VENTICA® SYSTEM
– Technology and Clinical Studies

CLINICAL NEED & SOLUTION

Lung function testing is the accepted cornerstone of diagnosis and monitoring of asthma. Currently, however, there are virtually no testing methods suitable for young children.

The Ventica® System allows for reliable testing of lung function during natural sleep, at home. The system records tidal breathing flow-volume curves overnight for subsequent analysis of signs of asthma.

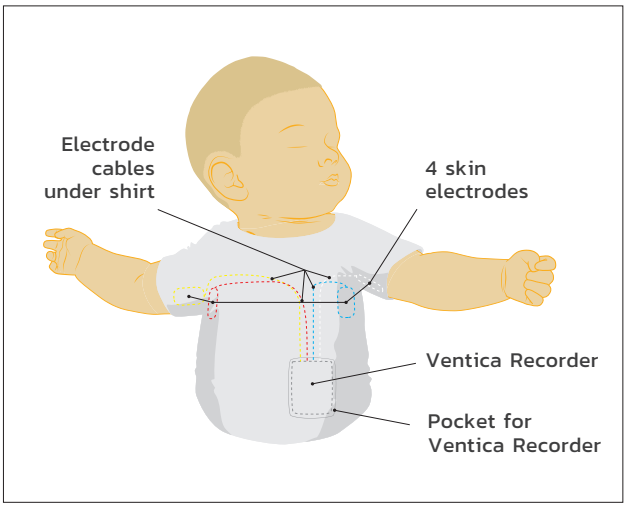

Figure 1. *Components of the Ventica® System*

TECHNICAL & PHYSIOLOGICAL BACKGROUND

Ventica® System is based on impedance pneumography, where changes in lung volume (breathing) are derived from changes in the electrical conductivity of lung tissues. The Ventica® System's proprietary algorithms convert the dynamic impedance signals into tidal breathing flow-volume curves[1].

Asthma is classically characterized by increased variability in lung mechanics (variable broncho-constriction)[2-5]. However, in tidal breathing patterns, bronchoconstriction causes *reduced* variability[6-11].

	Lung mechanics	Tidal breathing pattern
Healthy	Variability: **LOW**	Variability: **HIGH**
Asthma	Variability: **HIGH**	Variability: **LOW**

Based on proprietary analysis, the Ventica® System derives the subject's EVI (Expiratory Variability Index). EVI describes the nocturnal variability of tidal expiratory flow-volume curves.

EVI is based on:

1. Measurement of all flow-volume curves during a night's sleep.
2. Screening the data to exclude sections containing artifacts caused, e.g., by movement or coughing.
3. Averaging the curves and extracting the 15-45% range of expired volume.
4. Calculation of the correlations between all curves, and the inter-quartile range (IQR) of those correlations.

Thus, for a subject whose nocturnal expiration has high variability, the EVI is high (healthy). For low expiratory variability, the EVI is correspondingly low (obstructive). The Ventica® analysis is performed on the early phase of expiration (15-45% of expired volume) as this early phase has been found to exhibit the highest variability and best at distinguishing between healthy and asthmatics (unpublished data).

The first reference sample for EVI was acquired from a sample of 39 healthy children aged 1-5 years (NCT03551236), measured over two or three consecutive nights (80 night measurements in total).

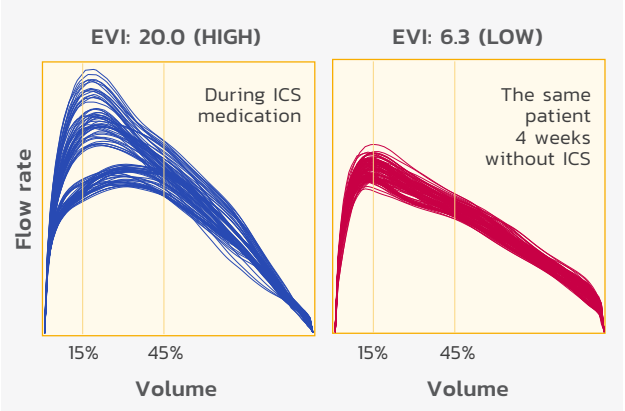

Figure 2. *Example expiratory flow-volume curves from the same 1y7m old child with recurrent wheeze as measured by Ventica®. Note the difference in curves while on ICS medication (left graph) and after 4 weeks off ICS medication (right graph). The patient's EVI was considerably higher when on medication.*

CLINICAL STUDIES

Technical validation (laboratory)

Studies have been performed validating the accuracy of the Ventica® indirect tidal flow signal measurement technology against direct pneumotachograph measurements:

- **Preschool children**[12] with wheeze measured during a methacholine challenge test
- **Infants**[13] with troublesome lung symptoms measured during methacholine challenge
- **Healthy adults**[14] during mechanical loading

A sensitive measure of asthma control (clinical setting)

70 patients, median age 2.5 years (range: 0.9–5.7 years) on ICS for three months due to at least three physician-witnessed acute lower airway obstructions were recruited (NCT02164968, Finland). Three overnight measurements were performed: at the end of the treatment period and at 2 and 4 weeks post-treatment. A control group of 39 healthy subjects, median age 4.3 years (range 1.5–6.0 years) was recruited and measured on 1–3 consecutive nights (NCT03551236, Croatia).

Calculated EVI was higher in the healthy controls than in patients with persistent wheeze, regardless of the status of their medication. Importantly, the patients with wheeze showed a further, significant decrease in EVI when taken off medication (p=0.007) at follow-up visits, 2 and 4 weeks later (see Figure 3).

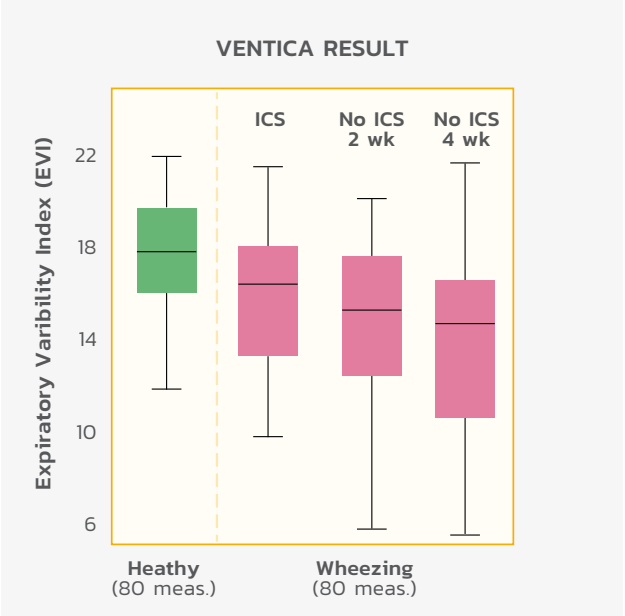

Figure 3. *Ventica®-calculated EVI results for children with recurrent wheeze on and off ICS vs. healthy controls.*

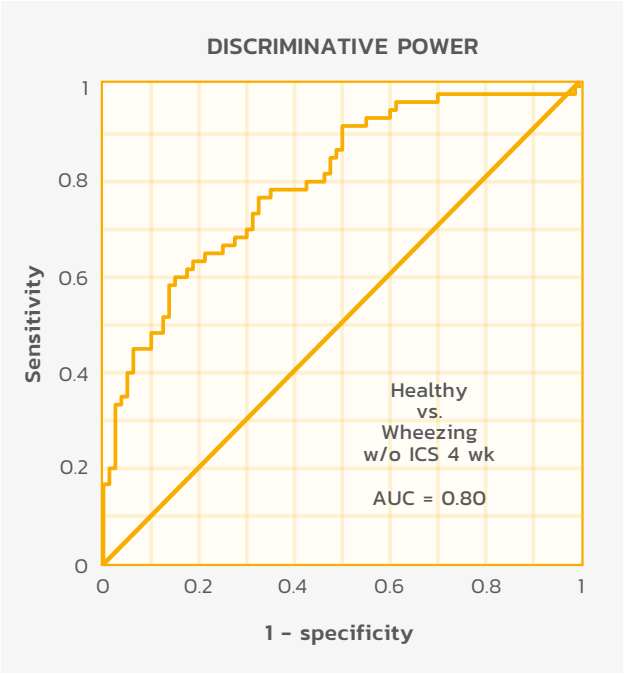

Figure 4. *Discriminative power of the Ventica® EVI algorithm.*

Overall, this clinical study highlights the value of Ventica® in assessing the level of asthma control in small children[15].

On-going studies:

- Ventica® in infants with different risk factors for persistent asthma (Finland)
- Comparing Ventica® with polysomnography in non-asthmatic preschoolers (NCT03408990, Croatia)
- Ventica® in preschool wheezers before and after starting ICS (NCT03377192, Finland)
- Ventica® in preschool wheezers during exacerbation and recovery (NCT03488303, Croatia)
- Ventica® in Pediatric Arm of DZL All-Age Asthma Cohort (ALLIANCE) (NCT02496468, Germany)

REFERENCES: **[1]** Seppä et al. Physiol Meas. 2011 **[2]** Troyanov S et al. Thorax 1994 **[3]** Que CL et al. J Appl Physiol 2001 **[4]** Lall CA et al. Eur Respir J 2007 **[5]** Czövek D et al. Thorax 2016 **[6]** Dames et al. Respir Physiol Neurobiol 2014 **[7]** Veiga. J Appl Physiol. 2011 **[8]** Frey. AJRCCM. 2017 **[9]** Hmeidi et al. Physiol Rep 2018 **[10]** Fouzas et al. J Appl Physiol 2017 **[11]** Usemann et al. J Pediatr 2018 **[12]** Seppä. J Appl Physiol. 2013 **[13]** Malmberg et al. Eur Respir J 2017 **[14]** Seppä et al. Proc IEEE EMBS 2013 **[15]** Seppä et al. ERS 2018 late-breaking abstract PA1299