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Acoustic analysis of cough in head and neck cancer patients with swallowing disorders

Submission date 09/09/2022	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 23/06/2023	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 02/10/2023	**Condition category** Signs and Symptoms	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims

Dysphagia is an impaired swallowing safety and/or efficiency. This impaired swallowing may lead to the passage of food or liquids into the lungs instead of the stomach. Patients who are treated for head and neck cancer (chemoradiotherapy) are particularly at risk for dysphagia. Indeed, this treatment may result in ineffective or absent coughing that does not protect the airways anymore, which can lead to life-threatening lung infections.

Coughing efficiency is a key factor in the assessment of dysphagia. However, the subjective nature of cough assessment (auditory assessment by caregivers) leads to many disagreements in the detection of dysphagia. This project aims to measure objectively the effectiveness of coughing by using methods of acoustic analysis in patients with dysphagia following head and neck cancer treatments.

Who can participate?

Healthy volunteers (to obtain reference values) and head and neck cancer patients treated with chemoradiotherapy

What does the study involve?

All participants will produce voluntary coughs, voluntary throat clearings, and induced reflexive coughs (coughs induced by inhalation of a lemon preparation). Patients will also undergo an objective examination of dysphagia with an endoscope (nasofibroscopy). During this examination, patients will swallow several food textures (liquid, semi-solid, solid), and simultaneously, natural reflexive coughs (if present) will be recorded.

What are the possible benefits and risks of participating?

Patients benefit from a thorough evaluation of dysphagia. This study is without risk for all participants.

Where is the study run from?

Jules Bordet Institute (Belgium)

When is the study starting and how long is it expected to run for?
December 2016 to September 2023

Who is funding the study?
Department of Radiation-Oncology, the Université Libre de Bruxelles, and has been supported by l'Association Jules Bordet (Belgium)

Who is the main contact?
Sofiana Mootassim-Billah (a speech therapist and research assistant) (Belgium)
sofiana.mootassim-billah@bordet.be

Contact information

Type(s)
Scientific

Contact name
Ms Sofiana Mootassim-Billah

ORCID ID
https://orcid.org/0000-0003-4917-7360

Contact details
Meylemeersch 90
Bruxelles
Belgium
1070
+32 (0) 2 541 72 02
sofiana.mootassim-billah@bordet.be

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Assessment of radio(chemo)therapy-related dysphagia in head and neck cancer patients based on cough-related acoustic features

Acronym
ACCOUGH-P/A trial

Study objectives
The ultimate goal of this study is to develop an innovative and non-invasive assessment method for dysphagia and aspiration in head and neck cancer (HNC) patients using acoustic features related to voluntary and/or reflex cough as biomarkers of dysphagia and/or aspiration in this population.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/07/2018, Ethical Committee of the Institut Jules Bordet (Rue Meylemeersch 90, 1070, Brussels, Belgium; +32 (0)2 541 35 95; comite.ethique@bordet.be), ref: BECT B079201836313) and Ethical Committee of Universitair Ziekenhuis Antwerpen (Wilrijkstraat 10, 2650, Edegem, Belgium; +32 (0)3 821 38 97; ethisch.comite@uza.be), ref: 20/05/053

Study design
Prospective two-phase multicentre study

Primary study design
Interventional

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Dysphagia and aspiration risk

Interventions
Firstly, the study will focus on healthy subjects to identify relevant acoustic features of cough, throat clearing, and voice quality (reference values).
Secondly, the study will focus on head and neck cancer patients to verify the applicability of the selected acoustic features in head and neck cancer patients and to identify relevant acoustic features of the risk of aspiration in this population.
This study is multicentric: Jules Bordet Institute and Universitair Ziekenhuis Antwerpen.
Participants will come one single time (+/- 45 minutes) and produce audible cough samples and voice samples in a silent room.

1. Cough audio sample recordings:
1.1. 5 voluntary coughs and 5 voluntary throat clearings (acoustic + aerodynamic equipment)
1.2. 2 induced reflexive coughs with 4 concentrations of citric acid (acoustic + aerodynamic equipment)
1.3. Natural reflexive cough with different food textures (acoustic equipment)
1.4. Simultaneously assessed with Fiberoptic Endoscopic Evaluation of Swallowing

2. Voice sample recordings (acoustic equipment):
2.1. Sustained vowel /a/ before swallowing
2.2. Sustained vowel /a/ after swallowing

Equipment:
1. Acoustic equipment for coughs recordings: skin-contact microphone + acoustic microphone, acoustic analysis with the software developed for the project

2. Aerodynamic equipment for cough recordings: facemask connected to a digital spirometer, nebulizer for tussigen inhalation, aerodynamic analysis (software developed by Medical Electronics Construction®)
3. Acoustic equipment for voice recordings: skin-contact microphone + acoustic microphone, acoustic analysis (software PRAAT®)

Endpoints of this study:

1. Construction of a set of valid acoustic cough features (ACCOUGH)
1.1. Identification of a new set of acoustic cough features in a sample of a healthy population (reference data)
1.2. Comparison between acoustic voluntary and reflexive cough features as well as acoustic features of throat clearing
1.3. Selection of valid acoustic cough features

2. Validation of the ACCOUGH features as biomarkers of penetration/aspiration in HNC patients (ACCOUGH-P/A)
2.2. Identification of the ACCOUGH features in samples of head and neck cancer patients
2.3. Investigation of the correlation between ACCOUGH features and observed penetration /aspiration in HNC-patients

3. Correlation between ACCOUGH and aerodynamic cough features
3.1. Investigation of the correlation in a sample of a healthy population
3.2. Investigation of the correlation in HNC-patients

4. Correlation between ACCOUGH-P/A and acoustic voice features in HNC-patients

5. Investigation of the relation between voice quality abnormalities and observed penetration /aspiration in HNC-patients

Intervention Type
Other

Primary outcome(s)
Identification of a valid set of reference acoustic features in healthy subjects measured using temporal and spectral analyses at baseline. The temporal analysis includes signal duration, amplitude, sample entropy (turbulence noise) and kurtosis (burst). Acoustic cough-related features are recorded using skin contact and acoustic microphones, and analyzed with software developed for the project. The spectral analysis includes relative signal energies in the bands (0 Hz – 400 Hz), (400 Hz – 800 Hz), (800 Hz – 1600 Hz), (1600 Hz – 3200 Hz), the interval between 3200Hz and half the sampling frequency (22050 kHz) as well as the weighted frequency.

Key secondary outcome(s))
1. ACCOUGH-P/A
1.1. Identification of ACCOUGH in HNC patients measured using temporal and spectral analyses at a minimum 3 months following radio(chemo)therapy
1.2. Investigation of the correlation between penetration/aspiration and ACCOUGH to determine a set of valid ACCOUGH features as biomarkers of penetration/aspiration in HNC-patients (ACCOUGH-P/A) measured using the temporal and spectral analyses as well as the FEES examination at minimum 3 months following radio(chemo)therapy.

2. Swallowing features
Swallowing features measured using the Penetration-Aspiration Scale (PAS), The Yale Pharyngeal Residue Severity Rating Scale (YPRS) and the number of swallows at minimum 3 months following radio(chemo)therapy.

3. Voice features
Pre- and post-swallow voice quality measured using acoustic features to investigate whether a change in voice quality occurs with penetration/aspiration at minimum 3 months following radio (chemotherapy). Fundamental frequency (F0), harmonics-to-noise ratio, jitter, shimmer and intensity (dB) will be examined before and after each swallow trial to report changes in vocal fold vibration with penetration/aspiration.

4. Aerodynamic features
Aerodynamic cough features measured using the peak expiratory flow rate (l/s) and the total expired volume (l) at baseline for healthy subjects and at minimum 3 months following radio (chemo)therapy for HNC-patients. The aerodynamic cough features will be correlated to the acoustic cough features.

Completion date
30/09/2023

Eligibility

Key inclusion criteria
1. Healthy volunteers
2. Head and neck cancer patients

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
71

Key exclusion criteria
Exclusion criteria for healthy volunteers:
1. Respiratory diseases
2. Dysphonia

Exclusion criteria for patients:
1. Respiratory disease

Date of first enrolment
04/01/2021

Date of final enrolment
15/09/2023

Locations

Countries of recruitment
Belgium

Study participating centre
Jules Bordet Institute
Rue Meylemeersch 90
Brussels
Belgium
1070

Study participating centre
Universitair Ziekenhuis Antwerpen
Drie Eikenstraat 655
Edegem
Belgium
2650

Sponsor information

Organisation
Institut Jules Bordet

ROR
https://ror.org/05e8s8534

Funder(s)

Funder type
University/education

Funder Name
Université Libre de Bruxelles, Department of Radiation Oncology

Alternative Name(s)
ULB

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Belgium

Funder Name
L'Association Jules Bordet

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analyzed during the current study are/will be available upon request from Sofiana Mootassim-Billah (sofiana.mootassim-billah@bordet.be) from 3 months after the overall trial end date (30/09/23).

1. Data controller of subject data
The sponsor (Institut Jules Bordet, Brussels, Belgium) is the data controller of the subject's encoded data. The protection of subject data and the related rights are guaranteed by the General Data Protection Regulation (European Regulation 2016/679), by the law of 22 August 2002 concerning subject rights in Belgium, by the law of 30 July 2018 concerning the data privacy in Belgium as well as any (new) applicable legislation in the participating countries.
All “personal data” are treated in accordance with data protection laws, including the General Data Protection Regulation (GDPR). Personal and clinical data related to our studies are stored on secured servers. Those servers protect data against loss, destruction, access, modification or dissemination by unauthorized persons. Only a limited and controlled number of persons are authorized to access the data.

To ensure compliance with GDPR, our IT Department has implemented the following set of measures: A rigorous policy of password management. Passwords must be at least 8 characters including numbers, letters, and special characters, and must be renewed after a maximum of 180 days. A procedure for the creation and deletion of user accounts. Access to the workstations and applications must be done using registered user accounts, and not “generic” (account1, compta2, etc.), in order to be able to trace the actions done on a file and empower all stakeholders. This rule is also applying to systems and network administrators of our organization.

A secure Local Area network.
Institut Jules Bordet network is secured against external attacks. Logical safety devices such as filter routers (ACLs), firewalls, intrusion probes, etc. ensure the first level of protection. Reliable protection against viruses and spyware is constantly updated, both on the server and on the user's workstations. Remote accesses to the information system are authenticated by the user and the post. Internet access to our tools needs to pass by strong security measures, including the use of IPsec, SSL/TLS, or HTTPS protocols.

Secured physical access to facilities.
Access to sensitive premises, such as rooms hosting computer servers and network components, is limited to authorized personnel. These premises are subject to special security: locked doors, digicode, and access controlled by name badges.

Anticipating the risk of loss or disclosure of data.
All of our servers are subject to regular backup. The backup media are stored in a fireproof safe room separated from the one that hosts the servers. An "emergency-rescue" procedure describes how to quickly reassemble these servers in the event of a major crash or disaster.

Information security policy.
All the rules related to computer security are formalized in a document (SOP) accessible to all users of our organization.

2. Subject identification
All data will be coded. A sequential identification number will be automatically allocated to each patient registered in the study. This number will identify the patient and must identify samples. In order to avoid identification errors, the patient's code (maximum of 4 alphanumerics) and date of birth will be recorded.

3. Consultation and use of encoded data
The encoded data can also be transmitted to service providers on the basis of contractual agreements. The subject's encoded data may be transmitted to regulatory bodies (including ethics committees) for regulatory purposes, for example for reporting relevant safety information, in order to receive marketing authorization or for discussions on the reimbursement and marketing of the drug being tested and diagnostic tests. Regulatory bodies may also use the encoded data to learn more about cancer and related health issues.

4. Storage of encoded data
Encoded data will be kept for at least 25 years after the end of the study. Subsequently, they may be kept for an additional period of time, for the above-mentioned scientific purposes or for any legal reason (change of obligations with regard to storage, for example).
Unencoded data can be consulted by the hospital investigator and other individuals who are working on the study or providing care to the subject. Individuals accessing the data are subject to professional secrecy. In addition, a limited number of the sponsor's employees, or its contractual partners, ethics committees, and regulatory authorities may consult the unencoded data, but solely to verify that the study is being conducted properly. These persons are bound by an obligation of confidentiality.

5. Informed consent
All patients will be informed about:
5.1. The aims of the study
5.2. Strict confidentiality of any patient data
5.3. Medical records possibly being reviewed for trial purposes by duly authorized individuals

The template of the patient's informed consent statement is given as a separate document dated and version controlled to this protocol. The translated informed consent documents will be submitted to ethics committees for approval. The competent ethics committee must approve the informed consent documents before starting the study. It is emphasized in the patient information sheet that participation is voluntary and that the patient is free to refuse further participation in the protocol whenever he/she wants to. This will not have any impact on the patient's subsequent care. The written informed consent form must be signed and personally dated by the patient or by the patient's legally acceptable representative.

6. Subject rights related to personal data
The subject may exercise the following rights related to his/her personal data:
6.1. Request information about the processing of data about him/her; however, he/she may not be able to access some data before the end of the study, without the risk of being excluded from the study. This measure may be necessary to protect the scientific integrity of the study.
6.2. Request the correction of the data about him/her if they are incorrect or incomplete. The subject has the right to restrict the processing of data about him/her.
6.3. Request the transfer of his/her personal data to himself/herself or to someone else in a commonly used format.
6.4. Withdraw his/her consent at any time without giving a reason. The subject also has the right to end his/her participation in the study by no longer coming, without having to justify himself /herself. However, this is not withdrawal in this case. Withdrawal means that the subject is actively withdrawing from the study and withdraws consent for data processing. This shall not affect the legality of processing data about him/her based on his/her consent given before withdrawal. However, after his/her withdrawal, data about him/her will no longer be collected.
6.5. At the same time as his/her withdrawal, the subject has the right to request the erasure of data about him/her if it is no longer necessary for the purposes of processing or if there is no other legal basis for further processing.
6.6. The subject also has the right to lodge a complaint concerning the way in which his/her data is processed with the supervisory authority responsible for ensuring compliance with data protection legislation in his/her country. If the subject wishes to exercise one of his/her rights relating to data about him/her, or if the subject wishes to know more about the measures to protect his/her personal data, he/she can send a request to the investigator or to the data protection officer of the study hospital.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		29/09/2023	02/10/2023	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes