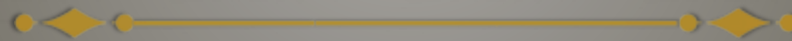


**Forced oscillation measurement technique
of pulmonary function:
An objective tool to assess respiratory
function in cattle**

From:
The Host-Pathogen Interaction Group
SLU/SVA



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BRSV: Continued losses due to disease: Vaccine development and refinement

Vaccine trials:

Hägglund et al: *Bovine respiratory syncytial virus ISCOMs - immunity, protection and safety in young conventional calves.*

Vaccine 2011

Safe and effective in the face of maternally-derived antibodies



Assessing protection vaccine provides?

Infection studies:

Reduction or absence of clinical disease (*ie: Ellis et al JAVMA 2011*).

✦ Clinical Scoring

- ✦ Fever, depression, dyspnea, tachypnea, abnormal lung sounds, nasal discharge, cough
- ✦ Most are subjective
- ✦ May not directly correlate to pulmonary disease

- ✦ Specific diagnostic sampling; *ie: chest X-ray, BAL/TTA lung biopsy/post mortem?*
- ✦ expensive, invasive, or unsuitable for serial sampling (*Pringle, Vet Clin NA Food Animal 1992 8:243.56*).

Vaccine development and refinement: Can we add objective markers of vaccine effect?

Hägglund et al: Bovine respiratory syncytial virus ISCOMs - immunity, protection and safety in young conventional calves. Vaccine 2011

Safe and effective in the face of maternally derived antibodies

Hypothesis: Clinical scores in experimental infection correlate to measurements of changes in pulmonary function in calves



Forced Oscillation: Background

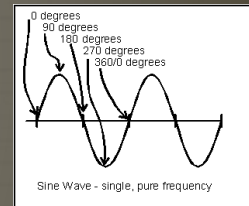
From Dubois
et al J Appl
Physiol 1956

✦ Sign wave of short pressure wave onto normal breathing-loudspeaker.

✦ Measure: (mathematically)

✦ Change in volume, versus pressure = resistance (R_s)

✦ Delay - compliance, elasticity; inertance reactance (X)



Forced Oscillometry in Large animals

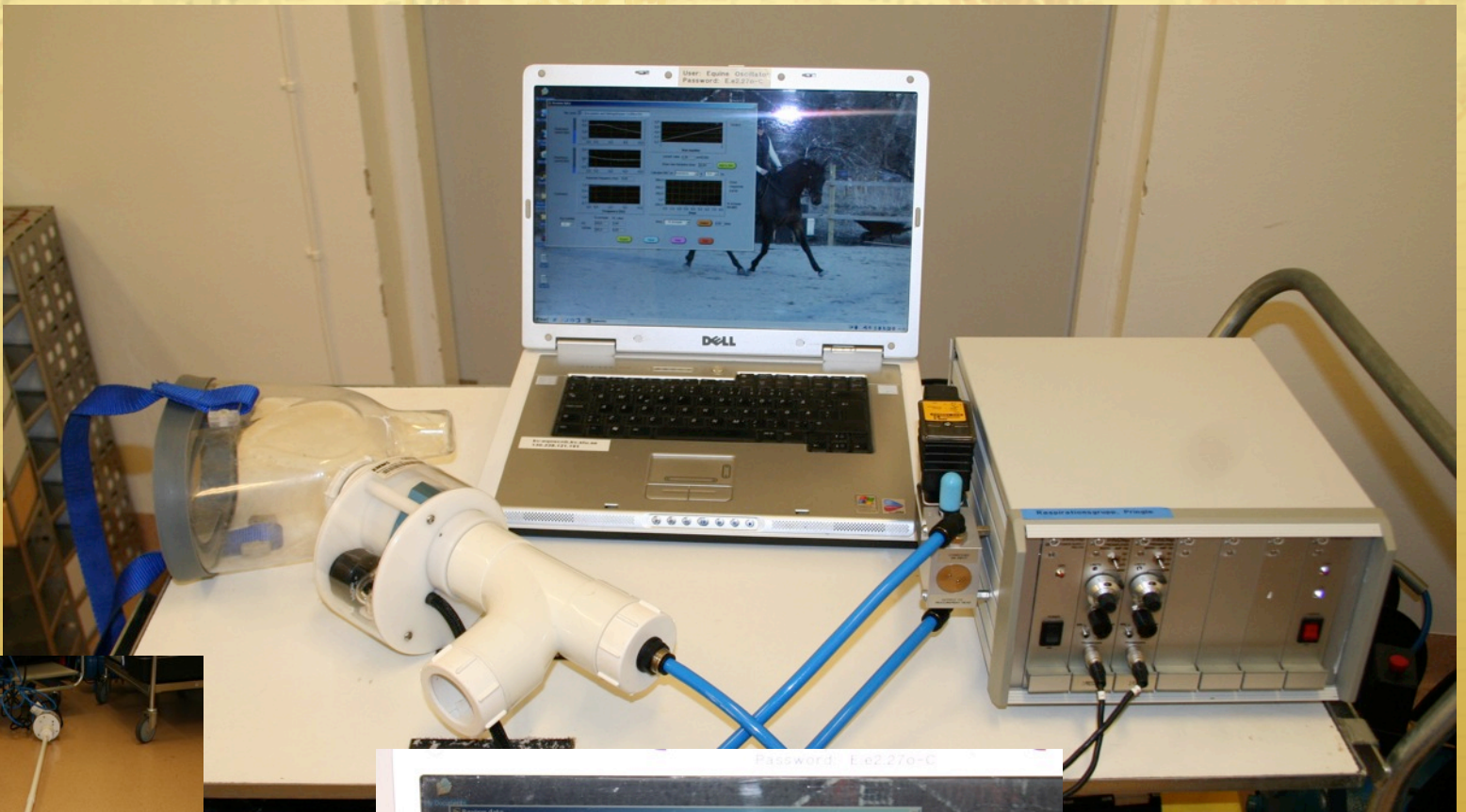


- ✦ Young & Hall: A rapid noninvasive method for measuring total respiratory impedance in the horse. Eq Vet J 1989
- ✦ Reinholt et al. Calves. Res Vet Sci. 1996 , Jaeger et al Vet Res 2007
 - ✦ Test frequency < 10Hz, carbachol and fenoterol, *Chlamydomphila*

Materials:

- ✦ Measurement head: calf adapted
 - ✦ EMMS Bordon, Hants UK GU35 9QF
 - ✦ www.electromedsys.com (EquineOscillation system vers 2.27)
- ✦ Face mask: Aeromask Trudell Medical International London Canada





Experimental protocol:

20 Swedish R&W, Holstein calves 3-8 weeks old:
grouped according to age and IgG to BRSV

Calf group: vaccine N= 5/group	Challenge infection (Day 0; 2 weeks after second vaccination)	Day 6 post-infection
PBS	Pulmonary function, aerosolize BRSV	Pulmonary function, sampling, full necropsy
BRSV protein	“ ”	“ ”
Adjuvant	“ ”	“ ”
BRSV-ISCOM	“ ”	“ ”

FOT portion in protocol

- ✦ Sampling: 3, 5, 7 & 10 Hz, Repeated 2 or 3 times
- ✦ Coherence: signal to noise) > 0.9 (mean 0.97)
- ✦ If cough, breath holding, vocalization: discard readings.

- ✦ Data analysis: Nonparametric: Wilcoxon ranked sign, two way testing - Each calf own control.

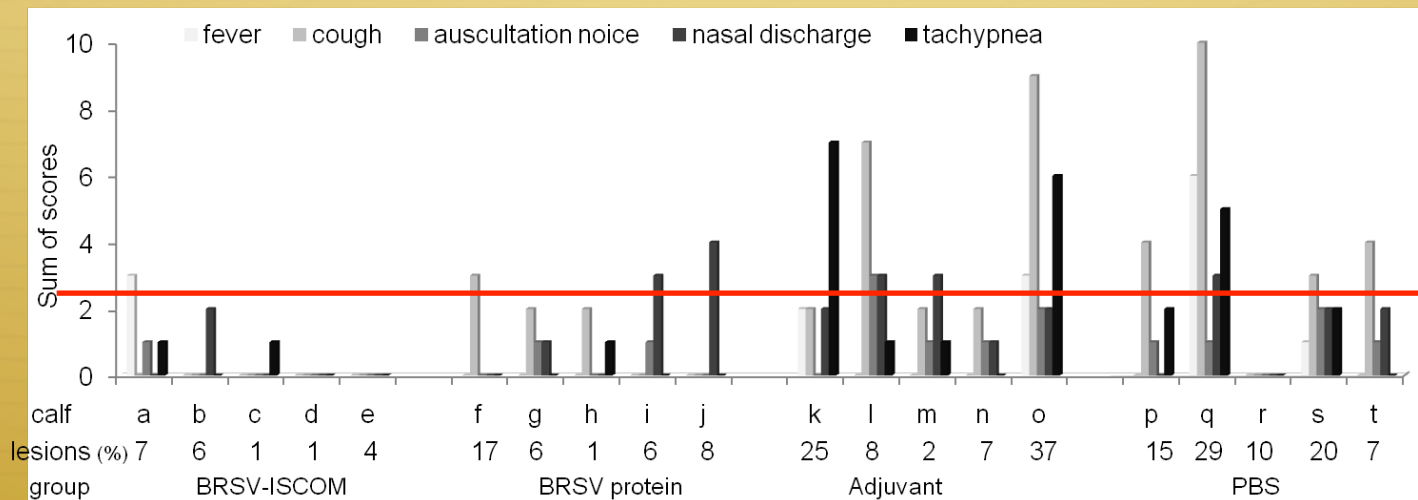
- ✦ **Hypothesis:** Clinical scores in viral infected calves correlate to FOT measurements indicative of impaired pulmonary function

Results: Pre-versus post infection: Resistance & Reactance (X) 3-10 Hz

PBS	P= 0.13- 0.81
Adjuvant	P=0.13-0.63
BRSV protein	P=0.06-0.44 (trend increased resistance 3&5 Hz)
BRSV & ISCOM	P= 0.11-0.88

Large SD: variation within calves. All groups showed frequency dependence of resistance, indicating lung function impairment. N=5/group

Results: Pre-versus post infection: Resistance & reactance (X) 3-10 Hz : Clinical score: lung sounds & hyperpnea



Score	Fever (°C)	Cough	Auscultation noise	Nasal discharge	Tachypnea (breaths/min)
0	≤ 39,5	no cough observed	No abnormal sounds noticed upon lung auscultation	normal nasal discharge	<49
1	39,6-39,9	only cough on compression of trachea	wheezing sounds noticed upon lung auscultation	serous and/or very little mucopurulent nasal discharge	50-54
2	40-40,4	spontaneous cough during 20 min observation		moderate mucopurulent nasal discharge	55-64
3	40,5-40,9			severe mucopurulent nasal discharge	65-74
4	>40,9				75-85



Clinical score compared to function:

Clinical score	Hz		Pre infection (cmH ₂ O/L/s)	Post infection Pre infection (cmH ₂ O/L/s)	P=
High clinical score (n=10)	3	Resistance (Rs)	2.6±0.5	4.6± 2.7	0.04
	5	Reactance (X)	0.28±0.18	-0.18±0.68	0.06
Low clinical score (includes 4/5in ISCOM group)	10	Reactance (X)	0.05±0.24	0.23±0.32	<u>0.06</u>

Two tailed Wilcoxon signed rank
No posthoc correction

Interpretation:

Increased Rs at low frequency: lung periphery, deeper, smaller airways

Decreased reactance (X): stiffer lungs



Conclusion:

◀ Pilot study ▶

FOT measures appeared to correlate to clinical score severity in calves with viral respiratory disease

FOT in calves has potential to provide quantitative serial noninvasive measures to assist in evaluation of clinical efficacy of respiratory vaccines.

✦ Supported by SLF and FORMAS



Principles of FOT

- ✦ Small amplitude pressure oscillations
- ✦ Force specific waveforms, Superimpose on normal breathing. Analyse the mechanical response of the respiratory system.
- ✦ Measure: pressure and flow changes
- ✦ Noninvasive, free from performing breathing maneuvers (no patient assistance!)
- ✦ Obtain
 - ✦ resistance/resistive properties of airways
 - ✦ Reactance: inertive and capacitive (elastic)

Oostveen et al, ERS
task force Eur Respir
J 2003

