

Voice related biomarkers focussing on glottal closure

Suggestion for a clinical protocol from the UEP Biomarker committee

Aim

To obtain (an) *objectively measured characteristic(s)* as an indicator of (faulty) *glottal closure*, *easy and handy* to administer, with a minimal intervention of a caregiver

Background

The voice is a multidimensional phenomenon and as such Dejonckere et al. has proposed an evaluation in 5-dimensions (Dejonckere, P., Bradley, P., Clemente, P. et al. A basic protocol for functional assessment of voice pathology, especially for investigating the efficacy of (phonosurgical) treatments and evaluating new assessment techniques . European Archives of Oto-Rhino-Laryngology 258, 77–82 (2001). <https://doi.org/10.1007/s004050000299>):

- **Perception:** the clinician/voice expert scores the voice quality according to one of the existing and validated rating scales, e.g. GRBAS(I), RBH, the Buffalo Voice Profile, IINFVo, ... of which the GRBAS is the most commonly used and preferred one (Webb AL, Carding PN, Deary IJ, MacKenzie K, Steen N, Wilson JA. The reliability of three perceptual evaluation scales for dysphonia. Eur Arch Otorhinolaryngol. 2004 Sep;261(8):429-34. doi: 10.1007/s00405-003-0707-7. Epub 2003 Nov 13. PMID: 14615893.). This perceptual rating is preferably performed on a text passage/running speech fragment.
- **Acoustics:** is an analysis of a voice signal/ voiced utterance -preferably a sustained open vowel, such as the vowel /a/- under standardized conditions (sound proof room, standardized source-microphone distance, quality microphone etc...). The acoustic analysis generates abundant results, of which F0, dB, NHR, Jitter, Shimmer... are the default parameters. Interesting is an observation reported by Dejonckere et al., regarding substitution voicing. The authors makes a distinction between voicing quantification and period perturbation parameters ad claim that in substitution voices voicing characteristics are more important than perturbation characteristics. (Dejonckere, P., Moerman, M., Martens, J.-P., Schoentgen, J., & Manfredi, C. (2012). Voicing quantification is more relevant than period perturbation in substitution voices: an advanced acoustical study. EUROPEAN ARCHIVES OF OTO-RHINO-LARYNGOLOGY, 269(4), 1205–1212. <https://doi.org/10.1007/s00405-011-1900-8>). Since substitution voicing usually also involves an insufficient closure, we assume/hypothesize that the same may apply for our objectives.

- Visualisation: videostroboscopy, high speed kymography, ... provides information about the glottal closure, the vibration pattern, etc.... A major disadvantage for our objectives is the need for a clinician performing this technical investigation.
- Aerodynamics: reveal information concerning the energy transfer required to get the vocal folds to vibrate. Important parameters are lung/vital capacity, subglottal pressure, the (trans)glottal flow, etc. However, measuring these one often has to rely on attributes or external devices (Rotenberg mask, spirometer, ...). Nowadays, inverse filtering of the acoustic voice signal seems a promising and handy alternative (Sopran, Aalto Aparat, Voice Clinical Systems- OnlineApp lab, ...)
- Self-assessment: this subjective rating is performed by the 'patient' him/herself, and reflects the personal experience of the voice quality. The most commonly used (disease specific QOL) questionnaires are the VHI, VHI-10, etc.

Side note: we must realize that except for acoustics and some of the aerodynamic measurements, none of these dimensions can be **objectively** measured

Towards a preliminary clinical protocol suggested by the UEP Biomarker committee

1st target population

Parkinson's disease, other neuromuscular disorders

The sample

- sustained open **vowel** /a/ on a comfortable loudness and pitch
- sustained vowel /a/ as loud as possible (but no shouting)
- sustained vowel /a/ as silent as possible (but no whisper)
- sustained vowel /a/ on the highest possible pitch (chest register- no singing)
- sustained vowel /a/ on the lowest possible pitch (chest register- no singing)
- **sentence** without fricatives (for Dutch "aan die bemiddeling willen we meedoen")
- phonetically balanced **text** passage (for Dutch "Papa en Marloes"; for German "Nordwind und Sonne"; for English "The Rainbow Passage", ...)

Aiming at a practical and easy accessible biomarker, recordings performed on pc or mobile phone by the 'patient' him/herself would be ideal. I Titze states that the influence of the internal noise of modern PCs is neglectable in perspective of the intra-individual variation (oral communication). Also smartphones appear to be a reliable alternative for voice recordings (Manfredi C, Lebacqz J, Cantarella G, Schoentgen J, Orlandi S, Bandini A, DeJonckere PH. Smartphones Offer New Opportunities in Clinical Voice Research. J Voice. 2017 Jan;31(1):111.e1-111.e7. doi: 10.1016/j.jvoice.2015.12.020. Epub 2016 Apr 7. PMID: 27068549.)

Important and easily accessible parameters with potential of leading to a biomarker for glottal closure

We suggest to keep **at least** the following parameters, considering their importance in the glottal closure:

- Perception: G & B from the GRBAS.
(In perspective of Voicing related parameters, the IINFVo perceptual rating scale might form an alternative (Moerman M, Martens JP, Crevier-Buchman L, de Haan E, Grand S, Tessier C, Woisard V, Dejonckere P. The INFVo perceptual rating scale for substitution voicing: development and reliability. Eur Arch Otorhinolaryngol. 2006 May;263(5):435-9. doi: 10.1007/s00405-005-1033-z. Epub 2006 Jan 11. PMID: 16404623.))
- Acoustics: NHR, Shimmer, dB, Voicing quantification parameters (What about: Fractal Dimension, Normalized Mutual Information – see presentation Ramon).
- Visualization: since this requires the intervention of a clinician, we ignore this for the moment. However, visualization of glottal closure can be used as a reference for the glottal insufficiency biomarker in a clinical trial.
- Aerodynamics: MPT. There is a need for further investigation (led by Ramon) of the added value of inverse filtering, for example the glottal closure quotient, the flow declination rate and to what extent this can reliably represent the glottal airflow characteristics (Sopran, Aalto Aparat). In addition, also the OnlineApp Lab tool and its glottal closure parameters is studied ('Biomechanical voice analysis').
- Self-assessment: it might be interesting to study which items of the VHI can specifically be linked to glottal closure/voicing. Other option: VAS scale – but how to formulate?
(In the appendix I have indicated in yellow the items that I **feel** tell something about glottal closure).

Next steps:

- examining the value of various *inverse filtering programs* -led by Ramon (Sopran, Aalto Aparat, ... OnlineApp Lab tool
- investigate which *VHI parameters* can specifically be linked to glottal insufficiency/voicing
- *putting the dimensions together*: come up with a way to link the different parameters each with its own weight (Alberto - AI?)
- *testing in practice*/clinical trials, with Parkinson's patients & other neuromuscular pathologies (Gavkhar? Valentina?)
- *The book* (Mette)