# The AspiRATE study IRAS No: 218224 STH No: 19484

Physiological investigations: clinical trial to study a novel intervention

## 1. Project details

1.1. Investigator details

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Dr Karen Kilner, Senior Lecturer in Statistics[5]

1. Sheffield Teaching Hospitals NHS Foundation Trust
2. Cambridge University Hospitals NHS Foundation Trust
3. Engineering Design Centre, University of Cambridge
4. Department of Engineering, University of Cambridge
5. Sheffield Hallam University

1.2. Sponsor details
Sheffield Teaching Hospitals NHS FT

1.3. Project title
The AspiRATE study: a proof-of-concept assessment of a novel intervention to acoustically detect silent aspiration in patients with acquired dysphagia.

1.4. STH Project Reference number
STH19484

1.5. Protocol version number and date
Version 2.2, October 10th 2017

1.6. Phase of Trial
Phase II: Proof-of-concept diagnostic novel intervention trial

## 2. Research question

Can silent aspiration during swallowing be reliably detected using acoustic signal processing plus pulse oximetry?

## 3. Abstract

This proof of concept trial, involving original research from a multicentre, multidisciplinary team, aims to establish whether silent aspiration can be detected in patients with dysphagia (swallowing difficulties), using a microphone array attached to the neck (to capture acoustic respiratory changes), pulse oximetry (to detect reduction in blood oxygen levels) and respiratory rate analysis, with data combined and analysed via post-capture signal processing techniques.

The project aims to develop equipment and signal processing algorithms to a point where a novel intervention has been established that allows semi-automated detection of safe versus unsafe (aspiration) swallows. The intervention will be trialed in patients with dysphagia within standard videofluoroscopy clinics under clinical supervision. There will be ongoing development of the intervention and signal processing algorithms during this process. Public and patient involvement work will feed back into the design process.

If the intervention performs successfully in this proof-of-concept study, we aim to proceed to a larger clinical trial to determine its sensitivity and specificity as a screening tool for aspiration, before final development into a commercial product.

## 4. Aim of the study

To answer the research question above, with the aim in future project work of developing the technology to ultimately create a semi-automated device to objectively detect silent aspiration in patients with swallowing difficulties.

The ultimate aim of the project is to enable objective, community based assessment of swallow safety for patients who cannot undergo hospital based assessments – for example those with severe cognitive challenges arising from learning difficulties or dementia and those who are bed bound. This would help resolve inequity of access to accurate swallow safety assessment for people with marked physical and/or cognitive challenges, and therefore reduce risks associated with aspiration in these patient groups.

## 5. Background

Dysphagia (swallowing difficulties) is commonly experienced as a symptom of neurological diseases such as amyotrophic lateral sclerosis (ALS), Parkinson's disease, stroke, dementia, multiple sclerosis (MS) or with traumatic brain injury. Dysphagia is also seen structural or dynamic changes to the caused by head and neck cancer or its treatment. Developmental disorders such as cleft palate, learning difficulty, or cerebral palsy may also cause dysphagia.

Aspiration may occur during dysphagia, whereby food, fluid, saliva or medication penetrates into the airway during swallowing. Aspiration usually triggers a protective cough reflex to clear the material, but in some people this protective mechanism is absent, and they have no indication that they have aspirated: this is called silent aspiration.

Aspiration predisposes to chest infection, which has a significant mortality and morbidity rate. It leads to hospital admissions, longer in-patient episodes, and poorer health outcomes and has been shown to be detrimental to an individual's quality of life.[1-6] Patients may require modified diet, fluids and medications – or if the dysphagia is severe, they may need feeding by tube. This can result in social isolation and many carers feel guilty eating or drinking in front of patients who are "nil by mouth" , treats and social gatherings are affected for all concerned.

It is therefore important to know whether someone is aspirating, as their diet or feeding methods can be changed to reduce the risk of aspiration and its complications.

While aspiration associated with coughing is usually clearly demonstrated by clinical examination by a speech and language therapist or other trained professional, suspected silent aspiration

(penetration of food and/or fluid into the airway without triggering of a cough reflex) is currently detected by one of two instrumental methods.

The first is Fibreoptic Endoscopic Evaluation of Swallowing (FEES), which involves a specialist passing a flexible endoscope down through the nose to directly observe the swallow process. This is time-consuming (taking on average 20 minutes), invasive, and some aspiration can be missed.

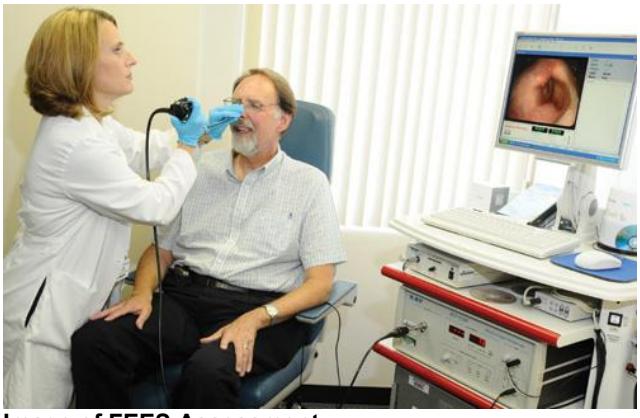


**Image of FEES Assessment**

The second method is video fluoroscopic assessment of swallowing, often considered the 'gold standard'. Videofluoroscopy (VF) requires the patient to swallow a radio-opaque liquid and barium coated solids, allowing a radiographer to follow the liquid/ food's passage through the mouth and pharynx using an x-ray. This investigation has good sensitivity and specificity, but it exposes the patient to radiation, is expensive, requires specialist assessors (usually 2) and can only be done in an appropriate x-ray suite.

**Image of VF Assessment**

Each of these assessments – while clinically valuable, require the patient to be able to come into hospital, to sit still and to have cognitive capacity to follow instructions. This means that currently they are not available to patients who have significant dementia, learning difficulty or those who are bed bound in the community, creating inequity of care.

A simple, portable screening test for silent aspiration is therefore highly desirable. This would facilitate equity of care and also fit with the care agenda aims of 'taking care to the patient' rather than transporting patients into hospital.

**Our innovation and proposed device:**

We aim to develop a portable, non-invasive, simple-to-operate and automated device that can be used to screen for silent aspiration. We believe that subtle changes to the breath sounds arising in the trachea and below the vocal cords may indicate if particles of liquid or food have been aspirated.

Similarly, changes in the breathing pattern or percentage blood oxygen saturation may indicate aspiration.

Once fully developed, we envisage that the proposed device would use multiple sensors and advanced signal processing techniques, to give a 'pass/fail' type response for the examiner looking for silent aspiration. We aim for the device sensors to be simple to apply using adhesive pads or a strap.

This study forms the first phase in working towards development of this technology. It builds upon foundation work done by groups using either a single microphone or accelerometers attached to the neck to assess the swallow and breath sounds associated with aspiration. These preliminary studies have provided promising results, but the focus has largely been on sounds heard above the vocal cords, and accuracy of the detection of aspiration has been limited.

The most interesting line of research has been the analysis of lower airway (tracheal) sounds during swallows, with one group reporting an accuracy of 86% for the detection of swallows with silent aspiration[7]. This method aims to detect the end result of aspiration (food or liquid below the vocal cords), and so should have a higher specificity than is found with other techniques.

Pulse oximetry has also shown some potential as a measure of silent aspiration, but current consensus in the literature is that, while it has value as an adjunctive measure, it is not sufficiently reliable for use in isolation[8].

The unique element to our work is a multi-channel approach using an array of microphones, and sophisticated processing of the audio and other sensor outputs. We will start by recording swallow and tracheal sounds via multiple microphones, in conjunction with pulse oximetry. Signal processing experts within the team will pick out characteristic signals associated with the normal swallow and episodes of aspiration. Through the development process we will narrow down the minimum set of sensors required to optimise test sensitivity and specificity. It may be that multiple measurements of the same type (sounds) or a mixture of measurement types (sounds and pulse oximetry) will give us the most information. We believe the microphone array and multi-channel analysis design can be superior in sensitivity and specificity when compared to existing reported techniques[7].

PPI evaluation will be undertaken to explore the acceptability/tolerability of wearing the equipment array, and also the potential perceived benefits of access in the community to objective swallow safety assessment, particularly for groups previously excluded by cognitive or physical challenges. Sheffield Teaching Hospitals NHS FT has access to a database of patients and carers who have previous or ongoing experience of swallowing problems, and who have agreed to act as reviewers for studies. A focus group consisting of these individuals will be arranged by letter of invitation.

A robust prototype will be designed and manufactured collaboratively by Sheffield Teaching Hospitals NHS FT and Cambridge University, to incorporate the final set of sensors and analysis software. The aim is for this equipment array to be approved for research use in patients, and assessed in a proof of concept trial.

5.1. Clinical significance

Patients and healthcare in general

Dysphagia and aspiration are common disorders, but with up to 59% of these patients suffering from silent aspiration, it can be difficult to detect [9, 10, 11]. If recognised, dietary modifications and swallowing strategies can be used to limit the condition's associated morbidity and mortality.

A common cause of dysphagia and silent aspiration is stroke [6]. In the acute phase after a stroke, the incidence of silent aspiration can be as high as 67%[9], and for many patients, aspiration then persists into the rehabilitation stage. Aspiration is strongly associated with an increased risk of

developing chest infection, and many stroke patients require dietary modification, or in some cases feeding tubes.

Aspiration is also seen in association with a wide range of other conditions such as neurodegenerative disorders (e.g. multiple sclerosis, Parkinson's disease) and vocal cord palsy[12]. It may also be caused by medical interventions, such as the treatment of nasopharyngeal, laryngeal and oral cancer[13,14].

Bedside investigations for dysphagia are available (such as the water provocation test[15]), though a recent systematic review concluded "although a wide variety of screening and assessment tests are available for use, none have acceptable sensitivity and specificity to ensure accurate detection of dysphagia"[11]. The detection of *silent* aspiration with these methods is almost impossible.

Currently, aspiration is diagnosed through FEES or videofluoroscopy, both of which require skilled staff, usually working in a hospital clinic that may only run weekly. For this reason, and due to the associated costs (videofluoroscopy costs the NHS £231 per test), these more accurate investigations are not available to all people presenting with dysphagia. Some hospitals do not have access to videofluoroscopy and need to transport patients out of district to a hospital which has this service.

Our proposed approach could revolutionise the way that dysphagia and aspiration are managed. A quick, automated screening test would allow any individual with basic training to test a patient with suspected aspiration at any time. In particular, regular non-specialist re-assessment would become possible, as would screening and testing in difficult circumstances. This would facilitate best ongoing management of oral intake and associated timely referrals to therapy and dietetic services.

5.2. Related research

A significant amount of research has been undertaken in the field of acoustic detection of aspiration. This stems from the longstanding use of stethoscopes to listen to the throat as a crude test of swallowing disorders. A full review of the literature was conducted prior to embarking on this project, and two existing reviews were also identified.

The first review by Dudik *et al.* (2015)[16] is very relevant to our work, providing an overview of cervical auscultation (the recording of sounds and vibrations from the throat) and signal processing techniques. The studies identified in the review provide a useful foundation for our work, establishing variables that may affect swallow sounds (e.g. food consistency), and investigating the impact of microphone position on the neck on the recordings obtained. No studies included in the review or identified in our own literature review have used multiple microphones to record sounds in an array. The review concludes that the addition of objective methods of data analysis has enhanced the diagnostic process, but that consensus on the best signal processing technique has not been reached. Signal processing to date has remained relatively basic, and has not integrated more than one type of sensor input.

The second review (2013) assesses the current evidence for the clinical assessment of aspiration following stroke[11], which is one of the leading causes of dysphagia. Non-instrumental assessment techniques ('bedside' tests e.g. the water provocation test) are comprehensively considered, finding that none have acceptable sensitivity and specificity to ensure accurate detection of aspiration. Regarding videofluoroscopy, evidence assessed in the review supports the technique as the best currently available for detecting silent aspiration, while noting the following disadvantages: i) The procedure is relatively complex, time consuming and resource intensive; ii) there is some exposure to radiation; iii) the test is not appropriate for some patients who may have difficulty in sitting upright in a chair. The results of the test can also be difficult to interpret and there can be significant variation among individual raters. The review states that limited evidence exists for pulse oximetry, leaving the association between aspiration and oxygen desaturation as inconclusive.

In addition to the reviews, two studies stand out as particularly relevant. The first was published by Shirazi *et al.* in 2014[7]. This group used a single microphone to record an increase in turbulent air flow within the trachea in response to a foreign body from aspiration. Analysing acoustic recordings with relatively basic signal processing techniques provided a sensitivity of 91% and specificity of 85%. We hope to build on this work by using multiple acoustic channel recording and combining this with pulse oximetry recording. The multi-channel approach in theory will improve signal detection and aid in the removal of background noise.

Relatively little work has focused on a paediatric population, and the second paper of note focuses on the joint analysis of swallow and breath sounds in children with a mean age 24 months[17]. Using an optimal combination of parameters relating to swallow and breathing sounds an accuracy classifying swallows as aspirating of 82% was achieved.

The above work provides a strong foundation for our study, which will investigate if a microphone array, combined pulse oximetry, complex signal processing and a focus on tracheal air flow can improve the classification of swallows as safe or unsafe.

## 6. Plan of the investigation

6.1. Methodology

***Preliminary testing / Public and patient involvement***

The team has agreement to access a database held by Sheffield Teaching Hospitals NHS FT of individuals who have or have had dysphagia, and who have consented to support the development of research studies. This database will be used to identify potential invitees for a focus group discussion. Refreshments will be provided and travel arranged/travel costs reimbursed. We hope to form a group of 6-8 patients and carers to discuss:

- their experiences of current screening and diagnostic options
- an outline explanation of the aims of this project
- discussion of any perceived benefits/challenges to any potential trial participants
- opportunity to see and try the proposed aspiRATE equipment

A clinician known to database members (but not a member of the research team) will send out the initial invitation letter. She will also host the group along with one person from the research team. We aim for a relaxed and open discussion in order to gain valuable feedback on the important considerations for users in any testing, and specific comments on the proposed study design. The team will be open to suggestions regarding modifications that may make the trial more user-friendly. The equipment array will be fitted to volunteers from the user group at this event to gain feedback on comfort and acceptability.

***Clinical trial***

The trial can be considered in two parts:

- Part 1, which will focus on tolerability during videofluoroscopy and ensure that there is no adverse impact on the usual clinical care
- Part 2, where dedicated trial staff will collect data with the equipment array alongside standard clinical care.

**Part 1.** The primary aim of part 1 of the trial is to ensure that the equipment array can be used alongside videofluoroscopy in a manner that doesn't impede the clinical utility of the examination. It will allow technical and radiology staff to familiarize themselves with performing the study protocol, additional time will be allowed for each of these procedures, in order to reduce time pressure and members of the research team will be on hand for support. We envisage 3-5 patients should be a sufficient sample to complete this first phase.

Eligible patients will be identified by the Speech and Language Therapy team at Sheffield Teaching Hospitals NHS FT. These will be patients who are known to experience at least occasional

aspiration, following initial videofluoroscopy as part of their usual clinical care.

Patients requiring follow up videofluoroscopy (either to check for deterioration or progress made in response to swallow therapy) will be sent a letter inviting them to their follow up appointment and explaining that they have the opportunity to participate in a research study on a voluntary basis. The letter will contain a patient information sheet explaining the study, and what participation will involve. Patients who express an interest in participating in the study they will be booked a double-length appointment to allow sufficient time for any delay that research participation may involve.

At their appointment the patient will be met by a research nurse and a study technician. The nurse will explain the study again, answer any questions and take written informed consent for study participation. The patient will have the option of declining to participate in the study with no effect on the planned videofluoroscopy study and ongoing clinical care.

The videofluoroscopy study will be performed in the standard manner, by two appropriately qualified Speech and Language Therapists and a Radiographer. In addition the aspiRATE equipment array will be attached by a study technician, in order to capture the additional data for the study so that it can be validated against the videofluoroscopy assessment.

Patients involved in Part 1 of the study will be asked to feedback on the design of the aspirate device, in particular the neck attachments. The radiographer performing the study will also be asked for feedback on the use of the device during videofluoroscopy, in particular to identify any hindrance to the acquisition or interpretation of images.

Once it has been confirmed that the equipment array can be easily applied, and does not interfere with standard videofluoroscopy, Part 2 of the study will be started. If it is found that the equipment array interferes with videofluoroscopy, progression to Part 2 will be halted until the issues are resolved.

**Part 2.** The primary aim of Part 2 of the trial is to collect data from a group of dysphagic patients using the proof-of-concept aspiRATE equipment array, allowing signal processing experts to develop the required multi-sensor analysis algorithms.

We aim to recruit up to 45 patients with dysphagia, according to referral rates within the timescale of the trial to the standard videofluoroscopy clinics within STH.
We will aim to recruit consecutive patients in one of three cohorts

1. Dysphagia with no aspiration
2. Dysphagia with clinically detectable aspiration (coughing, wet voice)
3. Dysphagia with silent aspiration

Potential trial participants will again be identified by the Speech and Language Therapy team at Sheffield Teaching Hospitals NHS FT. Once again a letter inviting trial participation will be sent, with a patient information leaflet enclosed.

On attending the clinic, the patient will be met by a research nurse to ask if they are interested in finding out more about the study. The nurse will explain the study again, answer any questions and take written consent for study participation. A study technician will attach the equipment array prior to the videofluoroscopy assessment, and be present to assist the radiographer if needed. Acoustic recordings and pulse oximetry data will be collected during the videofluoroscopy examination with no change to the standard protocol. The patient will be asked for feedback and their involvement in the trail will finish at the end of the clinic appointment.

For the purpose of the study videofluoroscopy findings will be interpreted using the Rosenbek Penetration-Aspiration Scale[18], and acoustic and pulse oximetry recordings from aspirating and non-aspirating swallows will be compared by signal processing experts to identify any characteristic

features in those where aspiration occurred.

6.2. Design
Exploratory cohort study to investigate proof-of-principle with an established reference standard (Level 2b)

6.3. Setting
Tertiary referral centre

6.4. Participants
Patients with dysphagia referred to videofluoroscopy clinic at Sheffield Teaching Hospitals NHS FT.

6.5. Sample size
The aim of the current work is not to establish diagnostic accuracy of the equipment array, but rather to develop the hardware and processing algorithms for use in a future larger clinical trial.

Based on experience from similar projects, a sample size of 20 - 45 has been chosen for Part 2 of the study, with an intention to recruit the 3 patient groups described above, aiming for up to 5 - 15 in each group but with the understanding that targets will be subject to referral patterns within the study timescale.

We will not know which groups patients will fall into before testing, and so consecutive cases will be approached and consented for the trial. After recording from the device and analysis of the videofluoroscopy examination, patients will be allocated to one of the three groups. Data collection will continue until all either: a) each groups has recruited 15 participants or b) recruitment time for the study is ended and data recorded from extra cases in already completed groups will still be entered into the analysis.

Age and sex matching will not be used, as is standard practice in this early stage of proof-of-principle research.

6.6. Recruitment: (see section 6.1 for recruitment procedures in context)

Part 1 clinical trial

Patient identification: by STH Speech and Language Therapy staff reviewing the medical notes of patients awaiting videofluoroscopy follow up appointments
Inclusion criteria: Dysphagia ± aspiration, age 18 and above
Exclusion criteria: Not competent for consent, previous neck surgery (not including thyroid surgery), cervical skin infection or defect, pregnant (or unknown pregnancy status).
Approach: By posted letter, with an enclosed trial patient information sheet
Recruitment: Through response to the letter
Consenting: On the day of testing, by a research nurse

Part 2 clinical trial

Patient identification: Patients attending a routine videofluoroscopy appointment at STH.
Inclusion and exclusion criteria: as above.
Approach: By posted letter, with an enclosed trial patient information sheet
Recruitment: On the day of testing, by a research nurse
Consenting: On the day of testing, by a research nurse

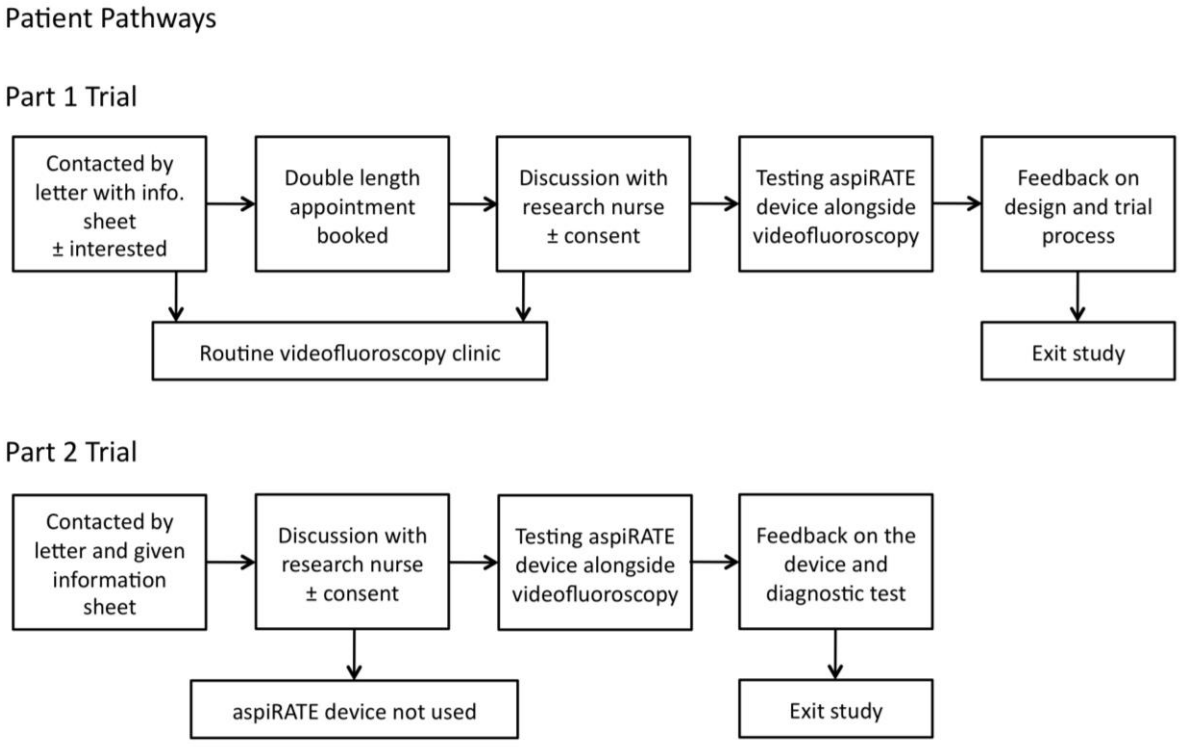
6.7. Outcome measure(s)
As a proof-of-concept study the outcomes of interest are primarily qualitative: feasibility of the use of the equipment array, characteristics of acoustic signals from cases and controls, equipment safety and patient group feedback.

No statistical comparisons will be drawn between the case-control groups identified by the equipment array. A future clinical study will establish sensitivity and specificity of the equipment array as a device for the detection of aspiration, with reference to videofluoroscopy. This will be powered for the primary outcome of diagnostic accuracy.

6.8. Analysis including statistical methods
Anonymized data (from both the equipment array and the videofluoroscopy) will be examined by the research team. Standard methods of analysis will be applied to acoustic recordings to assess the differences between those from aspirating and non-aspirating patients, and to compare these findings with the aspirating and non-aspirating videofluoroscopy data. An auditory processing algorithm that can be applied to future recordings will be developed.

Data from the device (index test) and videofluoroscopy (reference standard) will be used to populate a standard 2x2 table, allowing calculation of the device sensitivity and specificity. Receiver Operating Characteristic (ROC) curve analysis will allow refinement of the signal processing algorithm and interpretation thresholds, although as a screening test false positives will be considered preferable false negatives.

6.9. Intervention:




**Flow chart indicating participant's involvement throughout the course of the study**

6.10. Safety assessment:
The following issues have been considered as part of the risk assessment process of the new equipment array.

- Device obscures visualization of swallow on videofluoroscopy due to inadequate radiolucency – Videofluoroscopy assessments will be conducted by speech and language and radiography professionals, and initial testing (part 1 trial) includes built-in time to allow

the device to be adjusted or modified to improve videofluoroscopy views. In individual patients testing will be terminated early if inadequate views can be obtained for clinical use.

- Equipment prevents adequate patient positioning for videofluoroscopy – The attachment of the equipment attachment will be designed in conjunction with Speech and Language Therapists ensuring that it should not prevent the expected patient positioning. Initial PPI and the Part 1 trial are designed to allow refinement of the design if positioning proves problematic. In individual patients testing will be terminated early if positioning is inadequate for clinical use.
- Patient aspirates during videofluoroscopy – Aspiration is expected in some patients during videofluoroscopy and the risk should not be increased by use of the new equipment array. Most episodes of aspiration during videofluoroscopy have no sequelae. The equipment will be easy to remove and will not interfere with the provision of supportive treatment after aspiration in the unlikely event this is required.
- Radiation exposure – All participants in this study will already be undergoing videofluoroscopy for clinical reasons. In a limited number of cases, during the examination (which required multiple swallows to be performed) additional swallows may be requested to provide data for use only in the trial. The recording of any additional swallows would expose the patients to small amounts of ionizing radiation. This risk has been assessed by Mr Giles Morrison, Head of Radiology Physics and Radiation Protection Adviser at Sheffield Teaching Hospitals NHS FT.
- Electrical shock risk – Only the low voltage microphones and pulse oximetry probe will make contact with the patient. The equipment array will be assembled and checked by medical engineering professionals to meet EU medical device safety standards.
- Allergy to medical adhesives used to attach the microphones – standard echo cardiology sensors will be sued with additional measures as per individual patient need
- Infection control risk. All research project equipment which would contact patients' skin will be for disposal single patient use. Research project equipment which will not be in contact with patients' skin and the usual videofluoroscopy equipment will be sanitized according to Sheffield Teaching Hospitals Infection Control guidance.
- The protocol has received scientific review from Sarah Wallace, Royal College of Speech and Language Therapy Advisor in Dysphagia (Manchester) and Clinical Lead in Dysphagia University Hospital South Manchester NHS Foundation Trust.

Adverse events will be discussed at pre-existing institutional audit sessions, and reported online using standard STH incident report forms. In addition regular meetings of the study steering committee (co-investigators and CUHP representative) will allow further discussion. If a concern arises regarding device safety recruitment will be suspended until the risk has been mitigated.

A serious adverse event (SAE) occurring to a participant will be reported to the REC giving favourable opinion to the study. An SAE will be reported if the Chief Investigator believes the event may be: 'related' (resulted from administration of any of the research procedures); and 'unexpected' (not listed in the protocol as an expected occurrence). Reports of related and unexpected SAEs will be submitted within 15 days of the Chief Investigator becoming aware of the event, using the NRES report of serious adverse event form.

6.11. Subject withdrawal and trial stopping/discontinuation rules

Individual subjects will be withdrawn if an adequate clinical service cannot be provided alongside the research. The trial would be discontinued in the unlikely event that the aspiRATE equipment array could not be made compatible with clinically safe videofluoroscopy.

6.12. Quality control: Monitoring and audit procedures

This is a low risk study with participation required only for the duration of one hospital trip. During the study the CI and co-applicants will review the recruitment and results at a monthly

teleconference.

6.13. Project plan with timescale and clearly delineated milestones
The following internal review milestones have been set:

- Initial testing and assembly of experimental equipment array - underway
- Part 1: Completion of initial patient trials with VF once feasibility has been confirmed and obtained data is consistent with the aims of the project (i.e. able to analyse breath and additional sounds, and record pulse oximetry). Estimated 5 patients required. Target: March/April 2018
- Part 2: Completion of data collection from 20-45 patients seen in clinic. Target: April – October 2018
- Completion of a study. Target: December 2018

**7. Statistical opinion**
Although detailed statistical analysis is not predicted, given the early stage of this research, we will consult statistical advice from Dr Karen Kilner, Senior Lecturer in Statistics at Sheffield Hallam University in order to ensure that data analysis potential has been optimized. Initial discussions and sharing of the protocol have been completed with a view to seeking further guidance once (anonymized) data is available for analysis.

**8. Project management**
Internal management and review will be conducted by the project group at regular tele-conference or face-to-face meetings. Liz Pryde, NIHR Devices for Dignity HTC Project Manager is part of the team and will provide expert project management overview. External review will be provided by Evgeny Dmitriev on behalf of the Cambridge Universities Health Partnership.

An application will be made for the study to be included in the NIHR Clinical Research Network (NIHR CRN) Portfolio, as it is part funded by NIHR via D4D and PRIDE.

As the equipment array is manufactured in-house in a health care establishment, and it is undergoing testing for proof-of-concept, it is not subject to the provisions of the Health Research Authority Medical Devices Regulations. In any future trial the Medicines & Healthcare products Regulatory Agency (MHRA) will be contacted, as commercialisation of a device may result from clinical data.

**9. Expertise**
A working relationship has been established for some time between the Cambridge University team and the Sheffield Teaching Hospitals team, and this has been strengthened by regular meetings and workshops since mid-2014. A strength of the current project team is its multidisciplinary nature, with both clinical and non-clinical members who have a track record of delivering medical innovation projects and working with the NHS and industry. There is experience of developing commercial applications using complex auditory signal processing, and of device manufacture and prototyping. Within the team there is also clinical and academic expertise from Speech and Language and Otolaryngology specialists.

Research Team members
Professor Sue Pownall has over 25 years of experience in the assessment and management of dysphagia. She has been CI on a number of trials which have successfully recruited to time and target. Sue is the Sheffield Clinical Lead in dysphagia, is a RCSLT Advisor in Dysphagia and is the RCSLT dysphagia representative on the RCP National Clinical Guidelines for Stroke.

Lise Sproson is a clinical researcher and Speech and Language therapist with specialist skills in dysphagia assessment and rehabilitation. She works for NIHR Devices for Dignity HTC and is

involved in a number of funded studies to enable people with long term health conditions. She is a committee member of the UK Swallow Research Group and has collaborated with dysphagia research evidence review for the RCP National Clinical Guidelines for Stroke.

Mr Matthew Smith is a senior specialist registrar in ENT Surgery regularly managing patients with dysphagia. He has been involved with a number of clinical studies during a period of full-time academic training and has led the development of an NIHR trial application.

Simon Godsill is a professor in statistical signal processing at the Cambridge University Engineering Department. He heads a team of researchers within the signal processing group, with particular interests in the processing and analysis of digital speech, audio, image and biomedical data.

Ian Hosking is a senior research associate in the Engineering Design Centre and the Cambridge University Engineering Department. Prior to joining the University he worked for 20 years in technology development in a range of sectors. Ian managed an EPSRC-NIHR funded network called PRIDE (Promoting Real Independence through Design Expertise) which has developed new tools for healthcare design. These have been applied to a range of projects covering new medical device development and service improvement. He is part of a collaborative project with Marie Curie Care and Sheffield Hallam University to develop a toolkit to enable the design of palliative care services. He sits on the British Standards Institute Committee (DES/001) that is providing input to the new European 'Design for All' standard.

Martin Slovak is a research associate within NIHR Device for Dignity HTC and clinical scientist in Specialised Scientific Physiological Measurement group within Sheffield Teaching Hospitals NHS Foundation Trust. He has been involved in a number of clinical trials in their design and setup. His research and clinical role is relevant for safe physiological measurements and trial data integrity according the guidelines for Good Clinical Practice.

Liz Pryde is an NHS Innovation Manager with NIHR Devices for Dignity (D4D) HTC, specialising in collaborative technology development projects that unite clinical, academic, patient and industry expertise to address unmet clinical needs. Liz has been involved in multiple projects involving defining user needs, developing technologies that integrate with existing healthcare practices and systems, and projects around practice change, adoption, and policy change within the NHS for the last 10 years. She has significant experience of projects in which the involvement of users (patients and the public, and other users including clinical staff).

**10. Ethical issues**

This is a low risk study where the normal patient care pathway is not significantly altered. The aspiRATE device will not be used in isolation for diagnosis or intervention.
The following ethical considerations have been identified:

- The target population includes vulnerable adults who may be suffering from cognitive impairment. Some patients may lack capacity to consent. – Only nurses trained in informed consent will discuss the project with patients and obtain written consent. If there is a concern that patients lack adequate capacity they will be excluded from study.
- Patients will only have a short period to consider trial involvement after speaking to the research nurse on the day of their clinic. – Information sheets using lay language and large font will be sent out with the invite letters to ensure that patients have the opportunity to discuss information with family members if they wish, in order to start the nurse-led discussion with a basic understanding of the trial. Contact details will be available in the information leaflet to allow interested patients to further discuss the trial with a member of the study team prior to the day of testing. It will be made clear that consent may be withdrawn at any point without detriment to care.
- The attachment of the aspiRATE equipment array could lead to discomfort – The equipment will be ergonomically designed from soft materials where possible to improve comfort and reduce the bulk of the attachment. Prior to clinical studies the equipment will be attached to

members of the target population during a PPI focus group event. Feedback will be obtained and the device modified if required to improve comport. Feedback on comfort will also be collected during clinical trials.

- All videofluoroscopy assessments will be arranged due to clinical need. Patients may be asked to repeat swallows for the purpose of additional acoustic recording, however trials will be supervised by a qualified Speech and Language therapist and a Radiographer and if the patient is felt to be at risk the device testing will be terminated. This is in line with usual practice during videofluoroscopy studies. Radiation risk assessment has been completed by Mr Giles Morrison, Head of Radiology Physics and Radiation Protection Adviser at Sheffield Teaching Hospitals NHS FT.

**11. Service users**

The project has been initiated by Speech and Language and Medical staff who meet with service users suffering from dysphagia and aspiration on a regular basis. It has been noted that there is a clear concern from clinical staff and service users that currently there are limitations to the reliability and accessibility of diagnosis and monitoring of swallow safety.

Prior to starting the study, service users will be consulted to influence the design of both the proof of concept equipment array and the study. This is detailed above under Methodology/Preliminary testing.

**12. Dissemination**

The findings of this proof of concept work will be disseminated via publication in scientific journals and presentation at academic meetings attended by relevant clinical staff. We will also report back to the PPI groups and locally to clinical teams.

**13. Taking the work forward**

If the aspiRATE equipment array demonstrates some ability to discriminate between aspirating and non-aspirating patients, the plan is for the equipment to be further developed to a point where the hardware and software can be replicated and used in a multisite clinical trial. It is envisaged that the primary outcome of this larger trial would be the sensitivity and specificity of the device for the detection of aspiration in a mixed population of dysphagic patients, thus building on the data collected in our proof of concept study. An economic evaluation would be considered as part of this trial given the current costly or ineffective diagnostic alternatives and also the potential cost and health benefits of avoiding costs associated with long term morbidity, hospital admissions and care requirements from aspiration associated complications.

**14. Intellectual Property**

A collaboration agreement has been produced for this project, to specify IP arrangements between the Cambridge and Sheffield-based parties.

In brief:
Background intellectual property will remain the property of the generating party. Royalty-free, non-exclusive license will be granted for the duration of the project to use Background Intellectual Property for the sole purpose of carrying out the project. Arising Intellectual Property will belong to the party generating the IP. If generated by two or more parties jointly, the Arising Intellectual Property will be jointly owned by those parties in equal shares.

**15. Costing schedule**

**Cost of development:**

- Materials required for proof-of-concept device (microphones/accelerometers, data capture card, ECG monitor) and development to a refined prototype £10,000.
- Laptop and software for data analysis £1,500
- Manufacture of bespoke parts (in Engineering department) £2,500

- Radiation assessments prior to ethics committee review £1,400
- Initial VF trials £4,616 (to pay for 2x normal double clinic appointment times for an estimated 10 volunteer patients)
- Research Nurse Band 6 (3.5hrs /week for 6 months , £22.51/hr): £2,049
- Clinical Engineering Support Band 7 (0.1 WTE for 6 months): £2,594
- Travel expenses @£30 per patient x10 £300
- Signal processing/data analysis (lab time) £2,500
- (PPI £400, covered separately by PRIDE)

**Total £27,459**

**16. Funding arrangements**

Funding in full has been secured for the project:
£5,000 from PRIDE (Promoting Real Independence through Design Expertise, an NIHR initiative)
£5,000 from D4D (Devices for Dignity, an NIHR initiative)
£17,648 from Cambridge University Health Partners (CUHP).

In total £27,648 has been secured for the project

If the results of our initial proof-of-concept work are promising we would aim to seek funding for a larger clinical trial from a national funding body such as the NIHR.

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Appendix 1: Additional documents

- Patient invitation letter
- Patient information sheet
- Patient consent form
- GP information letter