PHAGENESIS®

Phagenyx®
Treat dysphagia, restore control

Phagenyx EPSB3 System User Guide

Medical device for the treatment of neurogenic dysphagia

Version 0
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Caution: Federal law restricts this device to sale by or on the order of a physician

Manufactured for Phagenesis Limited - Enterprise House, Manchester Science Park, Manchester M15 6SE, United Kingdom

PHAGENESIS®

Transforming the lives of people with dysphagia using revolutionary treatments developed through a commitment to scientific and clinical excellence

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1 Introduction

Prior to the use of the Phagenyx System for dysphagia treatment, users should read and familiarize themselves with the contents of this User Guide paying particular attention to the warning information outlined in Section 9.

Phagenyx devices and consumables are manufactured for and supplied by Phagenesis Limited whose primary contact address is Enterprise House, Manchester Science Park, Manchester, M15 6SE, United Kingdom and registered address is The Elms Courtyard, Bromesberrow, Ledbury, HR8 1RZ, United Kingdom.

1.1 Intended use

The intended use of the Phagenyx System is to restore swallow function using neuro-stimulation and to provide nutritional support for patients who require liquid feedings as a substitute for solid food.

1.2 Indication for use

Phagenyx is a neurostimulation device delivering electrical stimulation to the oropharynx, to be used in addition to standard dysphagia care, as an aid to improve swallowing in patients with severe dysphagia post stroke.

1.3 Contraindications and Cautions

While there are relatively few absolute contraindications to the use of Phagenyx system, the physical aspects of the Phagenyx PNX-1000 catheter should be considered in a similar clinical category to standard nasogastric feeding tubes. Therefore, Phagenyx treatment is generally contraindicated in circumstances where it is not possible to pass a standard NG tube, for example, nasal, oral or pharyngeal anatomical abnormalities that preclude passage of a feeding tube, history of esophageal perforation, stricture or pouch. In addition;

1. The Phagenyx PNX-1000 catheter should not be used if the patient has a cardiac or respiratory condition (for example severe heart failure or end stage COPD) where the insertion of a catheter into the throat might impact on their respiratory status.

2. Phagenyx treatment is contraindicated in any patient with an implanted electrical device or any invasive device with active electrical components that cannot be safely removed for the duration of treatment.

3. The Phagenyx PNX-1000 catheter should not be left in place if a patient is to receive an MRI scan. Insertion of the catheter should either be delayed until such time as the MRI has been completed, or the Phagenyx catheter should be removed and disposed of and a new catheter inserted after the MRI is completed.

4. Phagenyx treatment should not be applied to pregnant women.

5. The Phagenyx system is for the treatment of neurogenic dysphagia in adults and should not be used in children.

6. The PNX-1000 catheter part may be used within an enriched oxygen environment i.e., delivery of treatment is allowed if the patient is receiving supplementary oxygen support via a nasal cannula. The Base Station part should not be exposed to enriched oxygen.

7. If prior to insertion of the PNX-1000 catheter, the patient presents with significant throat pain, this should be investigated and the presence or absence of an infection confirmed. Any such infection should be treated and resolved before the catheter is inserted.

8. The PNX-1000 catheter is provided as a sterile single patient use device. The EPSB3 Base Station is not suitable for sterilization.

9. Suitable personal protective equipment must be worn when inserting the PNX-1000 catheter in patients to minimize the likelihood of infection. Follow local or national best practice guidelines in relation to catheter insertion for patients suspected of having transmissible infections such as COVID-19 or equivalent.

10. Any equipment in contact with the patient should be disinfected as per the instructions in this guide before being used with another patient.

1.4 Known Side Effects and Patient Management

A small number of rare side effects have been seen, either as a result of Phagenyx stimulation, or due to the physical presence of the treatment catheter. These are listed below together with the actions to be taken in the event that they occur.

1. Jaw chattering or facial/ear pain – These are rare events associated with active stimulation. If they occur, pause treatment and adjust the catheter further in to the patient by 1-2cm and retry treatment. If the chattering or pain persists consider stimulating at a lower current level. If this still does not resolve the issue discontinue treatment and remove the catheter.
2. Hypersalivation – Some patients produce excess saliva during treatment. This is not considered harmful. Suctioning to remove the saliva at the end of treatment may improve patient comfort.
3. Arytenoid edema or Pharyngeal abscess – In common with any indwelling catheter, the physical presence of the Phagenyx catheter may give rise to contact irritation over time. In rare cases this might give rise to an abscess. In the event the patient reports pain or discomfort that persists (>4hours) after the end of stimulation, the catheter should be removed on completion of the treatment regimen and replaced with a standard nasogastric feeding tube if enteral feeding is still required.

1.5 Method of operation

Phagenyx is intended for the treatment of neurogenic dysphagia. It should only be used by appropriately trained health-care professionals in accordance with the instructions in this guide. It is designed for use within a hospital setting only. The EPSB3 Base Station must be used only with PNX-1000 catheters. The Phagenyx system must not be used for any application other than that intended by the manufacturer.

2 System Overview

2.1 Treatment Principle

The Phagenyx system has been designed to treat oropharyngeal dysphagia arising due to disruption of or damage to the cortical centers for swallowing control or the peripheral swallowing sensory neurological architecture (neurogenic dysphagia). It works by delivery of electrical stimuli to the sensory nerves located in the mucous membranes of the oropharynx. The location of the stimulus and its frequency, have been optimized to promote neuroplasticity in the areas of the brain associated with swallowing control. The effect of the stimulus is to induce and accelerate a cortical reorganization process whereby responsibility for the control and coordination of swallowing activity is moved from the area affected to a complementary area of the cortical centers with intact function. Treatment also increases local levels of swallow related neurotransmitters in the oropharynx.

The electrical stimuli are delivered to the patient via two ring electrodes located on the outer surface of a single patient use catheter. Guide marks on the catheter facilitate electrode positioning, and the system applies continuous monitoring of the quality of contact between electrodes and target tissues during treatment to ensure that the correct tissues are stimulated and the amount of stimulus is controlled.

The catheter also conveniently incorporates the means to safely deliver enteral nutrition. Whilst this is not essential to the treatment of the underlying dysphagia, it provides the advantages that only one catheter is needed to fulfil both functions, and that the means to deliver the treatment (the electrodes on the catheter surface) may be left in place between successive stimulation treatments.

The Phagenyx system includes the EPSB3 Base Station and the PNX-1000 catheter.

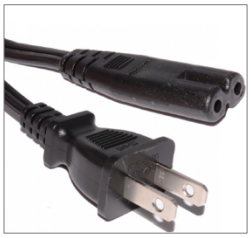
2.2 Base Station construction

The EPSB3 Base Station is used to optimize and generate the stimulating current. It also provides the means for recording and storing patient and treatment information. It incorporates a touchscreen menu driven user interface, a USB port for data transfer, a cable for connection to the mains power supply, and a cable for connection to the catheter.

a) Touchscreen – a touch sensitive screen presenting the User Interface
b) Casework – high density easy clean ABS
c) On/Off switch – push button switch with integrated LED indicator
d) USB port cover – provides protection and access as required to the USB port
e) Active output indicator – LED indicator to show when stimulation output is active
f) Treatment cable to catheter connector – connection point to catheter
g) Cable clip – securing point for Treatment cable
h) Cable tidy – storage for Treatment cable
i) Treatment cable to Base Station connector – connection point to Base Station
j) Cable groove – retaining feature on cable tidy

2.3 Additional Parts

There are three additional parts that are supplied with the Phagenyx Base Station - the USB Stick, Treatment Cable and Power Cable. Details of the correct method of use for all items are outlined throughout this guide.

Part and Part Number	Picture	Description
USB Stick (EPSU)		Used to transfer patient records from the Base Station to a hospital patient information system
Treatment Cable (EPSA)		A detachable component used to connect the Base Station to the Phagenyx PNX-1000 catheter
Mains lead (PLUS006)		Used to connect the Base Station to a mains power supply for operation
Case and key (EPSCC)		Used to store and protect the Base Station and additional parts during transport

3 Getting Started

3.1 Connecting to power and switching on

1. Connect the power lead to the power socket on the rear of the Base Station and the plug to the mains supply

2. Start up the Base Station by pressing the On/Off switch. The system takes approximately 30 seconds to launch and the On/Off switch should not be pressed again during this period.

3. During loading the screen below will briefly be displayed. The first screen displayed once loading is complete is the Log-In screen.

Start Up screen

IMPORTANT!! – Ensure that easy access is possible to disconnect the power lead from the rear of the Base Station or from the mains supply if required.

3.2 Logging In

New Operators

New operators must be added by a Phagenyx trainer or administrator using an authorization code. The new operator should type their name/ID and a password of their choice into the Operator and Password fields respectively. The trainer or administrator will then enter the 'New Operator' authorization code into the Authorization field. This will only have to be completed once for each new operator added to the system. Once the information has been entered, press the "Save to Disk". The system will ask if the information is to be saved, press the tick button to confirm. The new operator can now log in to the system.

Existing Operators

Users that have been previously authorized should type in their name/ID and the password they chose when originally authorized into the Operator and Password fields respectively.

The system software will automatically recognize user information once completely entered and will present a Tick Box button. Press the tick box button to progress to the next screen.

Deleting Users

If an Operator needs to be deleted, type in the Operator name followed by the Delete Operator authorization code (provided by the product supplier) in the Authorization field.

Once this is complete the Delete Operator button will appear. Once pressed the system will ask the user to confirm that the Operator is to be deleted.

Changing passwords

If an authorized user forgets their password or wants to change it, the administrator should type in the Change Password authorization code in the Authorization field once the user has typed in their details into Operator field.

Once this is complete the Change Password button should be pressed. The system will ask the operator to type in the new password and then will ask for confirmation that the new password should be set for this operator.

Passwords should be kept confidential and not disclosed to third parties or other users.

3.3 Checking Device Settings

When the correct operator and password details have been input, the system will progress to the system and settings screen. The operator should check that the time and date settings are correct.

Time and Date - The time and date settings can be adjusted and saved

Sound - The sound level from the inbuilt speaker can be adjusted using the up and down buttons

Keyboard - Either a QWERTY or a QWERTZ keyboard can be selected from the drop-down menu

Language - The preferred language can be selected from the drop-down menu

Save - If any changes are made these should be saved by using the Save Changes button in the bottom right corner of the screen.

Home button - Once all of the settings have been checked and changes have been made if necessary, the user should proceed to the Home screen by pressing the Phagenesis icon button in the top left of the screen.

3.4 Home screen

The Home screen is the starting point for key operations. There are four buttons – Treatment, Records, Settings and Log Off. The function of each is described below.

Treatment
This allows the user to begin the process of testing and optimization prior to treatment.

Records
This is used to search, display and transfer patient treatment records to the USB

Settings
This takes the user to the System and Settings screen where the time, date, sound language and keyboard layout can be adjusted as required

Log Off
This button is used to change user or log off prior to switching off the base station

Home button
The Phagenesis icon is located on most screens and can be pressed to bring the user back to the Home screen

3.5 Logging off and switching off

If the Log Off button is pressed on the Home screen the message ‘Are you sure you want to log off?’ is displayed. Pressing the Tick button will bring the operator to the Log-In screen. Pressing the ‘X’ button will return the operator to the Home screen.

If at any time the On/Off switch on the front of the device is pressed the message ‘Power Off?’ is displayed. Pressing the Tick button will result in the device being powered down. Pressing the ‘X’ button will return the operator to the Home screen.

If the On/Off switch is pressed and held for longer than 3 seconds the unit will switch off without any message being displayed. In the event the user interface is non-responsive for any reason this method should be used to power down the device.

4 Patient Records

4.1 Creating or mapping a patient record

Before a patient can be treated, a record that includes their name and hospital code or unique identification must be created. This record is then saved on both the Base Station and automatically transferred to the electronic chip within the catheter.

If there is no patient information stored on the chip in the catheter, the system will open the New Patient Information screen. This allows the operator to create a new record that will be used to store all the information relating to the treatment of that patient.

Add New Patient

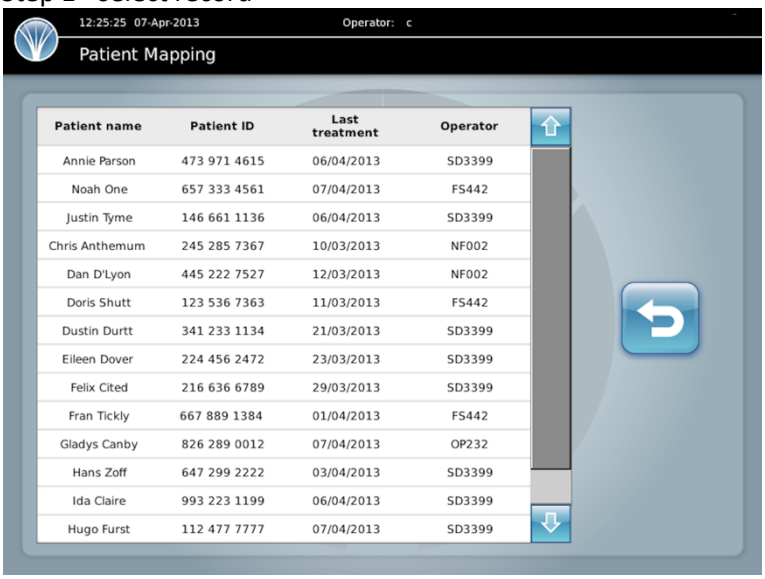
Once the information in the form of the patient name and identification has been input, press the Add New Patient button. The next time the catheter is connected to the Base Station via the treatment cable, the software will automatically detect the patient information and open the correct patient record.

Map Patient Information

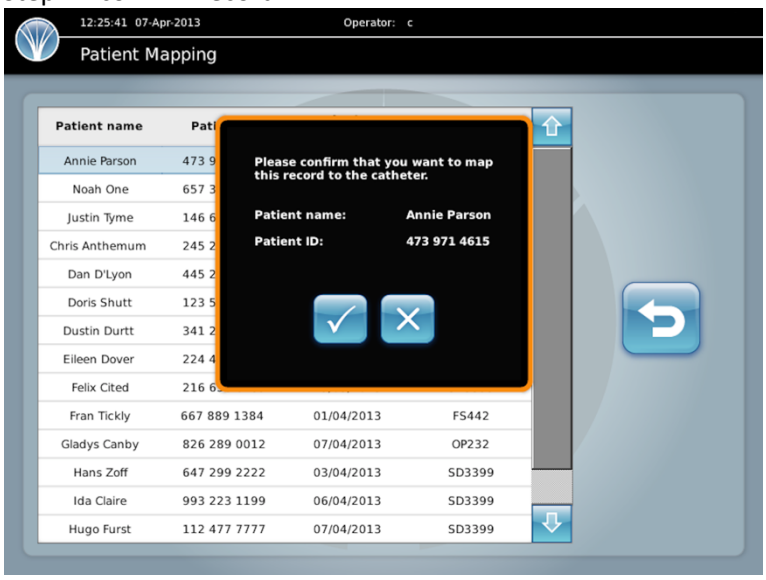
A patient record stored on the Base Station can be transferred onto a new catheter. This might be needed if the patient has already received treatment and the catheter used in that treatment has had to be replaced. When a replacement catheter is inserted into the patient and is connected to the treatment cable connector, press the Map Patient Information button. This will call up the list of patient records in a Patient Mapping window. Choose the correct patient record to be mapped. The system will ask for confirmation that this is the record to be mapped. If it is, press the Tick button and the patient information will be copied onto the chip in the catheter.

Mapping a patient record

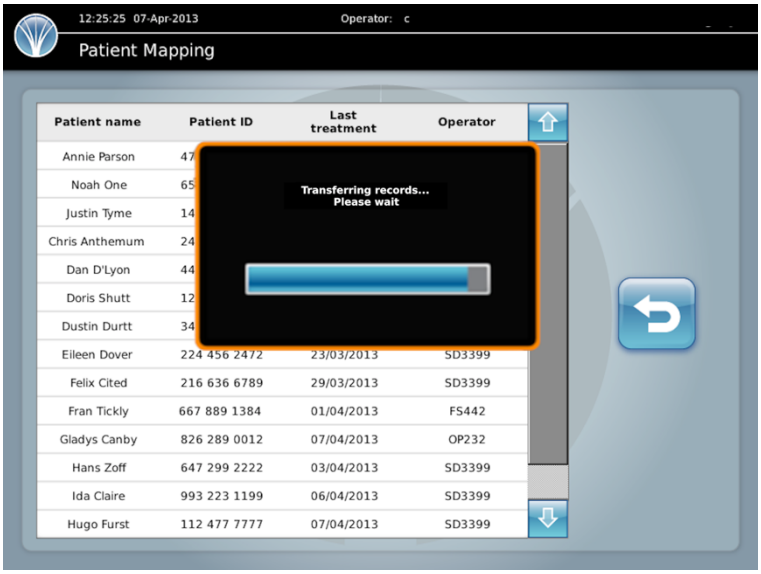
Step 1 - select record



Step 2 - confirm record



Step 3 - record mapped

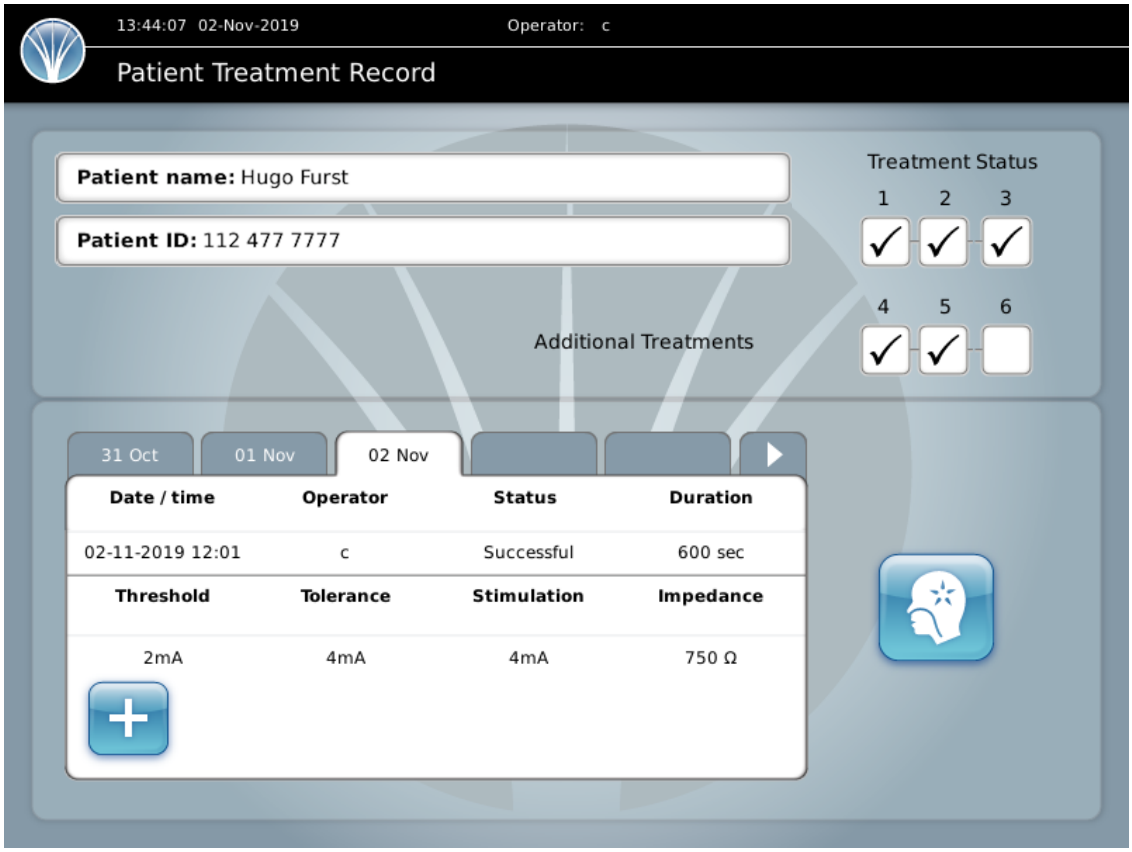


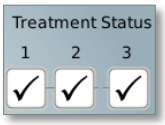
Transfer Patient Details

If there is patient information present on the chip in the catheter, but no corresponding record on the Base Station (this may occur if a site has multiple Base Stations in use), then the message below will display. The patient and treatment information can be transferred from the chip in the catheter but any associated comments will not transfer. For this reason, every effort should be made to use the same Base Station wherever possible for complete treatment of a given patient.

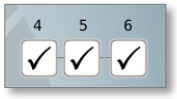
4.2 Record Format

The Patient Treatment Record contains data relating to the time, date and operating parameters used for each treatment. It is opened automatically when the treatment cable is attached to the catheter and the Treatment button on the Home screen is pressed. Each treatment is presented on a separate tab based on the date it was carried out. A number of parameters are saved for each treatment including the operator who carried out the treatment, the measured currents and the total duration. Comments associated with each treatment can also be recorded by the operator.





A summary of the treatment status is presented with each tick representing a successfully delivered treatment.



Where additional treatments have been delivered these are recorded here.

Treatment Optimization - Press this button to begin the process of optimizing the stimulation current for treatment

Add Comment - Press this button to add a comment to an individual patient treatment record

4.3 Searching Records

To search for a particular record press the Records button on the Home screen. The Patient Record Search screen will be displayed. Records can be searched by using at least one of four possible search terms - patient name, patient ID, operator and treatment date.

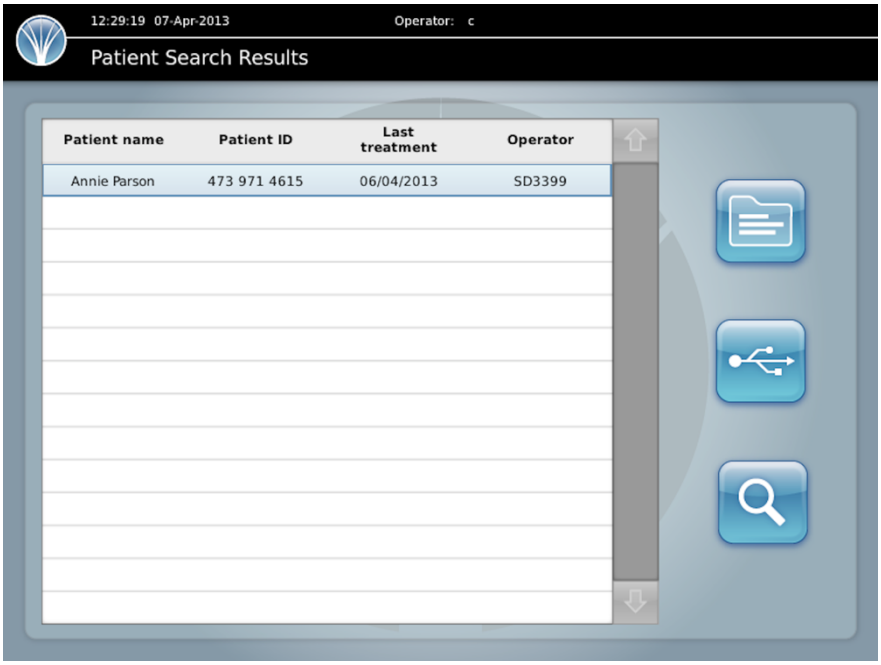
Searching is not case sensitive and the software will allow partial words to be input in all fields other than the treatment date.

Once the information is typed into the relevant field press the Search button. If there are matching records they will be listed in summary on the Patient Search Results screen (see below).

Display - Press this to display the chosen record

Save to USB - Press this to transfer the record to a USB stick. *

Search - Press this to return to the Patient Record Search screen

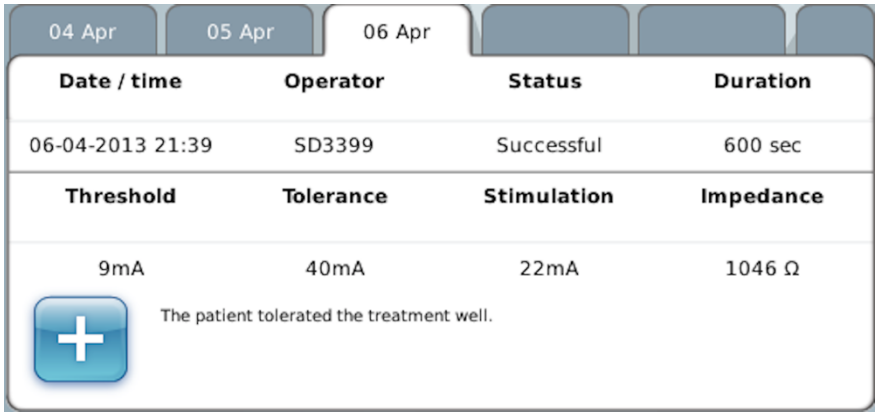


*Multiple records can be chosen and transferred together if required

4.4 Adding Comments to Records

To add a comment to the patient record, press the Add Comment button on the Patient Treatment Record screen.

Type in the information and press save. The information will appear at the bottom of the patient record. Please note that separate notes can be recorded for each treatment and will be displayed next to that treatment only.



4.5 Reports

Reports containing patient and treatment information are automatically generated in two formats

1. A pdf file suitable for printing or saving as an image
2. An XML file suitable for importing as data into an electronic patient record

Example pdf record

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Patient name	Patient ID	Generated by	Treatment Summary	Catheter Batch Number	Report Generated
Annie Parson	473 971 4615	c	2 of 3 complete	999	07-Apr-2013

Session	Date and Time	Operator	Status	Duration	Threshold	Tolerance	Stimulation	Impedance
1	04-Apr-2013 21:12	SD3399	Successful	600 sec	10 mA	32 mA	25 mA	1041 Ohms
2	05-Apr-2013 21:12	SD3399	Contact	600 sec	6 mA	33 mA	25 mA	1036 Ohms
3	06-Apr-2013 21:12	SD3399	Successful	600 sec	9 mA	40 mA	22 mA	1046 Ohms

Phagenyx Patient Treatment Record

The data is stored as a zipped file and is password protected. Suitable software to unzip the files must be loaded on any computer planned for receiving the copied data from the Base Station. Please see your local administrator for permission to load the software.

The password to unlock the files is the same password used to log in to the Base Station. Only the operator that transferred the patient record (or an administrator with copies of all log in passwords) will be able to unlock specific patient files.

An example of the zipped file format is shown below. Each zipped file is in the form of a folder (containing both the .pdf version of the patient file and the .xml version of the patient file) and is prefixed with the word 'Phagenesis' followed by the name/ID of the operator that transferred the record and the date the transfer was made

Phagenesis_c_07-Apr-2013.zip

When the file is unzipped the two files in the folder can be seen. An example of the unzipped file format is shown below. Files are saved in the folder using the unique patient identifier, in this case 473 971 4615 (not the patient name) followed by either .pdf or .xml depending on the file type.

473 971 4615.pdf
473 971 4615.xml

To open the files click on them and type in your Operator password.

4.6 Transferring Reports via USB

On any screen where this button is displayed a patient report can be generated and transferred onto a USB stick inserted into the USB port on the front of the Base Station. On the Patient Search Results screen multiple records can be selected and reports generated and transferred for each in parallel.

It is important that the USB stick is not removed during the transfer of data. Please ensure that you wait until the 'Transfer successful' message is displayed before attempting to remove the USB stick from the USB port on the Base Station otherwise the data may be corrupted.

If multiple files are being transferred it may take some time before the transfer is complete.

The USB stick should not be inserted into the USB port during treatment optimization or treatment delivery.

5 Patient Treatment Overview

5.1 Treatment Optimization

Sensitivity to sensory stimuli varies naturally in the population and may be further affected in a variable way in patients by the location and severity of cortical damage post stroke. It is important therefore to establish on a patient-by-patient basis the lowest current at which the patient can first detect an incrementally increased current (the Threshold Level) and also the highest level of current the patient can comfortably tolerate, as the current is further increased (the Tolerance Level). The Stimulation Level is then automatically calculated by the Base Station as per the formula below.

Stimulation Level (mA) = ((Tolerance – Threshold) x 0.75) + Threshold

(E.g., If Threshold = 5mA and Tolerance = 21mA then Stimulation Level = ((21-5) x 0.75) + 5 = 17mA)

As both the Threshold and Tolerance levels for a given patient can change over time, the process of establishing the correct currents for both of these levels ***must*** be carried out for each treatment. All other parameters are identical for each patient as summarized in the table below.

Parameter	Value
Frequency	5Hz
Pulse width	200µS
Waveform	Square wave
Duration	10 minutes per session

5.2 Number of Treatments

The number of treatments needed to deliver maximum therapeutic benefit varies from patient to patient. The standard treatment regimen is three treatments - one per day over three consecutive days. The majority of patients will respond to this number of treatments. For the minority of patients that don't show signs of improvement at this point, it is possible to deliver additional treatments. A maximum of 6 treatments in total can be delivered to the patient after which point the catheter will be electronically locked to prevent further treatments from being delivered to the patient.

As there are many factors that can impact a patients' ability to respond to the therapy it is not possible to predict in advance which patients are likely to respond to the standard three-treatment regimen. It is recommended that patients are assessed after three sessions before a decision on further treatments is made.

Assessment of patients on completion of Phagenyx treatment should follow local best practice. Any change to patient management should reflect observed improvements in patient swallowing and/or secretion management.

5.3 Treatment Regime and Rules

Standard treatment comprises three 10-minute treatment sessions. Additional treatments, up to a total maximum of six treatments, are possible if required. Software guidance is provided regarding the number and timing of treatments. A summary of the rules relating to treatment numbers and timing is given below.

1. Timing of first session – The first treatment may take place from 2 hours post catheter insertion.

2. Timing of subsequent sessions – The sessions should ideally take place on consecutive days but the interval must be no longer than 48 hours between completed sessions and no shorter than 14 hours. This is monitored and controlled by the Base Station software. There is no upper limit on the interval between the 3rd and 4th treatments to provide an opportunity for patient assessment.

3. Session time – The software is designed to deliver electrical stimulus for 10 minutes in each session. The session may be manually paused by the operator if required or automatically by the Base Station if it detects an electrode contact problem. In either case the treatment must be continued within 4 minutes of the pause initiation or else the session is classified as incomplete and must be repeated.

4. Retry – In the event of an incomplete session, and if the patient agrees to continue with treatment, it is possible to attempt to retry a session up to 2 more times within that 14-hour period.

5. Contact quality – The Base Station is designed to check the quality of contact for each pulse of stimulus delivered (5 pulses per second). In the event that contact quality falls below the acceptable level for a continuous period of 10 seconds then the software will alert the operator and automatically pause the session. This then provides an opportunity for the operator to adjust the position of the catheter or patient in order to restore contact.

6. Treatment counter – If the 48-hour interval between the treatments is unavoidably exceeded, then the treatment counter in the software is re-set and some treatments must be repeated. The counter is re-set to zero if the 48-hour interval is exceeded in between any of the first three treatments. The counter is re-set to 3 if the interval is exceeded after 3 treatments have already been delivered. Note: The 48-hour maximum interval does not apply between treatment 3 and 4 in order to allow the user to assess patient response to the standard three treatment sessions.

7. Total treatments - In the event the 48-hour limit is unavoidably exceeded on multiple occasions due to problems (and the treatment counter re-set to zero more than once) as many as 9 complete treatments may theoretically be delivered. No more than 15 treatment sessions (made up of both complete and incomplete treatments) are allowed for a single patient.

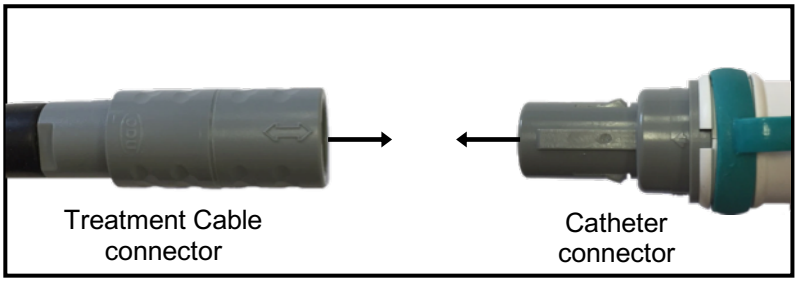
5.4 Insertion and use of the Catheter for feeding

Follow the guidance in the Phagenyx Catheter IFU for insertion, use and maintenance of the catheter.

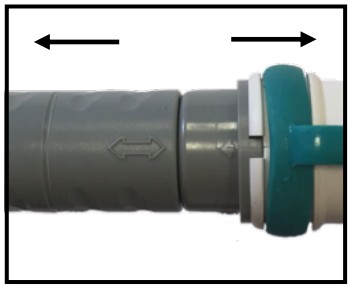
Ensure appropriate protective equipment (e.g., gloves, masks, face-shield, disposable apron) are used. Follow local or national best practice guidelines in relation to catheter insertion for patients suspected of having transmissible infections such as COVID-19 or equivalent in order to minimize the risk of infection.

5.5 Connection of the Catheter to the Treatment Cable

1. To connect the catheter to the Treatment cable first remove the cap from the catheter connector. Align the raised section or key on the catheter connector with the ⇔ sign on the Treatment cable connector and push the connectors together until a click is heard.



2. To disconnect the catheter from the Treatment cable pull them apart without turning them in any way. Replace the cap on the catheter connector.



Do not twist or turn the connectors or cables when connecting or disconnecting as this may damage the Treatment cable or catheter. Use a push or pull movement only.

The catheter contains metal parts and is not MRI safe. The catheter must be removed prior to carrying out an MRI scan.

5.6 Checking electrode position prior to treatment

In addition to the nasal guide, the catheter also incorporates an oral positioning guide. This can be seen at the back of the throat by oral exam. The oral guide provides an optional additional method for confirming that the electrodes are in the correct position. The oral guide is used as follows:

Ensure appropriate protective equipment (e.g., gloves, masks, faceshield, disposable apron) are used in line with local best practice guidelines for managing infection risk to carry out inspection of the oral guide.

1. Ask the patient to open their mouth. Examine the part of the catheter visible at the back of the throat. If any green bands are visible no further adjustment is required.

2. If no green bands can be seen on the catheter, or a thin black band or the electrodes can be seen, the catheter needs to be inserted further.

3. To insert the catheter further, carefully detach the tape from the catheter, loosen the tubing from the Garment clip and insert the catheter 1cm at a time until a green band can be seen (up to a maximum of 3cm).

4. Re-secure the catheter to the patient as per the guidance in the catheter IFU.

In the majority of patients, the catheter does not need to be adjusted after it is inserted for the first time. For some patients it may also not be possible to see the oral guide in the throat. Treatment may still be carried out in these patients.

If the catheter is adjusted, record this in the patient notes and specifically record the new 'X' number at the entrance to the nostrils. Please be aware that the nasal guide may no longer be visible after adjustment.

6 Treatment Protocol

The Threshold, Tolerance and Stimulation levels can vary substantially from patient to patient and also in a single patient between individual treatment sessions. The process of optimization should be followed <u>each time</u> a treatment is carried out.

The patient must be supervised at all stages of treatment and not left unattended at any point.

Inspect the catheter for damage prior to each treatment. If damage is seen (such as damage to tubing, exposed wires or broken connectors) discontinue use of the catheter and remove and replace it.

6.1 Preparation

1. Arrange the patient in a supported semi-reclining and comfortable position in a bed or suitable chair. Explain the procedure and agree a signal with the patient for them to confirm their willingness to proceed with a given step in the procedure or not to proceed. Obtain informed consent prior to proceeding to the next step.

2. Bring the Base Station on a suitable trolley to the side of the patient nearest to the electrical connector on the catheter. Inspect the Base Station, cables and connectors for damage (such as damage to tubing, exposed wires or broken connectors) and if there is any present do not proceed with treatment and contact your Phagenesis representative.

If the Base Station is mounted on a trolley it should be stable, at an appropriate height for visibility and ease of use and the brakes should be applied during treatment.

3. Switch the Base Station on and log in.

4. Compare the number on the printed guide on the surface of the catheter at the entrance to the patient nostril with the insertion distance recorded in the patient notes. Ensure they are the same. If they are different it may indicate that the catheter has moved at some point. If this is the case any feed being delivered should be stopped, the catheter adjusted to the correct distance, and a pH reading taken to confirm the end of the catheter is in the stomach. To take a pH reading follow the guidance in step 5 below or, if not required proceed directly to step 6.

5. Connect a 20mL ENFit syringe to the clear connector on the feeding tube part and use it to slowly withdraw approximately 2ml of stomach aspirate. If an aspirate cannot be obtained and it is safe to do so, position the patient on their left side and wait 5 minutes before trying again. Check the pH of the aspirate by placing it on the pH paper and using the labelled recess in the tray provided. A pH of 5.5 or less is indicative that the end of the tube is in the stomach. If it is not possible to obtain an aspirate, or the pH of the aspirate is more than 5.5, then an X-ray should be carried out to ensure the end of the catheter is not located in the airways.

6. Check the oral position guide if possible and practical to do so and ensure that a green band can be seen. If not follow the guidance in section 5.6.

7. Carefully unwind the treatment cable from its position at the back of the Base Station and connect it to the catheter via the electrical connector. Press the Treatment button on the Home screen. If the

patient details have already been input these will automatically be read from the chip in the catheter and displayed on the screen. If the patient details have not been input, then a new patient record must be created (as per Section 4.1).

8. Press the Treatment button on the Patient Treatment Record screen. This will open the Stimulation Optimization screen. This screen allows both the Threshold and Tolerance current levels to be established and also confirms that the electrodes are in good contact with the target tissues.

Contact quality - This window displays whether the contact between electrodes and patient tissues is sufficient to proceed to optimization and treatment. ✓ indicates good quality contact and ✗ indicates poor quality contact.

Increase Current - Press this button to increase the current by 1mA increments.

Back - Press this to reset the current value in the test window to its starting value or to go back to the previous test window.

Acceptable - Press this button to accept the set value and to proceed to the next step in the process.

Active Output Indicator – When the Base Station is delivering electrical stimulation this LED indicator located on the front of the Base Station is yellow. It flashes on and off during level optimization. If this LED is yellow when stimulation is not expected then stop use of the device, switch it off and contact your Phagenesis representative. If this LED is not yellow during treatment (when it should be illuminated) stop use of the device, switch it off and contact your Phagenesis representative.

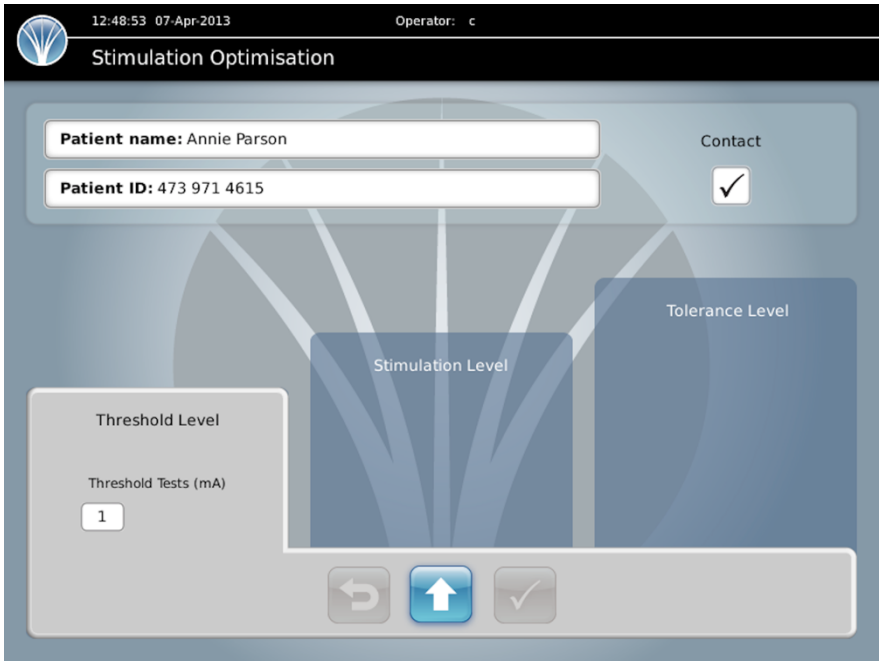
6.2 Establishing the Threshold Level

The first stage in the optimization process is to establish the Threshold Level. This is the average lowest value at which the patient can detect any sensation from the stimulating current. The patient most often feels a light vibration or a 'pins and needles' sensation at these low currents. Three separate Threshold Tests are carried out and the average of the three readings (which is calculated by the base station) provides the Threshold Level.

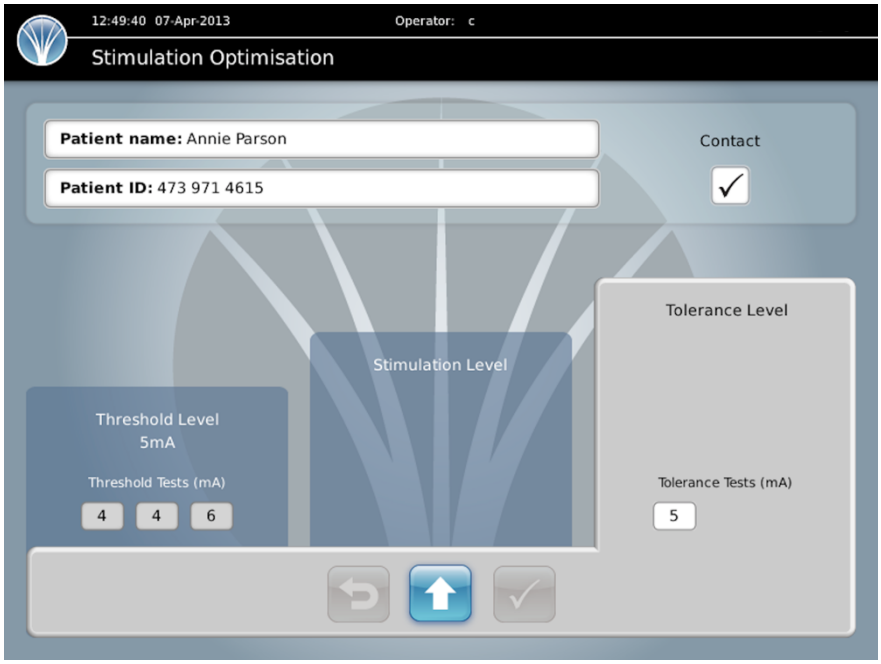
Procedure

1. The Contact Quality window needs to be displaying a ✓ icon indicating that good contact has been made. If the 'X' icon is visible then adjust the catheter until the '✓' icon is consistently displayed.

Please see Section 6.5 for how to adjust the catheter to restore electrode contact.



2. Agree with the patient a verbal or non-verbal signal to allow them to confirm the first time they feel the stimulation sensation in their pharynx. Press the Increase Current button repeatedly and slowly to increase the current by 1mA until the patient confirms that they can feel the stimulation. Press the Acceptable button. Repeat a further two times until the Threshold Level is obtained.



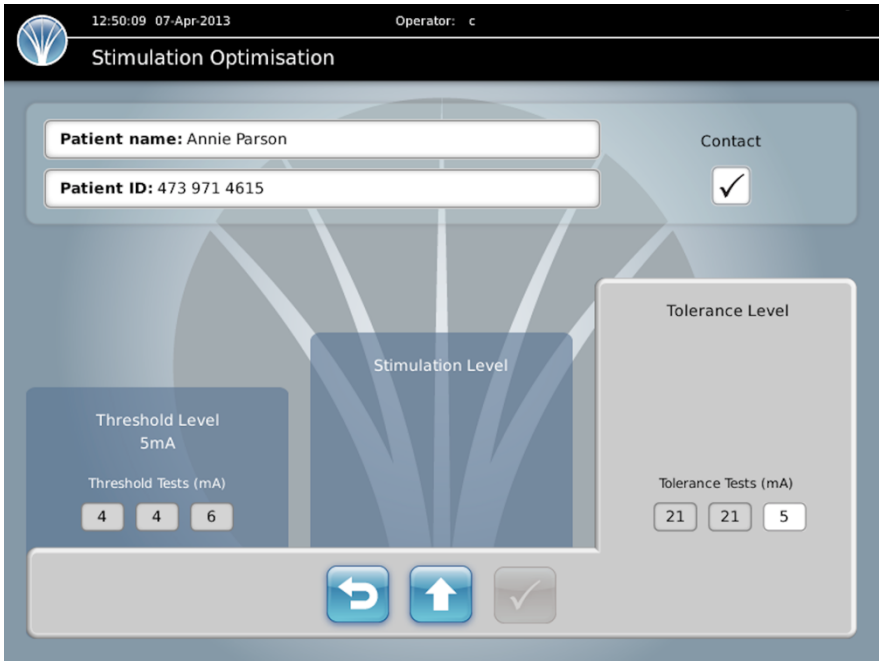
6.3 Establishing the Tolerance Level

The second stage in the optimization process is to establish the Tolerance Level. This is the average highest level of current the patient can tolerate. Three separate Tolerance Tests are carried out and the average of the three readings provides the Tolerance Level.

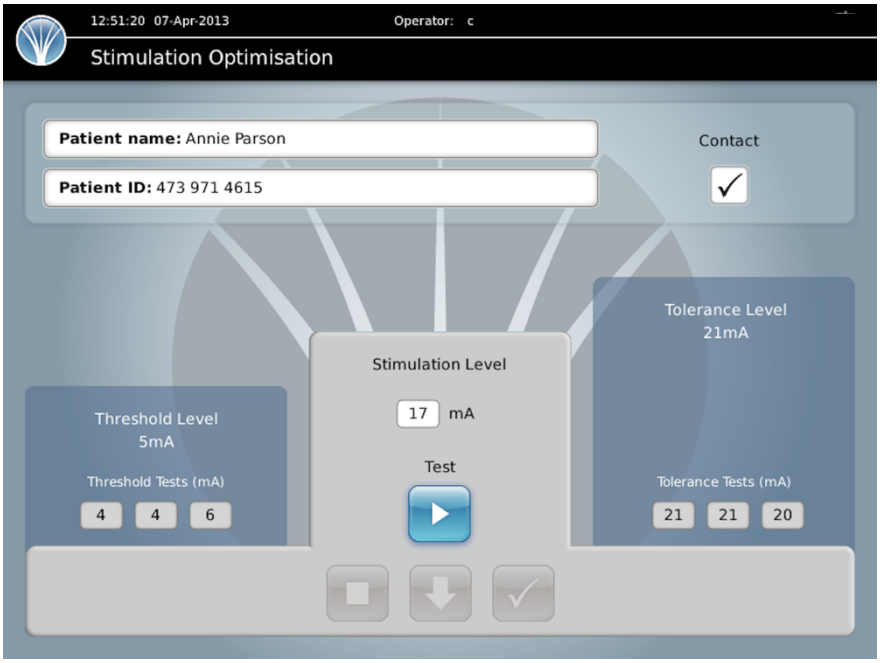
Procedure

1. Agree with the patient a verbal or non-verbal signal to allow them to indicate that the stimulation is at the highest level that they can tolerate.

Press the Increase Current button repeatedly and slowly to increase the current by 1mA until the patient confirms that they have reached their tolerance level. Then press the Acceptable button. Repeat a further two times until the Tolerance Level is obtained.

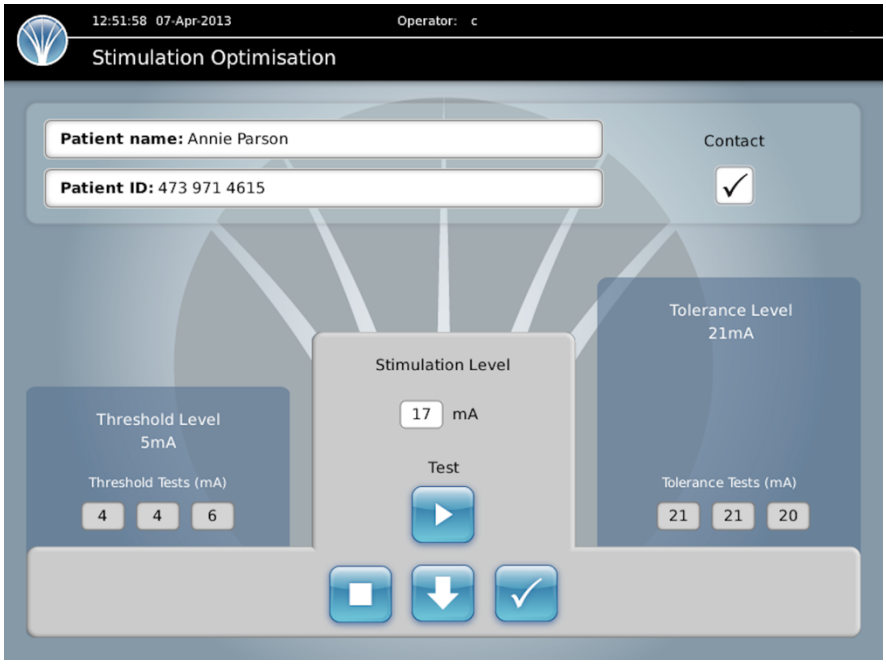


2. The software will then use the Threshold and Tolerance Levels to calculate the Stimulation Level



6.4 Level Test

In order to ensure that the patient is capable of tolerating the calculated Stimulation Level when applied over the 10-minute treatment, the Level Test allows the operator to deliver an 8 second period of stimulation at the Stimulation Level identified by the software as a final check of patient comfort before proceeding to treatment.



Begin Test - Press this button to start the 8-second test period of the Stimulation Level

Interrupt Test - Press this button to interrupt the test during the 8-second test period

Acceptable - Press this button on completion of the test to confirm the level is acceptable

Decrease Current - Press this button to decrease the Stimulation Level by 1mA prior to re-testing

Procedure

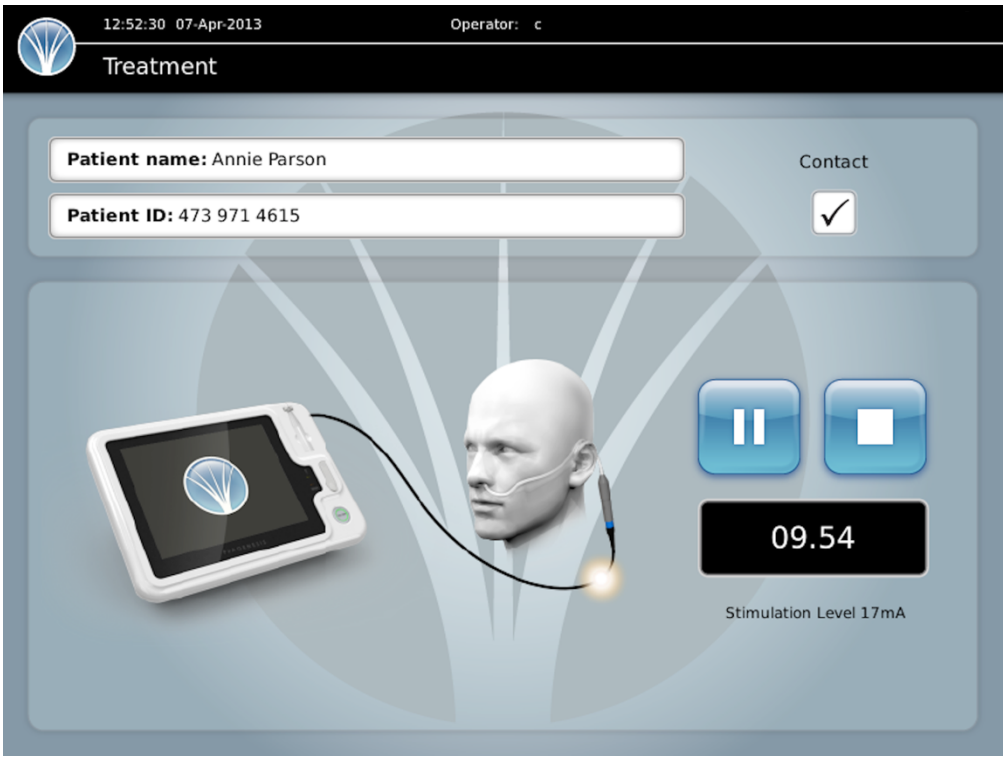
1. Explain to the patient that this is a final check of the stimulation current before the full 10 minutes treatment and then, when the patient is ready, press the Begin Test button.

2. At the end of the 8-second test stimulation ask the patient if they are agreeable to being treated at this level. If the patient asks for the stimulation level to be reduced, reduce the current by 1mA increments and re-test the patient until a tolerated level is reached.

3. Once the level is established press the Acceptable button and proceed to treatment.

6.5 Treatment

During treatment the screen below is displayed.



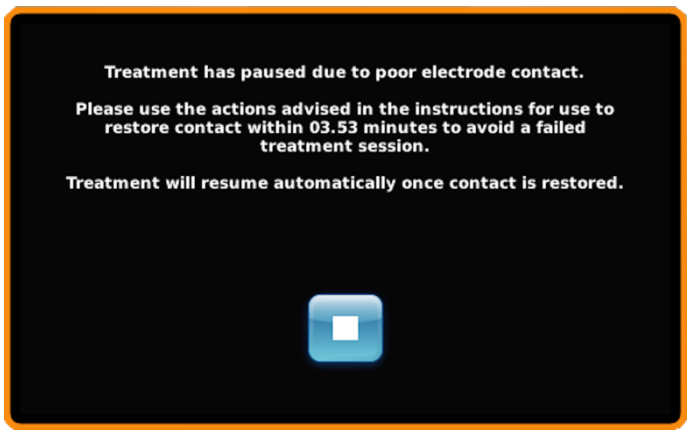
Pause - Press this button to pause the treatment. Treatment must be resumed within the time indicated on the pop-up message displayed

Stop - Press this button to stop the treatment. Stopping in this way before the full 10-minute treatment period is complete will not be recorded as a successful treatment

Procedure

1. The patient should be supervised throughout the 10-minute treatment process to ensure they are comfortable, they do not attempt to withdraw the catheter and the quality of contact between electrodes and target tissues is acceptable (as demonstrated by the '✓' icon in the Contact window).

2. Electrode contact with the patient oropharynx is monitored throughout the treatment process. If contact quality drops below acceptable levels the software will automatically pause the treatment process and prompt the operator to adjust the catheter until such time as contact is restored.



3. If a poor contact event occurs and the system pauses treatment, take the following actions while monitoring the screen to see if consistent electrode contact is restored. Once electrode contact is restored the system will automatically continue the treatment process.

a) Tell the patient that an adjustment to the catheter is needed
b) Ask the patient to tilt their chin downward slightly and attempt a dry swallow. Check if that restores contact. If it does, continue treatment. If not try step c.
c) Remove the tubing from the Garment clip and detach any dressing that may be in place to secure the catheter. Insert the whole catheter approximately 1cm further into the patient. Check if this restores contact. If it does, replace the dressing to secure the catheter re-insert the tubing into the Garment Clip and continue treatment. If it doesn't, then try step d.
d) Holding the catheter near the entrance to the nostril, twist the catheter slowly 180 degrees in a clockwise direction. Place a suitable dressing on the catheter and affix to the patient to hold it in this position. Check if this restores contact. If it does, continue treatment. If it doesn't, then try step e.
e) Remove the securing dressing and introduce a further 1cm of catheter into the patient. Check if this restores contact. If it does, continue treatment. If it doesn't, then discontinue treatment and try treating the patient at a later time.

4. The treatment may be paused or stopped by pressing the relevant button.

If the treatment is paused it must be re-started within the time indicated on the pop-up screen displayed.

If the treatment is stopped before the end of the 10-minute period the session will not be counted as part of the treatments sessions that make up the complete treatment regime.

5. At the end of the 10-minute treatment period the software will automatically stop delivering the electrical stimulus and a message will be displayed indicating whether the treatment was successful.

6. Disconnect the treatment cable from the catheter. Carefully wind the treatment cable back into place on the Base Station.

7. In the event that the catheter had to be adjusted during treatment, check that the distal end of the tube is still in the stomach by measuring the pH of a stomach aspirate sample (instructions for how to do this are provided in Section 6.1 - step 5). If a suitable pH reading cannot be obtained feeding should not be resumed until such time as the correct location of the distal end of the tube has been confirmed by other means such as X-ray.

8. The Treatment cable must be disinfected between patient treatments as per guidance in section 8.

The cap to cover the electrical connector on the catheter should be kept in place at all times when the catheter is not connected to the treatment cable on the Base Station. This ensures the pins on the connector are protected from contamination or inadvertent contact with a voltage source.

7 Alerts and Messages

The Base Station software is designed to ensure that the number of treatments and timing of treatments is controlled and correct. In the event that the operator attempts to carry out a procedure that is not consistent with the correct protocols the appropriate messages are displayed. In addition, the Base Station may display a message under conditions of fault.

Message	Explanation or Action
“Patient X has already received 6 consecutive complete treatments. No further treatment is allowed.”	This is the maximum number of complete consecutive treatments allowed for a single catheter. Do not attempt to continue to deliver treatment with this catheter.
"Patient X has already received total of 9 non-consecutive complete treatments. No further treatment is allowed."	This is the maximum number of complete non-consecutive treatments allowed for a single catheter. Do not attempt to continue to deliver treatment with this catheter.
"Patient X has already received 15 consecutive/non-consecutive complete treatments. No further treatment is allowed."	This is the maximum number of treatments (partial or complete) allowed for a single catheter. Do not attempt to continue to deliver treatment with this catheter.
"It has been less than the minimum interval of 14 hours since patient X was last treated. Wait at least another X hours before attempting treatment."	14 hours is the minimum treatment interval. Wait the specified time before attempting another treatment.
"Catheter inoperable"	There is a fault with the catheter. Do not continue to attempt to deliver treatment. Contact your Phagenesis representative.
"Catheter disconnected"	Connect the catheter. If it is connected there may be a fault. Contact your Phagenesis representative and do not use the catheter for treatment.
"Treatment has paused due to poor electrode contact. Please use the actions advised in the instructions for use to restore contact within X minutes to avoid a failed treatment session. Treatment will resume automatically once contact is restored."	Refer to the instructions for use as indicated.
"Check catheter connection. Please restore contact within X minutes to avoid a failed treatment session."	This will display if the catheter becomes disconnected from the Base Station during treatment. Reconnect the catheter to allow treatment to continue.
"Empty password not allowed"	Input the password
"Operator already exists"	Ensure new operator details are input
“Operator does not exist”	Ensure operator details have been input and saved
"Communication failed"	Contact your Phagenesis representative and do not use the Base Station until authorised to do so.
"Connect catheter to Base Station"	Connect the catheter. If it is connected there may be a fault. Contact your Phagenesis representative and do not use the catheter for treatment.
"No records found"	Check the search information input for correctness
"Error current outside of +/- 20%"	Poor contact or system fault. Contact your Phagenesis representative for guidance
"Stopping now will result in an incomplete treatment."	This will display if the Stop button is pressed.
"Catheter inserted does not match patient record. Treatment cannot commence until correct catheter is inserted."	Ensure the correct patient is being treated
"Patient X ID already exists. Patient X has already received 6 consecutive complete treatments. No further treatment is allowed."	Do not attempt to deliver further treatments to this patient
"Patient X ID already exists. Patient X has already received a total of 9 non-consecutive complete treatments. No further treatment is allowed."	Do not attempt to deliver further treatments to this patient
"Patient X ID already exists. Patient X has already received 15 consecutive/non-consecutive treatments. No further treatment is allowed."	Do not attempt to deliver further treatments to this patient
"Patient X ID already exists. Patient X has already been treated with a different catheter. Map patient information?"	This will display if a second catheter is being used on the same patient. If the patient has not received their full treatment regimen then map the new catheter as per section 4 of the IFU
"Patient mapping failed"	Re-try the mapping procedure. If it fails again contact your Phagenesis representative for further guidance.

In the event that any other message is displayed please note down the content of the message and contact your Phagenesis representative for further guidance.

8 Cleaning and Disinfection

The base station should never be immersed in water or other liquids. Do not apply any surplus liquid to the device. Use wipes or single use cloth dampened with the recommended cleaning solution or disinfectant. Should any liquid inadvertently be added to the area around the screen, on/off switch or USB port remove immediately with a clean dry cloth.

Before cleaning or disinfection ensure the Base Station is switched off and disconnected from mains power supply. Ensure the power cable plug has been disconnected from the mains supply before removing from the Base Station. Do not touch any exposed pins on the plug, cable or Base Station for at least 10 seconds after disconnecting from the mains power supply.

Do not apply surplus liquid and avoid any liquid coming in to contact with the pins of the power cable plug or entering the open apertures of the connector ends of the treatment cable.

Once cleaning or disinfection is complete, ensure all surfaces are dry before further use of the Base Station.

Solutions or wipes should be used in compliance with manufacturer guidelines with regards to make up, concentration, suitability and contact time.

8.1 Catheter

- The catheter incorporates sensitive electrical components and must not be immersed in liquids or exposed to liquid sprays or excess liquid of any description.
- During the period when the catheter is in place, the parts of the catheter external to the patient may be cleaned if required using a cloth or gauze dampened with water. No other cleaning agents should be used. Care should be taken not to introduce any liquid into the electrical connector on the catheter.
- The cap for the electrical connector should be left in place when the electrical connector is not connected to the Base Station via the Treatment cable.

8.2 Base Station

Cleaning

- The Base Station screen and casework should be inspected for physical contamination. Surface cleaning of the Base Station should always be carried out prior to disinfection when physical contamination is present.
- Physical cleaning of the base station casework, screen and cables can be carried out using a single use cloth dampened with a mild detergent and water or detergent wipes. When cleaning or disinfecting the Base Station it is advised that the USB tab should remain closed for the duration of the surface cleaning or disinfection.

Disinfection

- Disinfection of the Base Station casework, screen and cables is carried out using wipes containing *quaternary ammonium compounds* as the active agent. The disinfecting agents should be prepared/used as per the manufacturer's recommendation. Contact time should be as per manufacturer's recommendation but for at least 1 minute.

- Alcohol wipes (70% IPA) may be used with care on the Base Station but ***must not*** be used on the power lead or Treatment cable, as over time this can lead to cracking of the cable cover material and may expose users to the risk of electric shock.

8.3 Hygiene Plan

The following hygiene plan should be followed when using or moving the Base Station.

	Base Station	Treatment Cable	Power Lead
On initial receipt of the Base Station	C D	C D	C D
After treatment	-	D	-
If equipment is moved between wards	D	D	D
External transport to another hospital	D	D	D
Following visible physical contamination	C D	C D	C D
Prior to return to manufacturer	D	D	D

- C = Cleaning D = Disinfection
- If required, additional cleaning and disinfection should be carried out to meet local infection control guidelines
- Level of disinfection achieved should align with local best practice

9 Warnings

Please read the following notices prior to use of the Phagenyx System.

9.1 Base Station

1. **USB port** - The USB port is for connection to a USB stick only and must not be connected to a PC, printer or memory device with an external power source. Data transfer is not possible during treatment. Do not insert a USB stick into the USB port when the device is being used for treatment.

2. **Inspection** - The device should be inspected before use. If any damage to the casework, cables or screen is seen do not use the device and contact your Phagenesis representative.

3. **Performance** – If there is a variation in performance such as a failure to power up or to switch off, powering off unexpectedly, lack of response from the touchscreen or excessive heat when touched discontinue use of the device and contact your Phagenesis representative.

4. **Maintenance** - The Base Station is not a serviceable device and no modification of this equipment (either Base Station or Catheter) is allowed. No maintenance operations are required by the operator other than the cleaning specified in Section 8.

5. **Transport and Storage** - If the Base Station is to be transported it should be placed in its carry case. Do not store the Base Station in direct sunlight and keep away from sources of heat or fire. Any trolley used to support the Base Station must be stable, level and the brakes applied while the Base Station is being used. If the Base Station is subjected to mechanical shock contact your Phagenesis representative.

6. **Use environment** – The Base Station should only be used in a hospital setting. Do not use the Base Station near active high frequency surgical or MRI equipment. The catheter part is not defibrillation proof.

Use of this equipment adjacent to or stacked with other equipment should be avoided because it could result in improper behavior. In addition, portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30cm to any part of the Phagenyx Base Station or cables. Only use the cables provided by Phagenesis. Otherwise, degradation of the performance of this equipment could result.

Where patients are being monitored with ECG or EEG, as soon as the Phagenyx Base Station is plugged in to the mains, before being connected to the electrical connector on the catheter and during the treatment period, the operator should be aware that the applied current may generate anomalies in EEG or ECG data being collected at the same time and this effect should be considered when using or reviewing such data.

9.2 Connecting to other devices

The only device that should be connected to the Base Station is a Phagenesis supplied USB stick and a Phagenyx Catheter.

The Base Station should never be connected to any other device other than the supplied USB stick via its USB port.

Simultaneous connection of a patient to a h.f. surgical equipment may result in burns at the site of the stimulator electrodes and possible damage to the stimulator

Operation within close proximity (e.g. 1m) to shortwave or microwave therapy equipment may produce instability in the stimulator output

10 Buttons and Icons

10.1 User interface action buttons and icons

Button	Description	Button	Description
	Go to the Log In/Log Out screen		Confirm
	Go to the System and Settings screen		No
	Go to the Patient Record Search screen		Pause treatment
	Begin process to treat patient		Stop treatment or interrupt test
	Go to Home screen		Decrease current level
	Save changes to settings or add new operator		Add patient
	Begin Treatment Optimization		Map existing record onto catheter
	Search records		Delete operator
	Return to Patient Search Results screen		Change Password
	Display patient treatment record on screen		Go back one step
	Transfer patient data to a USB stick		Begin test
	Add comment to patient record		Good electrical contact or treatment successful
	Increase current level		Poor electrical contact

10.2 Phagenyx System icons

Icon	Description	Icon	Description
	Date of Manufacture / Country of Manufacture		Batch code
	Type BF applied part		Use by date
	Class II equipment		Single sterile barrier system sterilized using EO
	Manufacturer		Do not re-use
	The device must not be disposed of in general or domestic waste		Do not re-sterilize
	Cable connection point		Do not use if package is damaged
	Catalogue number for product		Keep away from sunlight
	Product serial number		Keep dry
	USB connection		Temperature limits
	Active electrical output to patient		Humidity limits
	General warning		Atmospheric atmosphere limits
	Not MRI safe		Follow instructions for use
	Medical Device		Unique Device Identifier barcode

11 Technical Data and Specifications

Performance

Parameter	Value
Stimulation fundamental frequency	5 Hz
Stimulation pulse width	200 µs
Controlled current range	1 mA – 50 mA (+/-20%)
Peak stimulation voltage	240 V
Peak energy per stimulation pulse	2.4 mJ

Load impedances for which these specifications are valid are 0 to 3kΩ. Tested with a 1kΩ nominal load

Waveform

The pulses are square wave and unipolar, and there is a small DC component of 0.1% of the requested pulse current.

Electrodes

The applied part is the PNX-1000 catheter. The catheter contains two 3.0mm long bipolar stainless-steel ring electrodes separated by a gap of 10mm. Max electrode outer diameter = 3.85mm. Surface area of each electrode = 0.36cm^2.

Operation

- Not suitable for use in the presence of enriched oxygen or flammable anaesthetic mixtures with oxygen or nitrous oxide. Catheter part may be used in the presence of enriched oxygen.
- Type BF Applied Parts
- Suitable for continuous operation

System and Power Supply system

- Safety - Class II protection (no functional or protective earth)
- Power Supply Input - IEC-C8 input connector, 100V-240V, 2.5A, 50-60 Hz

Environmental conditions for the Base Station

- Storage: 10°C – 40°C, 20-85% Relative Humidity non-condensing, 50kPa - 106kPa
- Operation: 10°C – 30°C, 20-85% Relative Humidity non-condensing, 50kPa - 106kPa
- Transport: 5°C – 40°C, 20-85% Relative Humidity non-condensing, 50-106kPa
- Equipment for indoor use only. Not protected against ingress of liquids.

Service and replacement parts

The Base Station does not require servicing. The power cable and Treatment Cable are replaceable parts. Contact your Phagenesis representative for further information.

Table 1

Guidance and manufacturer's declaration – electromagnetic emissions		
The Phagenyx System is intended for use in the electromagnetic environment specified below. The customer or the user of the Phagenesis Phagenyx system should assure that it is used in such an environment.		
Emissions test	**Compliance**	**Electromagnetic environment - guidance**
RF emissions CISPR 11	Group 1	The Phagenesis Phagenyx system uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
RF emissions CISPR 11	Class A	The EMISSIONS characteristics of this equipment make it suitable for use in industrial areas and hospitals (CISPR 11 class A). If it is used in a residential environment (for which CISPR 11 class B is normally required) this equipment might not offer adequate protection to radio-frequency communication services. The user might need to take mitigation measures, such as relocating or re-orienting the equipment.
Harmonic emissions IEC 61000-3-2	Class A	
Voltage fluctuations/ flicker emission IEC 61000-3-3	Complied	

Table 2

Guidance and manufacturer's declaration – electromagnetic immunity			
The Phagenyx System is intended for use in the electromagnetic environment specified below. The customer or the user of the Phagenyx System should assure that it is used in such an environment.			
IMMUNITY test	**IEC 06061 test level**	**Compliance level**	**Electromagnetic environment - guidance**
Electrostatic discharge (ESD) IEC 6100O-4-2	± 6 kV contact ± 8 kV air	± 6 kV contact ± 8 kV air	Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material the relative humidity should be at least 30%.
Electrical fast transient/burst IEC 6100O-4-4	± 2 kV for power supply lines ± 1 kV for input/output lines	± 2 kV power supply lines ± 1 kV for input/output lines	Mains power quality should be that of a typical commercial or hospital environment.
Surge IEC 6100O-4-5	± 1 kV line(s) to line(s) ± 2 kV line(s) to earth	± 1 kV differential mode ± 2 kV common mode	Mains power quality should be that of a typical commercial or hospital environment.
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 6100O-4-11	<5 % UT (> 95 % dip in UT) for 0.5 cycle 40 % UT (60 % dip in UT) for 5 cycles 70 % UT (30 % dip in UT) for 25 cycles <5 % UT (>95 % dip in UT) for 5 s	<5 % UT (> 95 % dip in UT) for 0.5 cycle 40 % UT (60 % dip in UT) for 5 cycles 70 % UT (30 % dip in UT) for 25 cycles <5 % UT (>95 % dip in UT) for 5 s	Mains power quality should be that of a typical commercial or hospital environment.
Power frequency (50/60 Hz) magnetic field IEC 6100O-4-8	3 A/m	3 A/m	If image distortion occurs, it may be necessary to position the Phagenyx System further from sources of power frequency magnetic field or to install magnetic shielding. The power frequency magnetic field should be measured in the intended installation location to assure that it is sufficiently low.
NOTE UT is the a.c. mains voltage prior to application of the test level			

Table 3

Guidance and manufacturer's declaration – electromagnetic immunity			
The Phagenyx System is intended for use in the electromagnetic environment specified below. The customer or the user of the Phagenyx System should assure that it is used in such an environment.			
IMMUNITY test	**IEC 06061 test level**	**Compliance level**	**Electromagnetic environment - guidance**
Conducted RF IEC 6100O-4-6 Radiated RF IEC 6100O-4-3	3 Vrms 150 kHz to 80 MHz 3V/m 80 MHz to 2.5 GHz	3 Vrms 3 V/m	Portable and mobile RF communications equipment should be used no closer to any part of the Phagenyx System including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter. **Recommended separation distance** $d = 1.2\sqrt{P}$ $d = 1.2\sqrt{P}$ 80 MHz to 800 MHz $d = 2{,}3\sqrt{P}$ 800 MHz to 2.5 GHz where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and d is the recommended separation distance in meters (m). Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey, "should be less than the compliance level in each frequency range." Interference may occur in the vicinity of equipment marked with the following symbol: 
NOTE 1 At 80 MHz and 800 MHz, the higher frequency range applies. NOTE 2 These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.			
a Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the Phagenyx System is used exceeds the applicable RF compliance level above, the Phagenyx System should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the Phagenyx System. b Over the frequency range 150 kHz to 80 MHz, field strengths should be less than 3 V/m.			

Table 4

Recommended separation distances between portable and mobile RF communications equipment and the Phagenyx System			
The Phagenyx System is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The customer or the user of the Phagenyx System can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and the Phagenyx System as recommended below, according to the maximum output power of the communications equipment.			
Rated maximum output power of transmitter W	**Separation distance according to frequency of transmitter** m		
	150 kHz to 80 MHz $d = 1{,}2\sqrt{P}$	**80 MHz to 800 MHz** $d = 1{,}2\sqrt{P}$	**800 MHz** to **2,5 GHz** $d = 2{,}3\sqrt{P}$
0,01	0,12	0,12	0,23
0,1	0,38	0,38	0,73
1	1,2	1,2	2,3
10	3,8	3,8	7,3
100	12	12	23
For transmitters rated at a maximum output power not listed above, the recommended separation distance *d* in metres (m) can be estimated using the equation applicable to the frequency of the transmitter, where *P* is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer. NOTE 1 At 80 MHz and 800 MHz, the separation distance for the higher frequency range applies. NOTE 2 These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.			

Written offer related to software used in this device.

This product includes free software including "Linux kernel", "BusyBox", "glibc", "alsa", "tslib", "U-boot", and "QT" which are released under the GNU Public license version 2.0 and 3.0 and the Lesser GNU Public license version 3.0. These licenses may be found under https://www.gnu.org/licenses/licenses.html.

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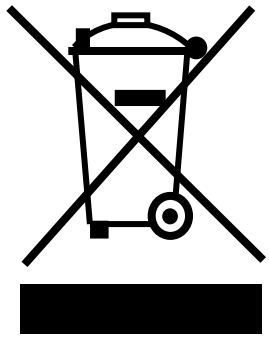
July 22, 2011 – Button click sound By KorgMS2000B (http://www.freesound.org/usersViewSingle.php?id=497386)

12 Disposal

12.1 Catheter

Once withdrawn from the patient, the catheter should be immediately disposed of in clinical waste. Any additional parts used with the catheter such as the Garment Clip should also be disposed of in clinical waste. Care should be taken when disposing of the Garment Clip as it contains a pin which has the potential to cause injury. Reuse of the catheter should not be attempted as this will expose patients to risk of infection. It is not possible to reprocess the catheter to allow use in another patient.

12.2 Base Station



This symbol on the products and/or accompanying documents means that used electrical and electronic products should not be mixed with general waste. This applies to the Base Station and additional parts (USB sticks, Treatment Cable and power lead).

Disposing of this product correctly will save valuable resources and prevent any potential negative effects on human health and the environment which could otherwise arise from inappropriate waste handling. If you plan to dispose of the Base Station or additional parts please contact your Phagenesis representative who will arrange for the device to be collected and disposed of.

Penalties may be applicable for incorrect disposal of this waste, in accordance with national legislation.

The above information is based on the European waste electrical and electronic equipment directive 2002/96/EC.

13 Summary of Clinical Studies to date

13.1 Clinical studies overview

Published studies to date using the Phagenyx system are presented in Table 5 below and summary study outcomes discussed in the following pages.

Table 5 *– Clinical studies using the Phagenyx System*

Company Sponsored		Independent	
Name	**Type and Design**	**Name**	**Type and Design**
STEPS	• RCT • 20 sites/5 countries • Dysphagia post stroke • (n=162)	**YOUSSEF**	• Independent • RCT • Single site • Dysphagic acute stroke • PAS, FOIS endpoints • (n=18)
PHAST TRAC	• RCT • 9 sites/3 countries • Dysphagic tracheotomized post stroke patients • Warnecke primary endpoint • DSRS secondary endpoint • (n=69)	**SUNTRUP**	• Independent • RCT • Single site • Dysphagic tracheotomized post stroke patients • Warnecke primary endpoint • (n=30)
PHADER	• Single arm PM registry • 14 sites/3 countries • Post stroke dysphagia • DSRS primary endpoint • (n=177)	**MUHLE**	• Independent • Single arm observational • Single site • Dysphagic tracheotomized post stroke patients • Warnecke primary endpoint • (n=23)

13.2 STEPS

Study summary - STEPS was a randomized sham controlled single blinded study to assess the effectiveness and safety of Phagenyx in treating patients with dysphagia post ischemic or haemorrhagic stroke in 20 hospital sites in the UK, Germany, Denmark, Spain and France. All patients received standard of care and in the treatment group, additionally received Phagenyx treatment. STEPS used the Penetration Aspiration Score (PAS) at 2-weeks post treatment as the primary endpoint measure.

Subject accountability - Of the 162 subjects randomized, 141 received at least 1 treatment. 84% of subjects were available for primary endpoint assessment at the first follow-up (FU1) dropping to 80% at the second follow up (FU2). Patient data was not available for a number of reasons including patient death, withdrawal of consent and loss to follow up.

Safety Results – The Phagenyx System was shown to be safe in this study based on extensive safety data collection and analysis. There were no device or treatment related serious adverse events or deaths. There were a small number of non-serious device related adverse events such as gagging or nausea linked to catheter insertion and one instance of hypersalivation. All events resolved without complications.

Effectiveness Results – The STEPS study was neutral for the primary endpoint. Post hoc analysis indicated up to 58% of subjects may have been sub-optimally stimulated, that baseline dysphagia severity was too low overall to readily see therapeutic treatment effects and that the control group may have received some level of therapeutic stimulation unintentionally (Bath et al 2016).

Publication - Bath et al. Pharyngeal Electrical Stimulation for Treatment of Dysphagia in Subacute Stroke: A Randomized Controlled Trial *Stroke* 2016 Jun;47(6):1562-70.

13.3 Suntrup et al 2015

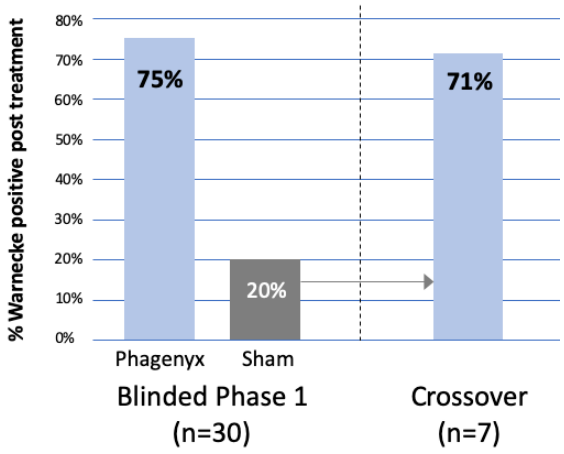
Study summary - The Suntrup study was an independent sham controlled single blinded RCT in post stroke patients with severe persistent dysphagia that were tracheotomized, where the dysphagia was the only remaining impediment to safe removal of the tracheostomy tube. Patients were considered suitable for inclusion if they were fully weaned from mechanical ventilation and were able to stay alert for at least 15 minutes. Dysphagia severity was assessed both at screening and for the primary endpoint by endoscopic exam using the Warnecke endpoint. This measures management of secretions, spontaneous swallow frequency and laryngeal sensitivity. Patients that passed Warnecke were eligible for decannulation of their tracheostomy tube based on the observed improvement in swallowing. All subjects received standard of care and the treatment group received the standard 3 x 10 minutes of Phagenyx treatment over 3 consecutive days.

Subject accountability – 51 subjects were screened and 30 randomized 2:1 to the treatment or sham arm. Post intervention or sham all 30 subjects were assessed with 72 hours using the Warnecke endpoint. 8 sham subjects that were Warnecke negative after primary endpoint assessment were offered treatment in an unblinded crossover but one of these was lost to discharge prior to treatment.

Safety Results – The authors reported that there were no device or treatment related adverse events.

Effectiveness Results – For the primary endpoint 75% of treated subjects passed the Warnecke assessment by comparison with 20% of the sham subjects ($p<0.01$). In the unblinded crossover phase 71% of subjects that received treatment passed the Warnecke assessment. None of the subjects subsequently decannulated on passing Warnecke from either phase required recannulation on follow up to the point of discharge.

Figure 1 *– Suntrup Study Outcomes*



Study Conclusions – Phagenyx treatment appears to be both safe and effective in improving swallow function and secretion management in patients with persistent severe dysphagia post stroke. Treatment outcomes in the blinded phase 1 of the study were replicated in the unblinded crossover phase suggesting that treatment effects are reproducible in this patient population. Treatment effects appear durable on the basis that no recannulations due to dysphagia were required for the duration of follow up.

Publication - Suntrup S., et. al., "Electrical pharyngeal stimulation for dysphagia treatment in tracheotomized stroke patients: a randomized controlled trial" *Intensive Care Med* (2015) 41:1629–1637

13.4 Youssef et al 2015

Study summary - This was an independent randomized controlled trial in patients with dysphagia post stroke. Patients were included in the study within 10 days of a hemispheric stroke event where dysphagia was confirmed via endoscopic exam i.e., Penetration Aspiration Score (PAS) of 3 or higher. Patients were randomized 1:1 into a treatment or sham control group. The sham group had the catheter inserted and went through a process of level optimization but did not receive the standard 3 x 10-minute optimized stimulation sessions over 3 days as per the treatment group. Both groups continued to receive standard of care. Treatment outcomes were assessed 2 weeks post the last treatment using a number of swallow measures and a patient global satisfaction measure.

Subject accountability – 18 subjects were recruited. All 18 subjects were assessed at baseline for PAS, FOIS, Pharyngeal Secretions and Pharyngeal Stasis and randomized to treatment or sham groups.

Safety Results – The authors reported that no serious adverse events occurred during the study

Effectiveness Results – Study outcomes are summarized in Table 6. All measures other than pharyngeal stasis showed a statistically greater improvement in the treated group by comparison with the sham group. Seven subjects reported satisfaction in the treatment group by comparison with 3 patients in the sham group at 2 weeks.

***Table 6** – Youssef study outcomes*

Outcome	Timing	PES group	Sham group	Difference p value
PAS	Baseline	5.7 +/- 1.1	5.1 +/- 0.9	
	Post treatment	2.3 +/- 0.37	3.58 +/- 0.78	0.017
FOIS	Baseline	2.8 +/- 1.54	2.58 +/- 1.79	
	Post treatment	5.18 +/- 1.7	4.33 +/- 0.98	0.024
Pharyngeal secretions	Baseline	2.2 +/- 0.35	2.3 +/- 0.65	
	Post treatment	0.7 +/- 0.47	1.52 +/- 0.81	0.032
Pharyngeal stasis	Baseline	3.1 +/- 0.6	2.9 +/- 0.9	
	Post treatment	2.2 +/- 0.69	2.1 +/- 0.7	0.116
Patient satisfaction	At 2 weeks	2.6 +/- 1.19	3.8 +/- 1.71	0.046

Study conclusions – Phagenyx treatment appears to be safe and effective in the treatment of moderate to severe dysphagia post stroke. The improvement in mean PAS, FOIS and Pharyngeal Secretions scores were statistically greater in the treated group by comparison with the sham group.

Publication - Youssef G., et. al. "The outcome of intraluminal electrical pharyngeal stimulation (EPS) on oropharyngeal dysphagia in acute stroke patients" *Al-Azhar Assuit Medical Journal* 2015 Vol 13 No.1 Jan, 67-72.

13.5 Muhle et al 2015

Study summary - This was an independent prospective single arm study in patients with severe persistent dysphagia post stroke fully weaned from ventilation with a tracheostomy tube still in place. The goals of the study were two-fold a) To establish the effectiveness of Phagenyx treatment in improving swallowing function as measured by Warnecke and; b) To establish whether Phagenyx treatment success correlated with an increase of a swallow related neurotransmitter 'Substance P' in the pharyngeal mucosa. Patients who could not be decannulated after the standard cycle of 3 treatments with Phagenyx were offered additional treatments in phase 2 and 3. Saliva samples were collected before and after each stimulation and Substance P concentration measured using and ELISA immunoassay.

Subject accountability – A total of 68 subjects were screened identifying 23 subjects suitable for treatment. All 23 subjects were given 3 Phagenyx treatments over 3 days and assessed within 24-72 hours after the third treatment using the Warnecke endoscopic exam. A total of 9 subjects that remained Warnecke negative after phase 1 were eligible for a second cycle of treatment but 6 of these subjects were discharged at this time prior to treatment. Of the 3 subjects treated in phase 2, 1 was discharged after treatment. A single patient was given one further cycle of treatment. All subjects that were Warnecke positive had their tracheostomy tubes removed based on the observed improvement in swallowing and were monitored along with Warnecke negative patients until discharge (mean LOS 35 days +/- 11 days).

Safety Results – The authors reported no device or treatment related adverse events occurred.

Effectiveness Results – A total of 61% of subjects were Warnecke positive after a single cycle of 3 Phagenyx treatments. This number increased to 65% of subjects after 2 cycles and 70% of subjects after 3 cycles (see Figure 2). All subjects decannulated on the basis of the improvement in swallow function and secretion management as measured by Warnecke were followed up to discharge and none required recannulation. This study also showed the effects of Phagenyx treatment on the levels of Substance P (SP) in the pharyngeal mucosa and its alignment with positive treatment outcomes (see Figure 3). 79% of patients with a positive Warnecke outcome post treatment demonstrated increased levels of Substance P versus only 11% of patients that were Warnecke negative post treatment.

Figure 2 – *Overall patient response to treatment*

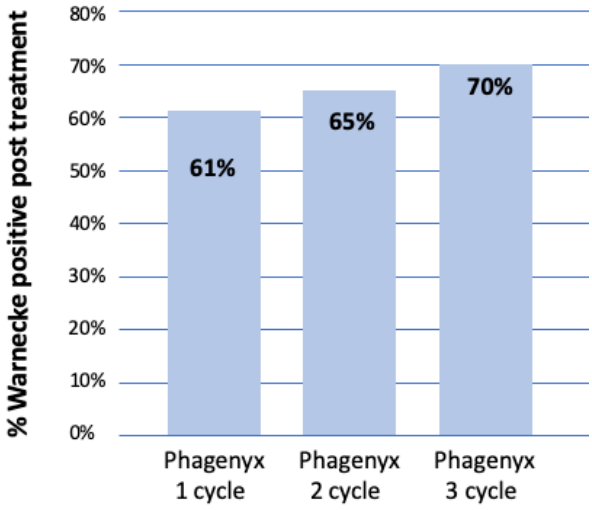
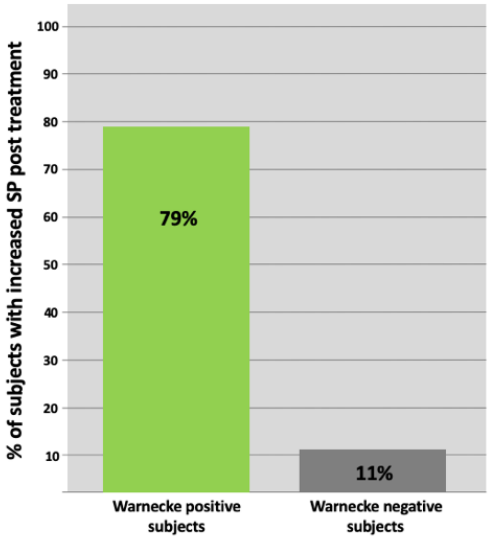


Figure 3 – *Substance P levels in responders*



Study conclusions – Phagenyx is safe and effective in the treatment of severe dysphagia post stroke. Certain patients may require a higher number of treatments to demonstrate improvement in swallowing. Treatment responders (i.e., those that pass Warnecke post treatment) are more likely to show elevated levels of Substance P in the pharyngeal mucosa.

Publication - Muhle P., et. al. "Increase of Substance P Concentration in Saliva after Pharyngeal Electrical Stimulation in Severely Dysphagic Stroke Patients – an Indicator of Decannulation Success?" *Neurosignals* 2017; 25:74-87

13.6 PHAST-TRAC 2018

Study summary - PHAST TRAC was a company sponsored prospective single-blind randomized controlled trial across 9 sites in Germany, Austria and Italy in tracheotomized patients with severe persistent dysphagia post stroke. Patients were randomized to receive 3 Phagenyx treatments or sham treatments. The primary endpoint was an endoscopically captured measure of swallowing function and secretion management (Warnecke). After primary endpoint collection (phase 1) the study had a second, open-label phase where the subjects initially assigned to the sham arm were offered treatment. In addition, any patients in the phase 1 part that had not responded to the standard regimen of 3 treatments were allowed an additional 3 treatments. The Dysphagia Severity Rating Scale (DSRS) was one of a number of secondary endpoints also recorded in this study.

Subject accountability – A total of 97% of subjects were available for primary endpoint assessment in phase 1 of the study. Of expected subjects, 94% were available for the endpoint assessment in the open label crossover. Thereafter 93% of subjects were followed up to discharge and 74% at the last follow up at 60-120 days. Subjects were not available for a number of different reasons including inability to pass the catheter, death, withdrawal of consent or loss to follow up.

Safety Results – There were no treatment or device related serious adverse events or deaths. There were a number of non-serious device or treatment related events such as catheter insertion difficulty, gagging during insertion and throat pain during stimulation. All events were resolved without complications.

Effectiveness Results – A total of 49% subjects passed Warnecke following treatment by comparison with 9% of sham subjects. When sham subjects were offered treatment in the crossover phase of the study a similar % of subjects, 53%, passed Warnecke post treatment (see Figure 4). In addition, when those treated subjects from phase 1 that had not passed Warnecke were given additional treatments, the total % of treatment responders in that group increased from 49% to 60% (Figure 5). DSRS results also showed that Warnecke positive subjects post treatment were more likely to return to oral intake (see Figure 6 on the next page).

Figure 4 – *Overall patient response to treatment*

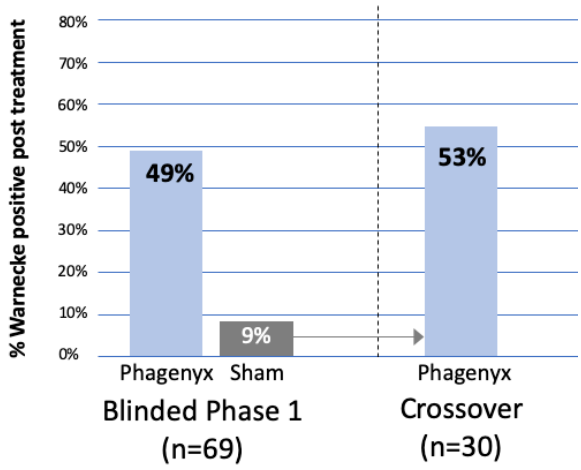
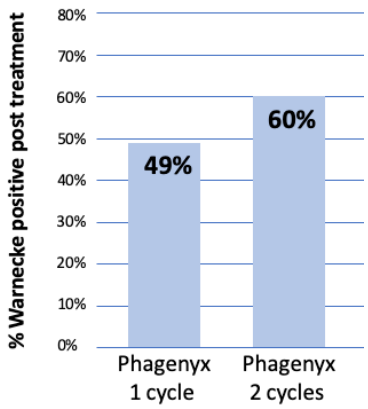
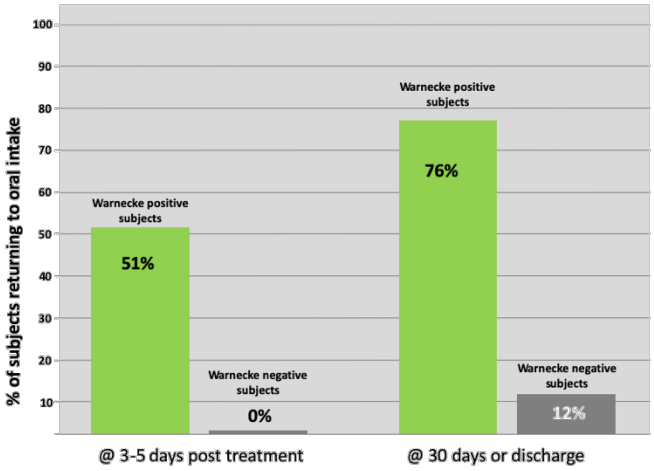


Figure 5 – *Substance P levels in responders*



Study conclusions – Phagenyx is safe and effective in the treatment of severe dysphagia post stroke. Treatment outcomes in the blinded phase 1 of the study were replicated in the unblinded crossover phase suggesting that treatment effects are reproducible in this patient population. Certain patients may require a higher number of treatments to demonstrate improvement in swallowing. Treatment responders (Warnecke positive) are more likely to return to oral intake in the days and weeks following treatment than treatment non-responders

Figure 6 – *Comparison of return to oral intake treatment responders and non-responders*



Publication - Dziewas et al. Pharyngeal electrical stimulation for early decannulation in tracheotomized patients with neurogenic dysphagia after stroke (PHAST-TRAC): a prospective, single-blinded, randomized trial. *Lancet Neurol* 2018; 17: 849–59

13.7 PHADER 2020

Study summary - PHADER was a company sponsored prospective single-arm observational post market registry study. It was designed to capture safety and effectiveness data in a broad range of patients with neurogenic dysphagia categorized into 5 different groups. PHADER Group A – Patients with dysphagia post stroke and PHADER Group B - Patients with dysphagia post stroke that also required ventilation and had been extubated, were two of the groups studied. The primary endpoint used in PHADER was the Dysphagia Severity Rating Scale (DSRS). DSRS data was recorded at baseline prior to treatment, at follow up 1 which was 2-3 days post last PES treatment, follow up 2 which was 7-21 days post last PES treatment and follow up 3 at 60-120 days post last PES treatment. Secondary endpoints included FOIS, PAS and hospital LOS. All patients in the study received standard dysphagia care and additionally received Phagenyx treatment.

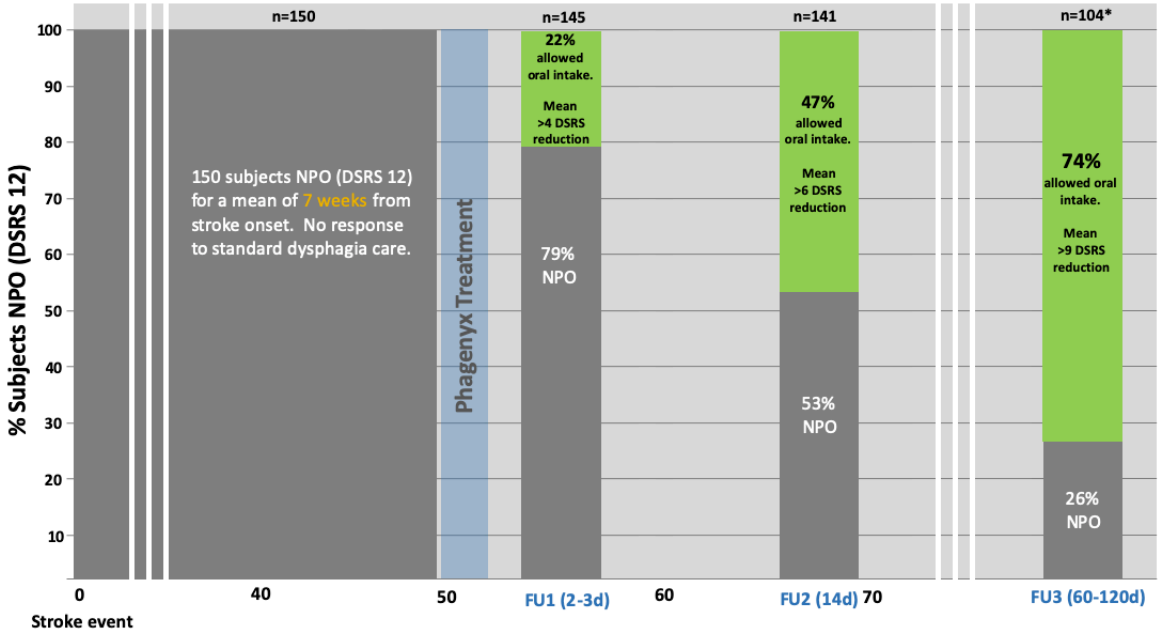
Subject accountability – Of the 188 subjects screened, 177 eligible subjects were identified and given at least one Phagenyx treatment session. A total of 170 subjects received all three treatments and 173 subjects were assessed at follow up 1 (98% expected). For follow up 2 (FU2) there were 86% of expected subjects and at follow up 3 (FU3) 77% of expected subjects. There were a number of deaths, consent withdrawals and losses to follow up over the course of the study.

Safety Results – There was one serious adverse event recorded as 'possibly device related' in this study where a difficult catheter insertion with coughing and copious secretions was followed within 24 hours by a chest infection. It was resolved without complications. There were a small number of non-serious device or

treatment related adverse events such as temporary headache, pain during treatment and jaw chattering. All events resolved without complication.

Effectiveness Results – Subjects showed significant improvements in DSRS, FOIS and PAS from baseline over the course of the study. The majority of subjects were NPO (DSRS 12) at baseline with mean onset to treatment time of 50 days where they showed no response to standard dysphagia care. Following Phagenyx treatment 22% of these persistently dysphagic NPO patients unresponsive to standard dysphagia care for 7 weeks returned to oral intake (DSRS 10) within 3 days. This % increased to 47% by follow up 2 (7-21 days) and to 74% of those assessed at follow up 3 (60-120 days). Those that responded to treatment (i.e., change from DSRS 12) showed a large improvement in their DSRS scores (mean of >4 DSRS at follow up 1, >6 DSRS at follow up 2 and >9 DSRS at follow up 3). This is illustrated in Figure 7.

***Figure 7** – DSRS outcomes for 150 subjects with a baseline DSRS of 12*



Study conclusions – Phagenyx is safe and potentially effective in the treatment of severe dysphagia post stroke in patients that do not respond to standard dysphagia care. Although this was a single arm study, the timing and size of improvement in DSRS seen in a significant % of subjects that had not responded to standard dysphagia care for many weeks strongly suggests a treatment effect. The single device related serious adverse event seen in this study was resolved without complication and was only possibly related to catheter insertion and not to treatment.

Publication - Bath et al. Pharyngeal electrical stimulation for neurogenic dysphagia following stroke, traumatic brain injury or other causes: main results from the PHADER cohort study, *EClinicalMedicine* 28 (2020) 100608