INSTRUCTIONS FOR USE

Pixyl.Neuro Release 1.7.2 via Pixyl's Web Interface

Version 5.0 of the document

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Pixyl.Neuro
Release 1.7.2
Manufactured in 2021
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Manufactured by:

Pixyl,
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Manufacture Date:

2021

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Consult user instructions manual

Caution

Federal law restricts this device to sale (or use) on the order of a licensed practitioner.

Additional Information	
List key components **Pixyl.Neuro**	Version Numbers **1.7.2**

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1. Device Description

Pixyl.Neuro is a web-based image analysis product that takes medical images of the brain from a magnetic resonance imaging machine (scanner) for analysis. Images in DICOM format are exported from the scanner and uploaded via the internet to the Pixyl.Neuro product. The user can view and download a report giving details of identified brain regions and lesions.

1.1. Intended Use

Intended Use	Pixyl.Neuro is intended for the automatic labelling, visualization and volumetric quantification of segmentable brain regions and lesions from a set of MRI images.
Intended Users	Medical Practitioners.
Intended Use location	In the healthcare facility.
Medical purpose	To support decision making when making a diagnosis or treatment planning in a subject with a neurological disorder. The application has been evaluated on data of patients with multiple sclerosis, white matter lesions, neuro degenerative disorders as well as age-normal subjects.
Multiple Use	As a software product this device can be used multiple times.
Patient population	Persons in the age range 18-90 years.
Part of Body	For use on the brain only.
Operator profile	Users responsible for supplying the input images to the application will be trained technologists working with medical images. The end user interpreting the report output by the application will be a certified medical practitioner with neuroanatomical experience and a full knowledge of the status of the patient being treated.
Application	To be used in the radiology or neurology clinic only when supported by other clinical information about the patient. The application will be used when an MRI scan is considered important to support patient planning and a quantitative report can aid decision making. The said MRI scans have been collected to a sufficient quality.

1.2. Contraindications



Automatic image-based measurements will not be accurate if the underlying image quality is not of a sufficiently high standard. This may be due to effects such as patient motion or gross underlying structural abnormalities or due to the way the images have been collected (inappropriate scanner settings). In addition, the underlying pathologies of the patient can also have a significant impact on the accuracy of the results obtained by the measurements.

This user manual provides guidance on image acquisition parameters, the accuracy of measurements made on images not conforming to this standard cannot be guaranteed.

The user is asked to review all reports thoroughly prior to making any decisions on patient treatment. Guidance for interpreting the report is provided in this user manual.

1.3. Device Classification

Pixyl.Neuro has been classified as a Class IIa Medical Device in accordance with Annex IX, Rule 10. The device has been categorized with a Software Safety Classification Class B, in accordance with IEC 62304:2006/Amd 1:2015. Minor injury or damage to health is possible.

1.4. Technical requirements

An internet connection is required for the online service to work.

Supported web browsers :

- Chrome, version >= 66.0 ;
- Firefox, version >= 60.0 ;
- Microsoft Edge, version >= 42.17.

Safari and Internet Explorer are currently not supported.

2. Privacy Statement

Pixyl is fully compliant with all aspects of the General Data Protection regulation (GDPR) ensuring the highest standards of privacy and security with respect to personal identifiable information (PII) and patient health records. This document describes data security relevant to the Pixyl.Neuro product.

What data does Pixyl store?

Users: User's first and last name, email address and affiliation (including address and contact number). This information will be used to provide the Pixyl.Neuro service to the user and may from time to time contact her/him to elicit feedback and provide her/him with updates on Pixyl.Neuro. Pixyl will not pass user's details on to any other parties.

Patients: To identify a patient in Pixyl.Neuro the user is asked to enter a Patient ID. This should not be the patient's name but should uniquely identify the patient for future reference. When downloading the report, the user has the option to add the real Patient Name into the pdf document.

Pixyl also stores patient images the user sends us and the results of the analysis. Note that upon transfer of images, DICOM headers are not modified and the user is advised to anonymise any data prior to upload.

Transfer and Storage of Data

All data is transmitted to our servers over a secure https connection. All servers running Pixyl.Neuro are located on Cloud Servers, offering a high level of security, backups and encryption of the data. More information can be provided upon request.

Who has Access to Data?

Pixyl.Neuro is strictly governed by user access controls to ensure only those users with permission to see patient information have access to see it.

Pixyl employees providing system software support will only access the system in the event of a problem. The system administrator who manages the Pixyl.Neuro deployment has had training in data privacy.

Policies and Procedures

All data received will be managed in accordance with Pixyl's Policies and Procedures which are fully conversant with GDPR.

3. Getting Started

3.1. Before you begin

Before attempting to work with this medical device, make sure that this manual and any Release Notes associated with the software have been thoroughly read and fully understood (refer to About page available from the Help Menu in the product interface).

3.2. How to register for a Pixyl.Neuro Account

Please contact the Customer Liaison Team at Pixyl to register for an account. They will provide you with a user account to access the web platform so that you can start analyzing patient data. Each user has their own account, if you require multiple users to access your institutional account, please let the team know.

3.3. Logging in for the first time

Please go to the URL: www.neuro.pixyl.io to access the login page. The first time you log in you will need to create your password. To do this follow these simple steps:

1. Click on the “Forgot Password” link
2. Enter your user name - this is the email address that you have provided
3. Check your email for a link to set your password
4. Enter your password twice to set your password

Log in with your user name and password and start adding patient data.

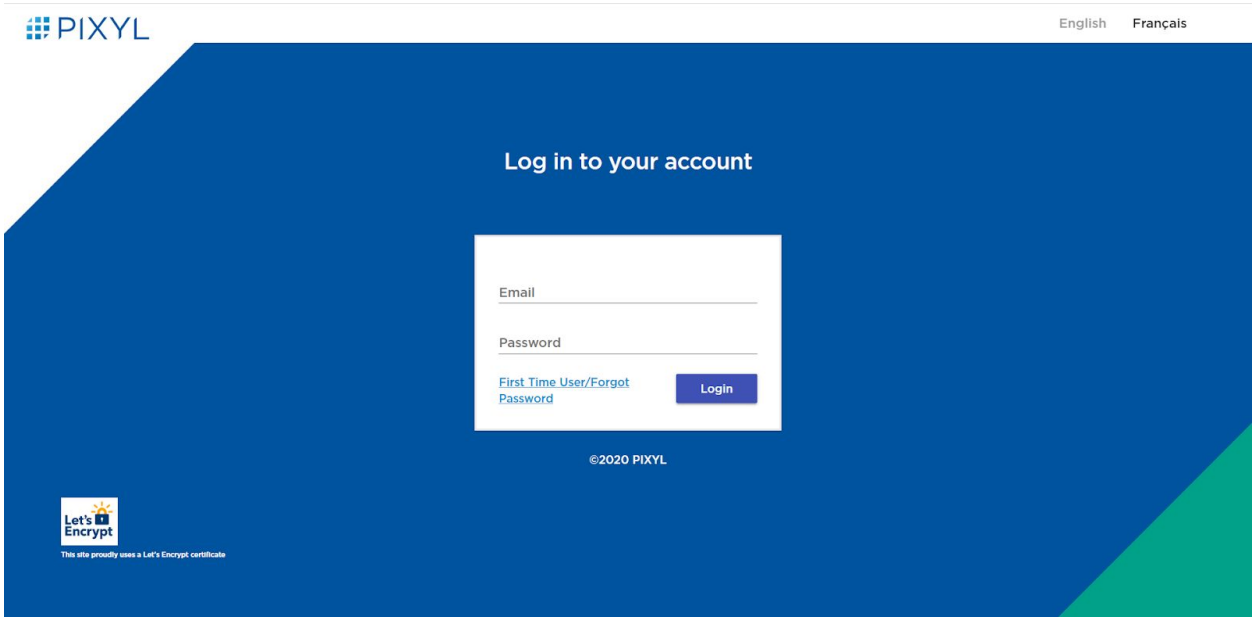


Figure 1: Login page.


Good to Know
Once you are logged in, your session remains open for 12 hours.
You can reset your password at any time by using the "Forgot Password" link
We recommend using Chrome when accessing Pixyl.Neuro.
Firefox, and Edge are also supported.
Do not use IE or Safari.
It is advisable to change uour password every few months to maintain the security of your account.
When setting your password, you must enter 8 characters: include at least 3 out of the 4 categories of characters (upper-case letters, lower-case letters, numbers, and special characters

4. Starting Analysis

4.1. An Overview

After connecting, you will land on the Analysis Overview page. Clicking on an Analysis type will show the patients associated with this Analysis.

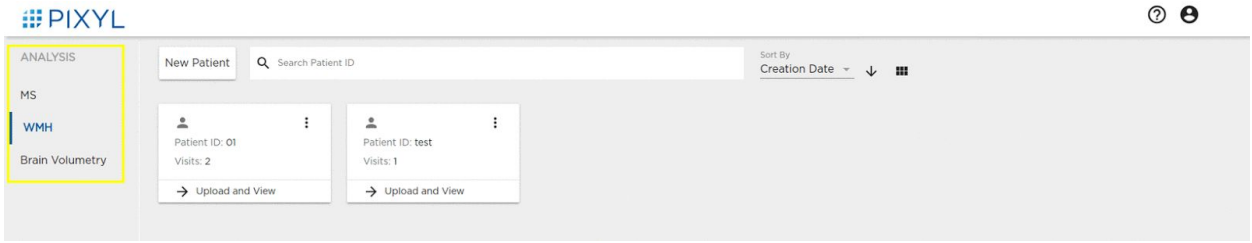


Figure 2: Select the appropriate analysis option for your patient.

You can be allocated access to up to three types of analysis. Each one of them corresponds to a different module in the product. A summary of these is provided in Figure 3.

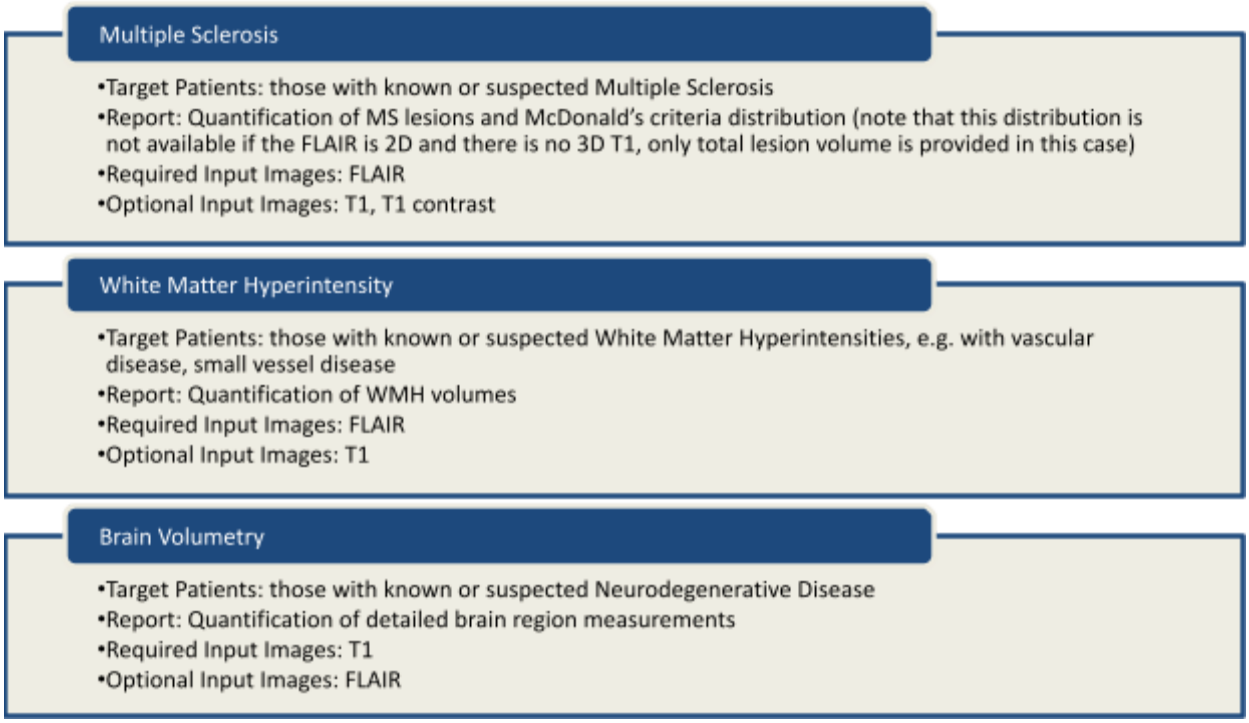


Figure 3: Analysis options available.

In order to start successfully using Pixyl.Neuro, it is useful to understand the structure of the product. See Figure 4.

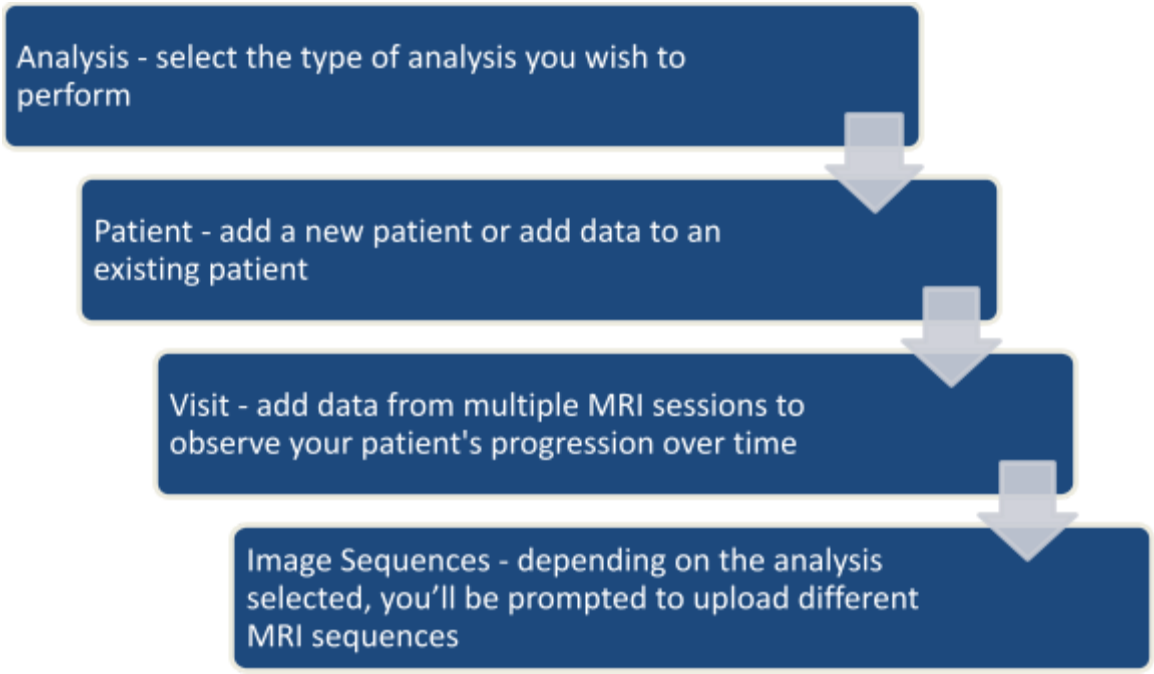


Figure 4: Data structure for Pixyl.Neuro.

4.2. Adding a New Patient

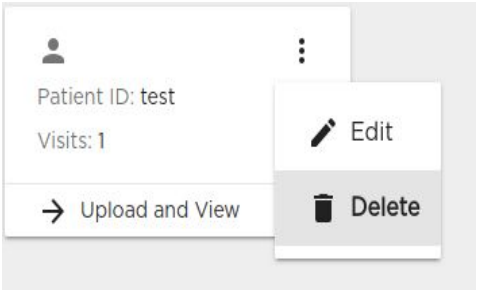
Having selected the analysis you wish to perform, you now create a new patient. Select the New Patient button at the top of the page. You will then be prompted to enter a Patient ID.



The identification of the patient is the responsibility of the user.
The Patient ID you enter should not be the patient name for security reasons. Use a pseudonym that will uniquely identify the patient. This ID will be shown throughout the system and on the report. You will need to know this ID in order to add patient visits at a later time. You will be able to add the Patient Name, Gender and Date of Birth to the report when you download it.

4.3. Edit or Delete a Patient

By clicking on the patient, you have the option to edit or delete the patient.



Delete is permanent and all patient data (images, analysis results) will be erased and will not be recoverable

Figure 5: Patient management, editing and deleting.

4.4. Adding a Visit and Images to a Patient

Once a patient has been created, you can upload MRI data. Select the patient you want to add data to and then select New Visit from the Patient Overview page.

You are prompted to upload DICOM sequences depending on the Analysis selected. The exam date is read automatically from information available in DICOM. If this information is missing for any reason, you must enter the exam date manually. You will also be prompted for the patient's year of birth. These two dates are used in the analysis to provide the comparison of brain regional volumes with a normal, age matched database.

Pixyl.Neuro is designed for patients between 18 and 90 years old. Any analysis performed on a patient whose age is out of this range will be considered irrelevant.

4.5. Monitoring the Analysis

Once the images have been uploaded analysis will begin automatically. On the Patient Overview page you will be able to see the status of the processing. All completed analysis will be listed according to the date of the visit. Data that remains in processing is indicated below the visit data by a rotating, processing symbol. If the images have failed in the processing, this will be indicated- you are advised to contact Pixyl if this is the case.

5. Accessing Analysis Reports

When the analysis has finished processing, you will see the analysis report from the Patient Overview page. There will be one report for each patient visit. As well as viewing the report on the web page, you can choose to download a PDF report.

Select Download Report to have the option to add the Patient Name, Gender and Date of Birth to the downloaded report.

6. Interpreting the Analysis Reports

6.1. Common Report Sections

Patient Information

Available in report: All
This section of the report contains personal information of the patient.

Name: Patient's name.
This field is left blank if the patient is anonymized.
It can be added at the time of downloading the report.

ID: Patient ID.
It is used to uniquely identify a patient within a project.

Gender: Patient's gender.
It is left blank if the patient data is anonymized.
It can be added at the time of downloading the report.

Year of Birth: Patient's year of birth, in the format yyyy.
It is left blank if the patient data is anonymized.
It can be added at the time of downloading the report.

Visit date: Date on which the current visit was acquired, in a format adapted to the selected language.

Prior visit date: If a prior visit is available, the report indicates its date.

Quality Control

Available in report: All
This section of the report contains a basic Quality Control of the current visit images and a comparison with prior visit images if available.

Status: Pass or Information.

Observations: Details of the Quality Control analysis.

Note: in all cases the analysis will be performed, but interpretation needs caution when the Quality Control returns some observations.

6.2. Multiple Sclerosis Report

Pixyl.Neuro Multiple Sclerosis analysis provides segmentation of multiple sclerosis lesions. This can be used to support the diagnosis, prognosis and follow-up of MS subjects.

Image Quality Requirements

The following requirements apply to input sequences for best segmentation results:

Sequence	Optimal Resolution (mm)	Minimum Resolution (mm)
FLAIR	1x1x1	1x1x3
T1W (optional)	1x1x1	1.2x1.2x1.2
T1 contrast (optional)	1x1x1	1.2x1.2x1.2

Images shall be acquired in AC-PC.

Lesion Segmentation

MS lesions are segmented on FLAIR images. Lesions on FLAIR sequences are labeled regarding their region of interest (ROI), to fulfill MS MRI criteria for diagnosis and follow-up:

- Periventricular
- Cortico-juxtacortical
- Infratentorial
- Deep white matter

For each ROI, lesions are counted, and their overall volume is computed.



Lesions less than 10 mm^3 in size are automatically removed from the results as they are not considered relevant.

Longitudinal Analysis

When you upload an additional exam to a patient, longitudinal analysis is performed with the previous exam. If you insert an exam between two existing exams (based on the exam date), then visits are reordered, and longitudinal analysis is performed against previous and following exams.

Longitudinal analysis computes new and enlarging (a threshold of 50% is applied to consider a lesion as enlarging) FLAIR lesions, regarding their region of interest:

- Periventricular
- Cortico-juxtacortical
- Infratentorial
- Deep white matter

To enable consistent comparison between exams, sequence quality must be similar. The following constraints apply on all sequences:

- Voxel size should not differ by more than 0.02mm;

- Contrast should not differ by more than 5% (mean and standard deviation).

Where possible, it is suggested that the same scanner, coil and sequences are used for each visit to give the most accurate results.

In the case these constraints are not fulfilled, a warning will be displayed in the interface.

Disease Activity

Available in report: Multiple Sclerosis
This section of the report contains a summary of the disease activity. It is based on the evolution of the number of lesions since the previous visit (Lesion Count). The section is empty if there is no prior visit unless a T1 with contrast image is available, in which case the **T1 with contrast** value will be shown.

T2 FLAIR New:	Number of new lesions since the previous visit.
T2 FLAIR Enlarging:	Number of enlarging lesions since the previous visit.
T1 with contrast:	Number of contrast-enhanced lesions that overlap T2 FLAIR hyperintensities. Only displayed if the modality is available.

Lesion load

Available in report: Multiple Sclerosis
This section of the report contains a summary of the MS specific White Matter Hyperintensities measured on T2 FLAIR images in different anatomical regions of the brain – **Periventricular**, **Juxtacortical**, **Infratentorial**, **Deep WM** (WM stands for White Matter) – and their sum, which is presented under the **Whole Brain** label.

Volume(ml):	Volume of lesions measured in the anatomical region, in milliliters (ml).
Change(ml):	Additional volume of lesions measured in the anatomical region since the previous visit, in milliliters (ml). Blank if no prior visit.
Lesion count:	Number of lesions identified in the anatomical region. The lesion count is based on the 2017 revision of the McDonald criteria and is presented with [0 to 8] or "≥ 9" for the whole brain, and "0" or "≥ 1" for the other anatomical regions. Note that the Barkhof MRI criteria for MS diagnosis includes at least 9 lesions on T2-weighted images.

6.3. White Matter Hyperintensities Report

Pixyl.Neuro White Matter Hyperintensity analysis provides segmentation of white matter hyperintensities lesions. This can be used for the diagnosis, prognosis and follow up of subjects with various pathologies including small vessel disease, vascular dementia, etc.

Requirements

The following requirements apply for best segmentation results:

Sequence	Optimal Resolution (mm)	Minimum Resolution (mm)
FLAIR	1x1x1	1x1x3
T1W (optional)	1x1x1	1.2x1.2x1.2

Images shall be acquired in AC-PC.

Lesion Segmentation

WMH lesions are segmented on the FLAIR. The overall lesion volume is provided.

Lesions less than 10 mm^3 in size are automatically removed from the results as they are not considered relevant.

Longitudinal Analysis

Longitudinal analysis consists of comparing the lesion volume between two timepoints.

White Matter Hyperintensity

Available in report: White Matter Hyperintensity
This section of the report contains a summary of the White Matter Hyperintensities measured on T2 FLAIR images in the whole brain.

Total Volume(ml): Volume of T2 FLAIR White Matter Hyperintensities, in milliliters (ml).

Change(ml): Volume change since the previous visit, in milliliters (ml).
Blank if no prior visit.

6.4. Brain Volumetry Report

Pixyl.Neuro Brain Volumetry analysis provides segmentation of brain regions. This can be used for the diagnosis, prognosis and follow up of subjects with various neuro degenerative pathologies.

Requirements

The following requirements apply for best segmentation results:

Sequence	Optimal Resolution (mm)	Minimum Resolution (mm)
T1W (3D, e.g. MPRAGE)	1x1x1	1.2x1.2x1.2
FLAIR (optional)	1x1x1	1x1x3

Images shall be acquired in AC-PC.

Regional Segmentation

Brain regions are segmented on the T1W image.

Longitudinal Analysis

Longitudinal analysis consists of comparing the regional volumes between two timepoints.

Segmentation and Comparison with Normal Values

Available in report: Brain Volumetry
This section of the report contains the Brain Volumetry analysis.

Volume(ml): Volume of the anatomical region, in milliliters (ml).

Change(ml): Volume change of the anatomical region since the previous visit, in milliliters (ml). Blank if no prior visit.

% of ICC: Percentage of the anatomical region volume compared to Intra Cranial Cavity volume.

Change(%): Percentage change of the anatomical region volume compared to the ICC volume. Blank if no prior visit.

Normative percentile: Percentile compared to age matched normal population. Normative percentile is computed if the patient is between 18 and 90 years old.

Change: Percentile change since the previous visit. Blank if no prior visit.

7. Further Help

If you did not find what you were looking for in this document and still require assistance, we will be happy to help. You can contact us by completing the form on the **Contact Us** page on the website, through the email addresses given or via the telephone number provided.

Pixyl follows device regulatory procedures to ensure that Pixyl.Neuro is correctly managed. All emails or online query submissions are internally monitored through a quality system and documented procedures followed to ensure any device problems that have been reported are effectively dealt with.

An email address for support is also available for any return concerning the product specifically: support@pixyl.ai.

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