Pharyngeal electrical stimulation for early decannulation in tracheotomised stroke patients with dysphagia (PHAST-TRAC): a randomised, single-blind, pivotal, superiority trial

Rainer Dziewas, Ingeborg van der Tweel, Shaheen Hamdy, Philip M Bath; on behalf of the PHAST-TRAC Investigators

P Bath: Professor of Stroke Medicine, University of Nottingham
Background

Swallowing problems (dysphagia) common after stroke:
- Admission ~50% of patients to ~15% at 6 months

Associated with poor outcome:
- Dehydration, poor nutrition, aspiration pneumonia, prolonged hospital stay (cost), poor functional outcome; increased death

Intensive Care after stroke (5-10%):
- Swallowing problems in stroke patients that need mechanical ventilation are common
- Tracheotomy for airway protection + severe dysphagia, or long term ventilation
- Long term cannula post-ventilator: uncomfortable, extended ICU/hospital stay (cost), readmission
- Decannulation often delayed because of severe dysphagia

Treatments:
- No definitive treatments
- Pharyngeal electrical stimulation (PES)?


Review
Restoration of swallow control after stroke

The natural recovery process post stroke involves compensatory reorganisation in the motor cortex of the non-dominant hemisphere.

Healthy brain
Both hemispheres active during swallowing but left hemisphere dominates.

Post Stroke
Lesion in left hemisphere (dominant side) - patient presents with dysphagia.

Recovery
Functional reorganization of control to unaffected hemisphere.

Pharyngeal electrical stimulation (PES)

Harvey et al., Phagenesis. PhEED CIP v1 2017
# PES studies in neurogenic dysphagia

<table>
<thead>
<tr>
<th>Condition</th>
<th>Stage</th>
<th>Site</th>
<th>Design</th>
<th>Size</th>
<th>Status</th>
<th>Name</th>
<th>Type</th>
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<td>SU</td>
<td>RCT x3</td>
<td>73</td>
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<td>Hamdy et al</td>
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<td>Commercial</td>
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<td>SU</td>
<td>RCT</td>
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<td>To start</td>
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<td>Suntrup et al</td>
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<td>Obs</td>
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<td>Muhle et al</td>
<td>Academic</td>
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<td>Subacute</td>
<td>ICU</td>
<td>RCT</td>
<td>≤126</td>
<td>Completed</td>
<td>PHAST-TRAC</td>
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<td>Published</td>
<td>Michou et al</td>
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<td>Resitvo et al</td>
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<tr>
<td>Mixed</td>
<td>Subacute</td>
<td>Hosp</td>
<td>Register</td>
<td>~300</td>
<td>Ongoing</td>
<td>† PHADER</td>
<td>Commercial</td>
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<tr>
<td>Subacute</td>
<td>ICU</td>
<td>RCT</td>
<td>Planned</td>
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</tbody>
</table>

† Mixed neurogenic dysphagia: Stroke – ventilation; Stroke – no ventilation; Traumatic brain injury or spinal cord injury; Other – ventilation; Other – no ventilation

Hosp: hospital; ITU: Intensive Care Unit; RCT: randomised controlled trial; SU: Stroke Unit; Obs: Observational study
PHAST-TRAC

Aim
- Safety & efficacy of PES in accelerating readiness for decannulation

Patients (adults)
- Supratentorial stroke (IS or ICH)
- Prior artificial ventilation and tracheotomy; weaned but persistent neurogenic dysphagia with unsafe airway
- Ineligible for decannulation 24-72 hours beforehand
- Cannot take food (FOIS=1)
- No sedation for ≥3 days
- Germany, Italy, Austria

Intervention
- Early PES (Phagenyx, CE Mark)
- PES again if persistent dysphagia

Comparator
- Sham then PES if persistent dysphagia = Late PES

Outcomes
1. Readiness for decannulation using FEES
2. Secondary
   - Need for recannulation
   - Need for, effect of, retreatment

Design
- International, prospective, randomised, single-blind parallel group trial; sequential design
- N=70-140

Funder/sponsor
- Phagenesis Ltd (UK)

Protocol

Sequential review:
N=50  Futility
N=70  Efficacy / sample size re-estimation
N=140  Maximum
PHAST-TRAC: Decannulation algorithm

- Protocol for determining readiness for decannulation using instrumental assessment - fibreoptic endoscopic evaluation of swallowing (FEES)
- Assessment made by independent investigator at each site
- Scoring: binary, ordinal

## PHAST-TRAC: Baseline

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>PES</th>
<th>Sham</th>
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<tbody>
<tr>
<td>Patients</td>
<td>69</td>
<td>35</td>
<td>34</td>
</tr>
<tr>
<td>Age, years</td>
<td>64.2 (11.9)</td>
<td>61.7 (13.0)</td>
<td>66.8 (10.3)</td>
</tr>
<tr>
<td>Sex, female, %</td>
<td>25 (36.2)</td>
<td>11 (31.4)</td>
<td>14 (41.2)</td>
</tr>
<tr>
<td>Premor. mRS&gt;0, %</td>
<td>3 (4.6)</td>
<td>1 (3.0)</td>
<td>2 (6.2)</td>
</tr>
<tr>
<td>mRS&gt;4, %</td>
<td>67 (98.5)</td>
<td>34 (100)</td>
<td>33 (97.1)</td>
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<tr>
<td>Previous stroke/TIA</td>
<td>10 (14.5)</td>
<td>7 (20)</td>
<td>3 (8.8)</td>
</tr>
<tr>
<td>Smoking, %</td>
<td>8 (11.6)</td>
<td>5 (14.3)</td>
<td>3 (8.8)</td>
</tr>
<tr>
<td>OTR, days</td>
<td>28.0 [22] (11-120)</td>
<td>28.0 [29] (11-120)</td>
<td>28.0 [22] (11-95)</td>
</tr>
<tr>
<td>Ventilation, days</td>
<td>15.0 [13] (3-131)</td>
<td>15.0 [15] (5, 131)</td>
<td>13.5 [13] (3, 60)</td>
</tr>
<tr>
<td>PEG tube, %</td>
<td>9 (20.5)</td>
<td>5 (22.7)</td>
<td>4 (18.2)</td>
</tr>
<tr>
<td>NIHSS, /24</td>
<td>17.5 (4.6)</td>
<td>17.6 (5.0)</td>
<td>17.5 (4.3)</td>
</tr>
<tr>
<td>Ischaemic stroke</td>
<td>49 (71.0)</td>
<td>27 (77.1)</td>
<td>22 (64.7)</td>
</tr>
</tbody>
</table>
PHAST-TRAC: Sequential analysis

- Two analyses performed: futility at N=50, efficacy at N=70
- Trial continued at N=50, not futile
- Trial stopped at N=70, for efficacy
- 1 patient excluded since catheter not inserted so N=69
PHAST-TRAC: Results

PES increased readiness for decannulation
# PHAST-TRAC: Results

<table>
<thead>
<tr>
<th>%</th>
<th>PES</th>
<th>Sham</th>
<th>OR/MD (95% CI)</th>
<th>p</th>
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<tbody>
<tr>
<td>Participants</td>
<td>35</td>
<td>34</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Investigators</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decannulation ready (%)</td>
<td>17 (48.6%)</td>
<td>3 (8.8%)</td>
<td>7.0 (2.4-19.9)</td>
<td>0.00082</td>
</tr>
<tr>
<td>Failing algorithm (/3)</td>
<td>0.5 [0, 3]</td>
<td>2 [2, 2.75]</td>
<td>-1.0 (-2.0, 0.0)</td>
<td>0.018</td>
</tr>
<tr>
<td><strong>Independent FEES RV</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decannulation ready (%)</td>
<td>10 (28.6%)</td>
<td>2 (5.9)</td>
<td>6.4 (1.3-31.9)</td>
<td>0.023</td>
</tr>
<tr>
<td>Failing algorithm (/3)</td>
<td>1.2 [0.4, 2.0]</td>
<td>2.0 [1.7, 2.7]</td>
<td>-0.7 [-1.0, 0.0]</td>
<td>0.009</td>
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<tr>
<td><strong>Actions</strong></td>
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<tr>
<td>Patients</td>
<td>17</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Re-cannulation ≤48h (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
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</tbody>
</table>
1ry outcome: pre-specified subgroups

Pre-specified subgroups

Significant interactions:

- Onset to randomisation
  - Efficacy if <28 days
- Time on ventilator
  - Efficacy if <15 days
# 1ry outcome: After open-label PES

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>PES</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Participants, open-label part</strong></td>
<td>45</td>
<td>15</td>
<td>30</td>
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<tr>
<td>Ready for decannulation (%)</td>
<td>20 (44.4)</td>
<td>4 (26.7)</td>
<td>16 (53.3)</td>
</tr>
<tr>
<td><strong>Participants, randomised &amp; open-label parts</strong></td>
<td>69</td>
<td>35</td>
<td>34</td>
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<tr>
<td>Ready for decannulation (%)</td>
<td>40 (58.0)</td>
<td>21 (60.0)</td>
<td>19 (55.9)</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>69</td>
<td>35</td>
<td>34</td>
</tr>
<tr>
<td>SAEs</td>
<td>18 (26.1)</td>
<td>10 (28.6)</td>
<td>8 (23.5)</td>
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<tr>
<td>Device-related SAEs</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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</table>

![Graph showing distribution of outcomes](https://via.placeholder.com/150)
PHAST-TRAC: Limitations & Strengths

Limitations
• Small: sequential analysis led to early stopping
• Single-blind: treater was unblinded
• Design meant no long-term follow-up

Strengths
• Multicentre, sham-controlled, well-defined participants
• Robust findings, blinded outcome
• Internal consistency
• External consistency (with pilot trial)
• Most patients offered PES irrespective of randomisation
Summary: Decannulation

- Results similar to Suntrup et al (single centre, N=30)
- Randomised comparison
- Subsequent treatment in sham group

**Suntrup et al. Int Care Med 2015; 41: 1629-37**
Pharyngeal Electrical Stimulation Evaluation for Dysphagia after Stroke (PhEED)

Aim: Pivotal trial
Patients: Post stroke dysphagia, in-patient rehabilitation. In US and Europe
Intervention: Catheter – stimulation PES x 3 days
Comparator: Catheter – no stimulation
Outcome: swallowing safety by videofluoroscopy
Status: Start Q1. Some US and EU sites identified; more interested US sites welcome

If interested, please contact:
• rharvey@sralab.org
  or
• philip.bath@nottingham.ac.uk

Thanks
Thank you
Declaration of Interests: P Bath

Chief Investigator:
- Cochrane post-stroke dysphagia National Institute Health Res

Trial Steering Committees
- STEPS CI Phagenesis Ltd
- PHAST-TRAC Chair Phagenesis Ltd
- PHADER Co-CI Phagenesis Ltd
- PhEED Co-CI Phagenesis Ltd

Advisor
- SONAR Nestle
PES: Tracheotomised stroke patients

Patients
- N=30, severe stroke; prior artificial ventilation and tracheotomy; weaned but persistent dysphagia with unsafe airway

Intervention
- PES 3 days (n=20)

Comparator
- Sham (n=10). Then PES if persistent dysphagia

Outcomes
1. Decannulation
2. Stimulation intensity; LoS; FOIS; mRS
3. Response in sham group

Results
1. Decannulation PES 15/20 v 2/10 (p<0.01)
2. LoS, FOIS, mRS all NS
3. PES in sham 5/7

Suntrup et al. Int Care Med 2015; 41: 1629-37