Atypical Parkinsonism (i.e., multiple system atrophy Parkinsonian variant (MSAp), or progressive supranuclear palsy (PSP)). The results of the neuropacs™ system are intended to provide supplemental information in conjunction with a standard neurological assessment and other clinical tests. Patient management decisions should not be made solely on the basis of analysis by the neuropacs™ system.

1.3 Contraindications

- Do not use in patients with stroke, brain tumor, and seizures.
- As necessitated by the risks of Magnetic Resonance Imaging, patients who have any type of implanted electrical device (such as a cardiac pacemaker or a neurostimulator), or a certain type of metallic clip in their body (i.e., an aneurysm clip in the brain), cannot obtain the necessary dMRI scan for use in the neuropacs™ system.

1.4 Warnings and Precautions

- The neuropacs™ system should not be used for purposes other than indicated in the Indications for Use section above.
- Caution: Federal law restricts this device to sale by or on the order of a physician.
- The neuropacs™ system has been tested with datasets from GE, Siemens, and Philips MRI scanners. It is not recommended to use scanners that have not been tested by neuropacs™.
- This software does not work with any other form of data other than dMRI acquired with the protocol specified in this user manual.
- Visually inspect the data to ensure that the MRI scan contains the full volume of the brain and is free of distortions due to patient motion or other forms of artifacts, such as tumors.
- Healthcare providers must follow the instructions from this manual on how to interpret the differentiation results.



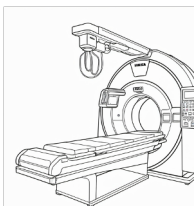
1.5 Intended Use

If a person is suspected to have a form of Parkinsonism, then the neuropacs™ software could be used as an aid in addition to standard of neurological care. The neuropacs™ system is a software-only device intended for use by neuroradiologists and neurologists interpreting diffusion MRI data for Parkinsonism diagnosis. The software analyzes diffusion MRI data using machine learning techniques to provide a diagnostic classification output in order to serve as an aid for neuroradiologists and/or neurologists to distinguish between Parkinson's Disease (PD), multiple system atrophy Parkinsonian variant (MSAp), and progressive supranuclear palsy (PSP) in patients 40 years of age or older with possible or probable diagnosis of PD, MSAp, or PSP. Patient management decisions should not be made solely on the basis of analysis by the neuropacs™ system.

1.6 Step-by-step Instructions for Health Care Providers

1

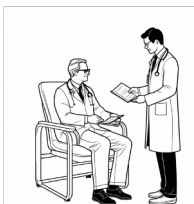
A patient experiences symptoms consistent with Parkinson's disease. The patient is 40 years of age or older with possible or probable diagnosis of PD, MSAp, or PSP. The neuropacs™ system can be used to assist with the differentiation between PD, MSAp, and PSP.

2

A diffusion MRI scan of the patient's brain must be acquired using the protocol parameters provided in this manual (section: Input Data Specifications). Basic image quality check is required through visual inspection to ensure that the scan contains the full volume of the brain and is free of distortions due to patient motion or other forms of artifacts, such as tumors.

3

The MRI scan can be submitted for analysis with neuropacs™ through a PACS or other software environment that provides the option to analyze data using neuropacs™.

4

The health care provider consults the result of the neuropacs™ analysis along with other clinical assessments and makes a diagnosis or other patient management decisions.



1.7 Example of results

The neuropacs™ analysis report contains the results from one or two independent classifiers:

- The classification result between PD and Atypical parkinsonism.
- If the first result indicates Atypical parkinsonism, then the classification result between MSAp and PSP is also contained in the report.

The report also contains a unique report ID and the date of the report for future reference.

Additionally, selected free-water biomarker levels included in the classification process, which produced the above results, are compared with those of control subjects.

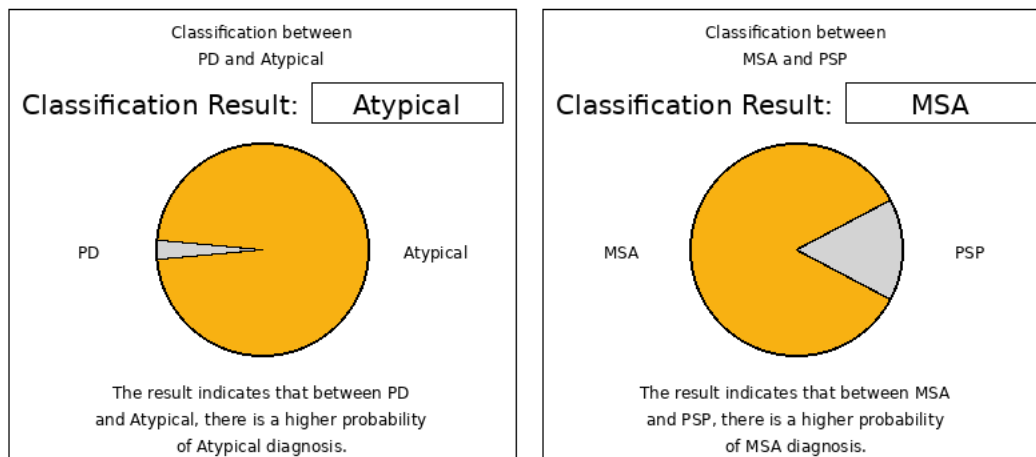
An example of the analysis report is shown below:



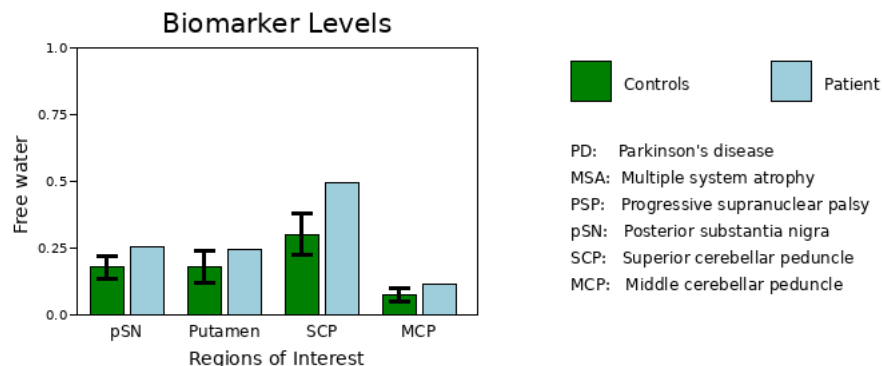
neuropacs™

ID: 42fb539f-beb1-4749-86be-91075820cfd8
Date (Y-M-D): 2024-06-17

Analysis: PD/MSA/PSP-v1.0
ML Version: 2BP20V6_29



Patient management decisions should not be made solely on the basis of analysis by the neuropacs system.





1.8 How to interpret the results

You must carefully read both classification results (PD vs. Atypical and MSA vs. PSP if shown) before making any diagnostic decisions. Patient management decisions should not be made solely on the basis of analysis by the neuropacs™ system.

Example 1: A physician evaluates a case of a 50-year-old patient with a possible or probable diagnosis of PSP. The physician orders a neuropacs™ analysis of the patient's dMRI scan to confirm the PSP diagnosis. The following differentiation result is obtained:

The result of the PD vs. Atypical classifier is: **Atypical**

The result of the MSA vs. PSP classifier is: **PSP**

- The results indicate that between PD and Atypical, there is higher probability of the subject being diagnosed with Atypical. This agrees with the physician's evaluation.
- The results indicate that between MSA and PSP, there is a higher probability of the subject being diagnosed with PSP. The result agrees with the physician's evaluation.
- Both results agree with the possible or probable diagnosis of PSP and confirm the physician's evaluation. The physician considers the PSP indication among other clinical tests and assessments in order to make patient management decisions.

In this case neuropacs™ was used to confirm the physician's initial assessment.

Example 2: A physician evaluates a case of a 66-year-old patient with a possible or probable diagnosis of MSA. The physician orders a neuropacs™ analysis of the patient's dMRI scan in order to confirm the MSA diagnosis before making any patient management decisions. The following differentiation result is obtained:

The result of the PD vs. Atypical classifier is: **Atypical**

The result of the MSA vs. PSP classifier is: **PSP**

- The results indicate that between PD and Atypical, there is higher probability of the subject being diagnosed with Atypical. This agrees with the physician's evaluation.
- The results indicate that between MSA and PSP, there is higher probability of the subject being diagnosed with PSP. This result differs from the physician's initial evaluation.
- The PSP indication questions the physician's initial assessment of MSA. The physician decides to perform additional clinical tests and assessments in order to better differentiate between PSP and MSA before making any patient management decisions.

In this case neuropacs™ questioned the physician's initial assessment.

Example 3: A physician evaluates a case of a 57-year-old patient with a possible or probable diagnosis of PD. The physician orders a neuropacs™ analysis of the patient's dMRI scan to confirm the PD diagnosis. The following differentiation result is obtained:



The result of the PD vs. Atypical classifier is: **PD**

The result of the MSA vs. PSP classifier is not reported because the first classifier indicated PD.

- The results indicate that between PD and Atypical, there is higher probability of the subject being diagnosed with PD. This agrees with the possible or probable diagnosis of PD and confirms the physician's evaluation.
- The physician considers the PD indication among other clinical tests and assessments in order to make patient management decisions.

In this case neuropacs™ confirmed the physician's initial assessment.

2 Technical Instructions

2.1 Product Requirements

- Internet connection (uploading speed of at least 300 Mbps is recommended).
- Access to a PACS or other software environment that provides the option to analyze data using neuropacs™.
- Access to patient's dMRI data.

2.2 Input Data Specifications

Whole brain diffusion MRI obtained with a single-shot spin echo EPI sequence sensitized to diffusion effect with the following acquisition parameters:

Scan Parameter Name	Value (or Range)
Magnetic Field Strength	3 Tesla
Repetition Time (TR)	6000 msec - 13000 msec
Echo Time (TE)	58 msec - 104 msec
Flip Angle	90°
Voxel Size	2 mm Isotropic
Number of Slices	≥ 80 Interleaved
Directions	> 30
Slice Gap	Zero
b-value	0 (x5), 1000 s/mm ²

The acquired MRI scans must be provided in DICOM imaging format (Digital Imaging and Communications in Medicine Part 10). The header of the DICOM images must contain the acquisition parameters using one or more of the following tags:



DICOM tag	Use
[0008, 0070]	scanner name
[2005, 1415] ^a	b-vectors
[2005, 1599] ^a	b-vectors
[0019, 10bb] ^b	b-vectors
[0019, 10bc] ^b	b-vectors
[0019, 10bd] ^b	b-vectors
[0019, 10e0] ^b	b-directions
[0019, 100e] ^c	b-directions
[0043, 1039] ^b	b-value
[0019, 100c] ^c	b-value
[0019, 1027] ^c	b-matrix
[0019, 100d] ^c	diffusion directionality
[0018, 1312] ^b	phase encoder

^a: usually used by Philips scanners.

^b: usually used by GE scanners.

^c: usually used by SIEMENS scanners.

2.3 Output specifications

The output contains the following information:

- request ID number [alphanumeric]
- the date of the processing request submission [yyyy-mm-dd]
- description of the input provided [text, example: "242 DICOM files"]
- the type of processing performed [text "PD/MSA/PSP-v1.0"]
- the version of the Machine Learning model used [text "2BP20V6_29"]
- the differentiation result between PD and Atypical [number between 0 and 1, with less than 0.5 denoting PD, and more than or equal to 0.5 denoting Atypical]
- description of the differentiation result between PD and Atypical [text "The result indicates that between PD and Atypical, there is higher probability of Atypical diagnosis." or "The result indicates that between PD and Atypical, there is higher probability of PD diagnosis."]
- If the previous result is Atypical, then the report will also contain the following two values:
 - o the differentiation result between MSA and PSP [number between 0 and 1, with less than 0.5 denoting MSA, and more than or equal to 0.5 denoting PSP]



- o description of the differentiation result between MSA and PSP [text “The result indicates that between MSA and PSP, there is higher probability of MSA diagnosis.” or “The result indicates that between MSA and PSP, there is higher probability of PSP diagnosis.”]
- biomarker levels of free water diffusion in the following brain regions:
 - o posterior substantia nigra [number between 0 and 1]
 - o putamen [number between 0 and 1]
 - o superior cerebellar peduncle [number between 0 and 1]
 - o middle cerebellar peduncle [number between 0 and 1]
- biomarker levels in control subjects [average and st. deviation] for each region:
 - o average value in posterior substantia nigra [number between 0 and 1]
 - o average value in putamen [number between 0 and 1]
 - o average value in superior cerebellar peduncle [number between 0 and 1]
 - o average value in middle cerebellar peduncle [number between 0 and 1]
 - o standard deviation in posterior substantia nigra [number]
 - o standard deviation in putamen [number]
 - o standard deviation in superior cerebellar peduncle [number]
 - o standard deviation in middle cerebellar peduncle [number]

2.4 Application Programming Interface

We provide an Application Programming Interface (API) for integration of neuropacs™ within your system. The API can be used in the following ways:

- Direct HTTPS requests to the API endpoints. Detailed technical specification of the endpoints is available at the following address:
<https://sl3tkzp9ve.execute-api.us-east-2.amazonaws.com/v1/api-docs/>
- Use the API through the neuropacs™ open-source examples that show how to perform the API calls from:
 - o JavaScript <https://github.com/neuropacs/neuropacs-js-api>
 - o Python <https://github.com/neuropacs/neuropacs-py-api>
 - o CLI (Command Line Interface) <https://github.com/neuropacs/neuropacs-cli>

Quick reference:

<code>init(apiKey, serverUrl)</code>	This function initializes the neuropacs object.
Returns: neuropacs object	Input: apiKey– String with a key provided upon registration serverUrl– The URL provided upon registration Output: A neuropacs object
<code>connect()</code>	This function establishes a secure connection with the neuropacs server.



Returns: String	Output: An alphanumeric connection ID or false if the connection was not established.
<code>newJob()</code> Returns: String	This function creates a new neuropacs order. An order ID is returned by the server to be used in subsequent references to this order. Output: String with the order ID.
<code>upload(dataset,orderId)</code> dataset: array orderId: String Returns: Integer	This function uploads a DICOM dataset file to a specific analysis order. Input: dataset – An array with File object orderId – String with the order ID. Output: An integer with the HTTP response code.
<code>runJob(productName,orderId)</code> productName: String orderId: String Returns: Integer	This function submits an order for processing. The type of neuropacs product to be used in this order must be specified. Input: productName – String with the product name. Example: "PD/MSA/PSP-v1.0" orderId – String with the order ID. Output: An integer with the HTTP response code.
<code>checkStatus(orderId)</code> orderId: String Returns: String	This function checks the status of an order. The result is returned as a JSON-formatted string with the parameters: started (true/false), finished (true/false), failed (true/false), progress (integer), info (string). Input: orderId – String with the order ID. Output: JSON-formatted string with the status info.
<code>getResult(format,orderId)</code> format: String orderId: String Returns: String (TXT, JSON, XML)	This function retrieves the result of a completed order in a specified format such as TXT, JSON, PNG, and XML. Input: format – String with the desired file format. orderId – String with the order ID. Output: A string (TXT, JSON, XML) or byte array (PNG) with the result.



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or bytes (PNG)

Example (in JavaScript)

```
//initialize the neuropacs object
const npcs = Neuropacs.init({serverUrl, apiKey});

//connect to the neuropacs server
await npcs.connect();

//create a new order for Parkinsonism differentiation
let orderId=await npcs.newJob();

//upload a DICOM dataset
await npcs.uploadDataset({dataset,orderId});

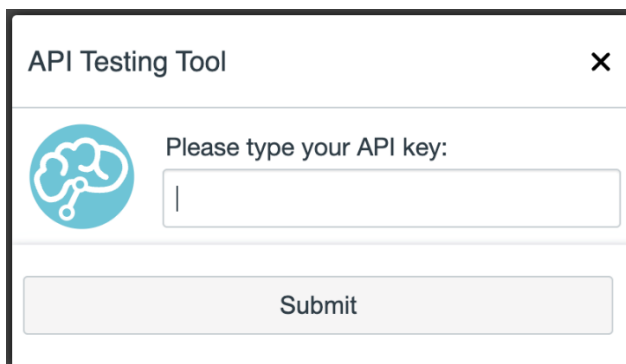
//submit the order for processing
await npcs.runJob({productName:"PD/MSA/PSP-v1.0",orderId});

//retrieve the results
let results=await npcs.getResults({format:"JSON",orderId});
```

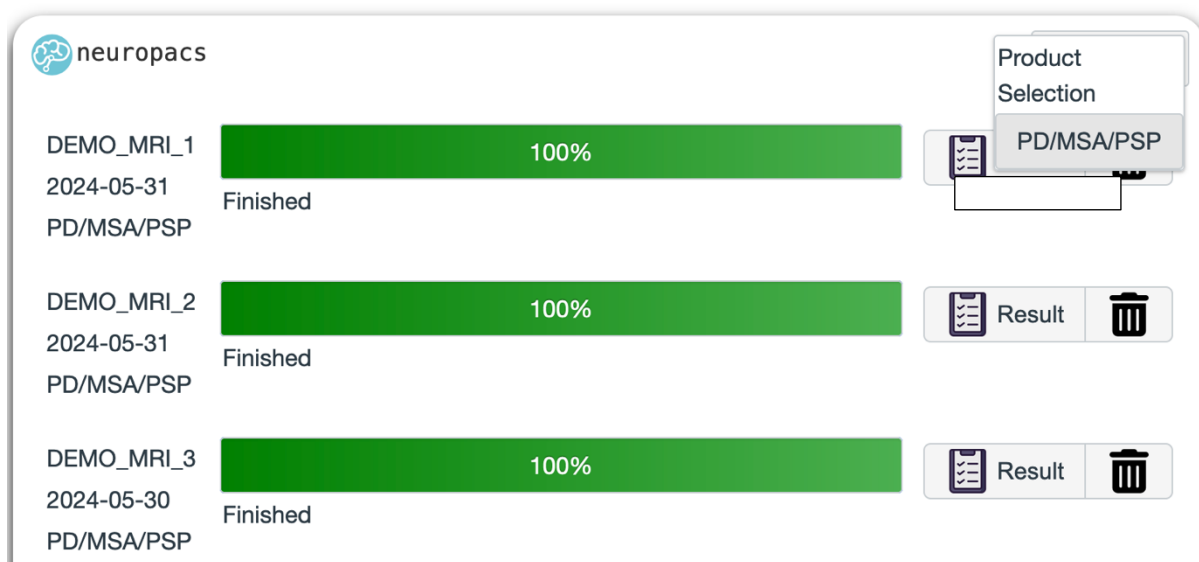
2.5 API Testing Website

We also provide a live demo of our API as a complementary product testing website. The purpose of this website is for customers to test and evaluate our products before they proceed with the integration of the products within their PACS environment.

The testing site, is located at: <https://neuropacs.github.io/demo/> and can be accessed using one of the following browsers: Google Chrome, Mozilla Firefox, Apple Safari, or Microsoft Edge. You must also type your testing API key as shown in the image below.




You can start a new order by clicking on the “New Order” button and select “PD/MSA/PSP” from the pop-up menu on the upper right corner. If you have previously used the testing site from the same browser, you will be able to check the progress of your previous orders and view the processing results. (See image below.)



Order ID	Date	Status	Progress	Product	Action
DEMO_MRI_1	2024-05-31	Finished	100%	PD/MSA/PSP	Result, Delete
DEMO_MRI_2	2024-05-31	Finished	100%	PD/MSA/PSP	Result, Delete
DEMO_MRI_3	2024-05-30	Finished	100%	PD/MSA/PSP	Result, Delete

After that, a pop-up window will prompt you to confirm that the patient meets certain criteria.

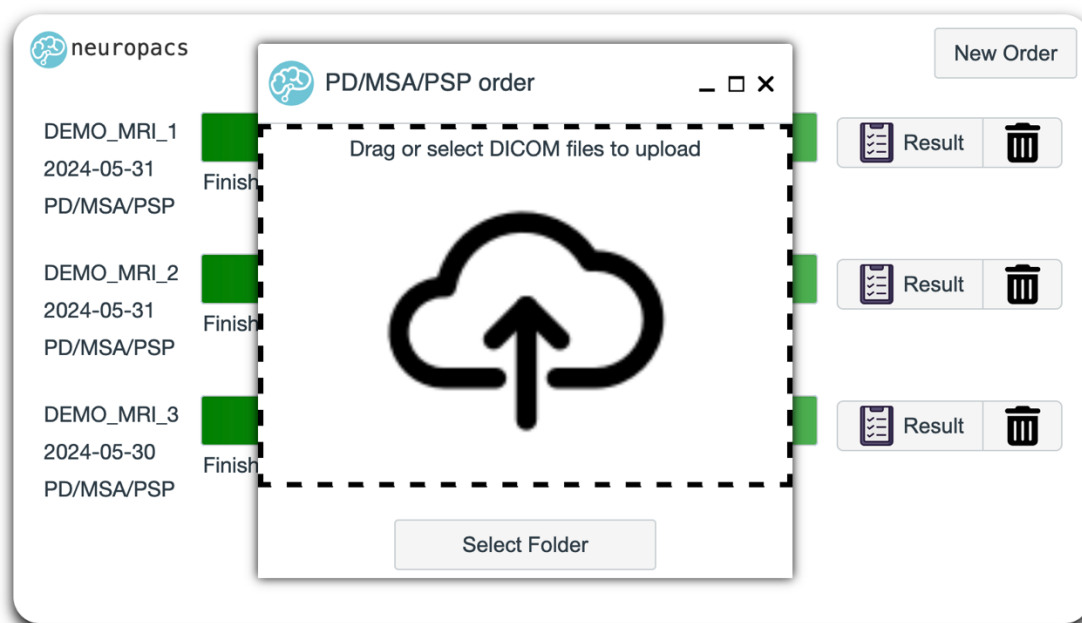

PD/MSA/PSP order
— □ ×

Please confirm the following:

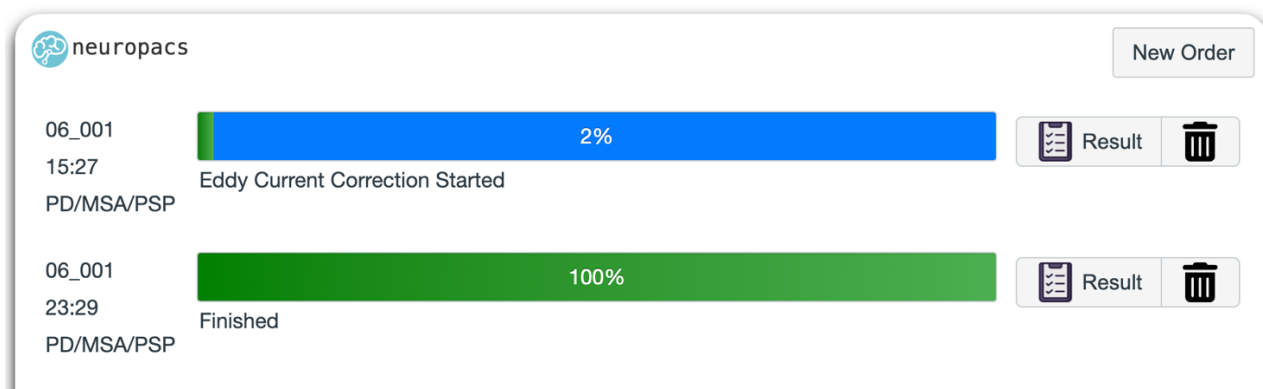
- ☒ The patient is 40 years of age or older.
- ☒ The patient experiences symptoms consistent with PD, MSA or PSP.
- ☐ The neuropacs diffusion MRI acquisition protocol has been followed.
- ☐ The MRI scan has been visually inspected to confirm that it contains the full volume of the brain and is free of distortions due to patient motion or other forms of artifacts.

Upload MRI


After that, a pop-up window will prompt you to drag or select DICOM files to upload for processing as shown in the image below.



After the file selection, an order number will be assigned to your processing request and the status of the process will be indicated on the top of the list of your orders. In the image below the status of the most recent order is 2%.



Once the processing is completed you can view the results by clicking on the “Results” button. In the example below the classification result between PD and MSA/PSP is indicating MSA/PSP. The classification result between MSA and PSP is indicating PSP. Furthermore, the result is supported by providing a chart of biomarker levels (free water) in four regions of interest (Posterior substantia nigra, Putamen, Superior cerebellar peduncle, and Middle cerebellar peduncle) and a side-by-side comparison with the corresponding biomarker levels in control subjects.



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DEMO_MRI_1
2024-05-31
PD/MSA/PSP

DEMO_MRI_2
2024-05-31
PD/MSA/PSP

DEMO_MRI_3
2024-05-30
PD/MSA/PSP

DEMO_MRI_3 - PD/MSA/PSP results

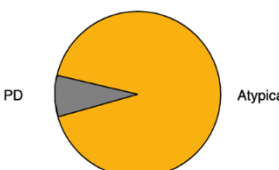
Download Print

neuropacs - Classification Report

Report ID: 183b21a1-15cb-4882-8aec-2d6bf4cd1d4d
Date (yyyy-mm-dd): 2024-05-30

Classification between PD and Atypical

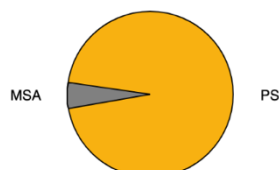
Classification Result: **Atypical**



The result indicates that between PD and Atypical, there is higher probability of Atypical diagnosis.

Classification between MSA and PSP

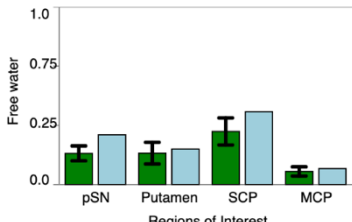
Classification Result: **PSP**



The result indicates that between MSA and PSP, there is higher probability of PSP diagnosis.

Patient management decisions should not be made solely on the basis of analysis by the neuropacs system.

Biomarker Levels




Free water


Regions of Interest


Controls Patient

PD: Parkinson's disease
MSA: Multiple system atrophy
PSP: Progressive supranuclear palsy
pSN: Posterior substantia nigra
SCP: Superior cerebellar peduncle
MCP: Middle cerebellar peduncle

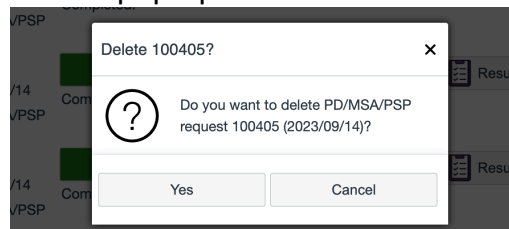
New Order

Result 

Result 

Result 

Finally, you can remove entries from your list of orders by clicking on the “trash bin” button and then “Yes” on the confirmation pop-up window as shown in the image below.





2.6 Recommended Security Controls

Cybersecurity Recommendations

It is recommended to keep your API KEY in secure digital storage such as a password vault.

Never share your API KEY with others.

Always use a new randomly generated AES key when you connect to neuropacs™.

It is recommended to follow the guidelines for AES-CTR encryption as specified in NIST SP800-38A, when sending data to neuropacs™ service for analysis.

Data de-identification Recommendations

Prior to sending data to neuropacs™ for analysis, it is recommended that all input images have been properly de-identified by removing the tags with sensitive information from the DICOM header, including but not limited to the following tags:

DICOM tag	Use
[0008, 0080]	Institution Name
[0008, 0081]	Institution Address
[0008, 0082]	Institution Code Sequence
[0008, 0090]	Referring Physician Name
[0008, 0092]	Referring Physician Address
[0008, 0094]	Referring Physician Telephone Numbers
[0008, 0096]	Referring Physician Identification Sequence
[0008, 1040]	Institutional Department Name
[0008, 1048]	Physicians of Record
[0008, 1049]	Physicians of Record Identification Sequence
[0008, 1050]	Performing Physician Name
[0008, 1052]	Performing Physician Identification Sequence
[0008, 1060]	Name of Physicians Reading Study
[0008, 1062]	Physicians Reading Study Identification Sequence
[0008, 1070]	Operators Name
[0008, 1072]	Operator Identification Sequence
[0008, 1080]	Admitting Diagnoses Description
[0008, 1084]	Admitting Diagnoses Code Sequence
[0010, xxxx]	Patient's information
[0032, xxxx]	Medical visit details
[0040, 0006]	Scheduled performing physician's name

It is recommended that other private tags are also removed.



2.7 Software Developer's Checklist

The following checklist must be completed when integrating neuropacs™ into your software solution.

<input type="checkbox"/>	Your neuropacs™ API key is securely stored in your software and is not shared with third parties.
<input type="checkbox"/>	The neuropacs™ report ID must be included in the report shown to the health care provider.
<input type="checkbox"/>	The neuropacs™ report date must be included in the report shown to the health care provider.
<input type="checkbox"/>	An indication that the results were generated by neuropacs™ must be included in the report shown to the health care provider.
<input type="checkbox"/>	The statement "Patient management decisions should not be made solely on the basis of analysis by neuropacs™." must be included in the report shown to the health care provider.
<input type="checkbox"/>	Before obtaining the report, the health care provider must be reminded that the patient must be 40 years of age or older, and must experience symptoms consistent with PD, MSaP or PSP.
<input type="checkbox"/>	A screenshot from the report generated from the provided test dataset in the intended format to be shown to the health care provider must be submitted to your neuropacs™ contact for approval. Prior to approval all diagnostic results generated by neuropacs™ will contain the text "Not for clinical use."
<input type="checkbox"/>	The data must be de-identified before submitted to neuropacs™ for analysis.

3 Software Version and Date of Manufacture

This device labeling is for neuropacs™ system (software) version 1.1. This revision of the device labeling (Rev. A) was issued on 7-Jul-2024.

4 Manufacturer Information



neuropacs
901 NW 8th Ave
Suite B8 #1077
Gainesville, FL 32601

Phone: 352-316-7923
Email: info@neuropacs.com
Website: <https://neuropacs.com/>