Innocor®

LUNG CLEARANCE INDEX METHOD

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1 LUNG CLEARANCE INDEX METHOD

1.1 SCOPE

The purpose of this document is to give an introduction to the Lung Clearance Index (LCI) Method used in Innocor. This section applies to users of Innocor with only limited experience in LCI measurements. This document will enable the reader to understand the LCI parameters measured by Innocor and the way they are determined.

For more detailed information about the LCI method, please contact Innovision A/S or consult the “Pulmonary Function testing in Preschool Children” in:

Am J Respir Crit Care Med Vol 175. pp 1328-1333	Section 7 – The Multiple-Breath Inert Gas washout Technique - of An Official American Thoracic Society / European Respiratory Society Statement: Pulmonary Function testing in Preschool Children.

1.2 INTRODUCTION

LCI is a physiological test that measures ventilation distribution in the lungs and the Functional Residual Capacity.

Spirometry is the commonest means of assessing lung function where diseases causing obstruction of larger airways eventually result in reduced expiratory flows and volumes. However, spirometry measurements are often normal in the early stages of peripheral airway diseases, and therefore changes (obstruction or restriction) in the peripheral airways associated with early cystic fibrosis disease, early chronic obstructive pulmonary disease or mild asthma cannot be detected by spirometry until the disease has progressed considerably because the small airways only contribute very little to the total airway resistance.

Peripheral airway diseases do, however, affect the way air mixes within the lungs and thus lead to increased ventilation inhomogeneity. Ventilation inhomogeneity may be assessed using the multiple-breath washout (MBW) test performed by washing out a previously washed-in tracer gas from the lungs during tidal breathing of room air. From this test Lung Clearance Index (LCI) can be determined as a sensitive marker of airway disease. It reflects differences in specific ventilation between well and poorly ventilated lung regions.

The LCI manoeuvre starts with normal tidal breathing during an Inert gas rebreathing (IGR) for rapid wash-in of a small amount of SF_6. When an even concentration is obtained in the lungs the subject is disconnected from the bag and the multiple-breath washout starts. The subject breathes room air until the end-tidal SF_6 concentration has fallen below 1/40th of the starting concentration.

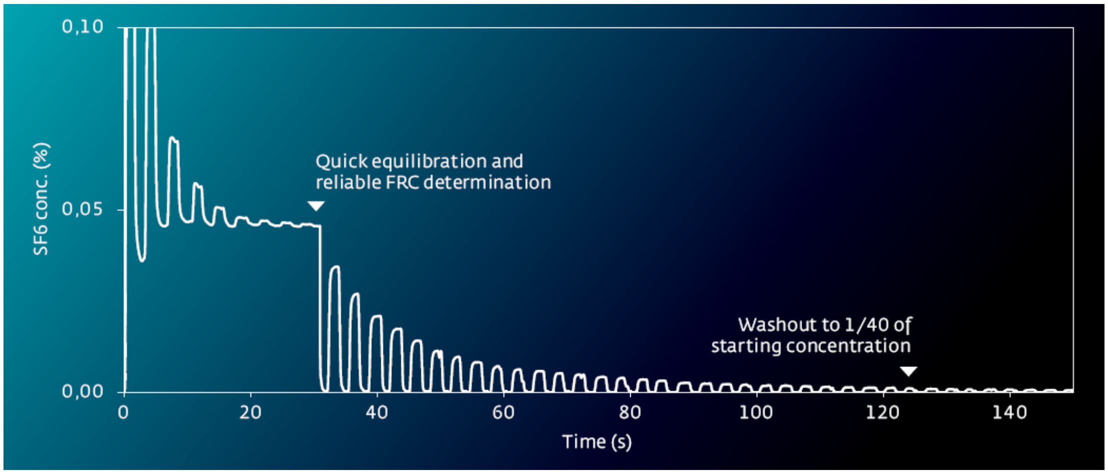


Figure 1.2–1 LCI manoeuvre.

1.3 LCI PARAMETERS

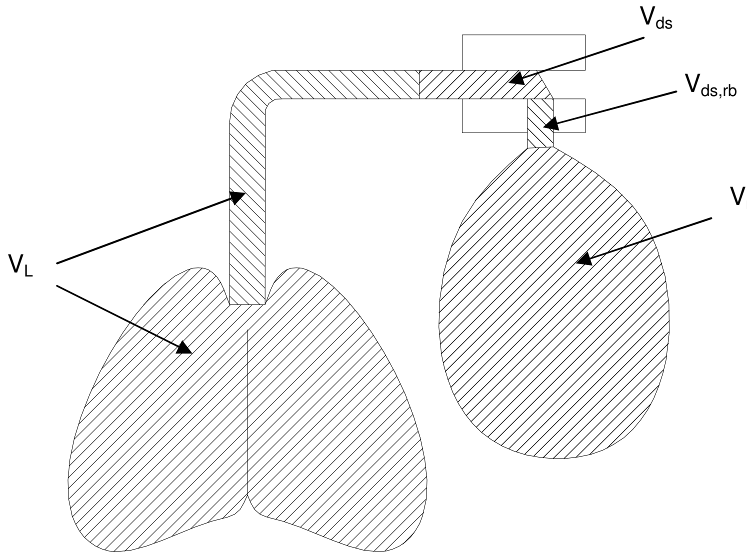
The LCI parameters measured by the Innocor are:

Abbreviation	Name	Unit
FRC	Functional Residual Capacity	L [BTPS]
LCI	Lung Clearance Index	

1.4 CALCULATION OF FRC

Calculation of the Functional Residual Capacity is based on a single-alveolar lung model.

1.4.1 Total systemic volume (Vs,tot)



Inert gas rebreathing allows the total systemic volume to be determined with high accuracy.

Figure 1.4.1-1 Systemic volumes.

The total systemic volume is defined as:

$$V_{s,tot} = V_L + V_{ds} + V_{ds,rb} + V_{rb}$$

where

V_L = Lung volume at the end of an expiration
V_{ds} = Dead space volume of rebreathing valve (RVU)
$V_{ds,rb}$ = Residual volume of bag when empty
V_{rb} = Volume of rebreathing bag

During the rebreathing / wash-in period the concentration of insoluble gas (SF_6) decreases from the initial value in the bag (F_i^0) to a final equilibrium ($F_{i,eq}$) value practically obtained after approximately 10 breaths (figure 1.4.1-2). Since the volume of the rebreathing bag is known, the total systemic volume can be determined simply from the dilution of the insoluble gas.

A typical SF_6 curve from a rebreathing / wash-in manoeuvre is shown in figure 1.4.1-2.

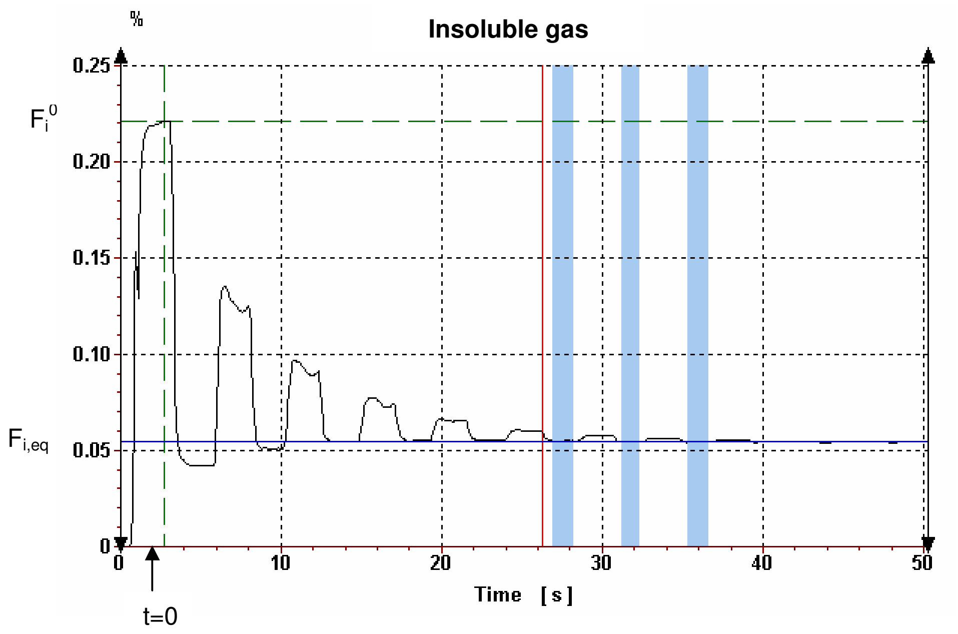


Figure 1.4.1-2 Insoluble gas concentration during rebreathing.

The total systemic volume is not constant during a rebreathing and wash-in manoeuvre. Initially the volume increases due to a constant oxygen uptake and an increased excretion of carbon dioxide. As the carbon dioxide quickly builds up in the lungs and bag, the gradient between the alveolar and capillary (mixed venous) CO_2 concentrations falls. This decreases the carbon dioxide excretion. The oxygen uptake is still constant. The result is therefore shrinkage in the total systemic volume.

The total systemic volume, referred to in this document, is the volume at the time “zero”. Time “zero” is defined as the middle of the first inspiration. This volume is difficult to measure directly since the volume measurements require the insoluble gas to be perfectly mixed. At the time zero this is not the case. Therefore the volume is determined by back extrapolation by drawing a straight line through the expiratory points of the insoluble gas where adequate mixing is obtained. The insoluble gas concentration at time “zero” is then determined as the point where the extrapolated line crosses time “zero” - see figure 1.4.1-2 ($F_{i,eq}$).

The total systemic volume at time “zero” is calculated using the following formula:

$$V_{s,tot} = \frac{F_i^0}{F_{i,eq}} \cdot V_{rb}$$

where

$V_{s,tot}$ = Total systemic volume
F_i^0 = Initial concentration of insoluble gas in the rebreathing bag
$F_{i,eq}$ = Equilibrium concentration of insoluble gas (back extrapolated to t = 0)

Example: Total systemic volume

How to calculate the total systemic volume from the data in figure 1.4.1-2:

The following data is assumed:

V_{RB} = 1.0 l
P_B = 763 mmHg
t_a = 23 °C
RH = 24%

Data from figure 1.4.1-2:

Initial concentration of SF_6 in the rebreathing bag, F_i^0 = 0.221%
Equilibrium concentration of SF_6, $F_{i,eq}$ = 0.056% (back extrapolated to t = 0)

The total systemic volume can now be calculated:

$$V_{s,tot}(ATP) = \frac{F_i^0}{F_{i,eq}} \cdot V_{RB}(ATP)$$

where

ATP = Ambient temperature, pressure and humidity

Example:

$$V_{s,tot}(ATP) = \frac{0.221}{0.056} \cdot 1.0 \ l = 3.95 \ l$$

The $V_{s,tot}$ is converted to STPD (see section 1.6.3) for further calculations:

$$V_{s,tot}(STPD) = \frac{273}{273 + t_a} \cdot \frac{P_B - \frac{RH}{100\%} \cdot P_{H2O}(t_a)}{760} \cdot V_{s,tot}(ATP)$$

Example:

$$V_{s,tot}(STPD) = \frac{273}{273 + 23} \cdot \frac{763 - \frac{24}{100} \cdot 21.1}{760} \cdot 3.95 \ l = 3.63 \ l$$

1.4.2 Functional Residual Capacity (FRC)

The Functional Residual Capacity (FRC) is defined as the gas volume in the lungs at the end of expiration.

The FRC can be determined by the equation from section 1.4.1:

$$FRC = V_{s,tot} - (V_{rb} + V_{ds,rb} + V_{ds})$$

When BTPS, STP and STPD conditions are used the equation becomes:

$$FRC(BTPS) = [V_{s,tot}(STPD) - (V_{rb}(ATP) + V_{ds,rb}(ATP)) \cdot C_1] \cdot C_2 - V_{ds}(BTPS)$$

where

$V_{s,tot}$ = Total systemic volume, STPD
V_{rb} = Volume of rebreathing bag, ATP
V_{ds} = Dead space volume of rebreathing valve (RVU), BTPS (containing expired air)
$V_{ds,bag}$ = Residual volume of bag when empty, ATP
C_1 = Conversion from ATP to STPD, see section 1.6.3.
C_2 = Conversion from STPD to BTPS, see section 1.6.3.

Example:

$V_{s,tot}$(STPD) = 3.63 l
V_{rb}(ATP) = 1.0 l
$V_{ds,rb}$(ATP) = 0.013 l
V_{ds}(BTPS) = 0.102 l
P_B = 760 mmHg
t_a = 23 ℃
RH = 24%

$$C_1 = \frac{273}{273+23} \cdot \frac{763 - \frac{24}{100} \cdot 21.1}{760} = 0.916$$

$$C_2 = \frac{273+37}{273} \cdot \frac{760}{763-47} = 1.205$$

$$FRC(BTPS) = (3.63 - (1.0+0.013) \cdot 0.916) \cdot 1.205 - 0.102 \text{ l} = 3.16 \text{ l}$$

Alternatively, FRC can be determined in the conventional way from the washout phase using breath-by-breath calculations on SF_6.

1.5 CALCULATION OF LCI

The LCI is calculated as:

$$LCI = \frac{V_{CE}}{FRC}$$

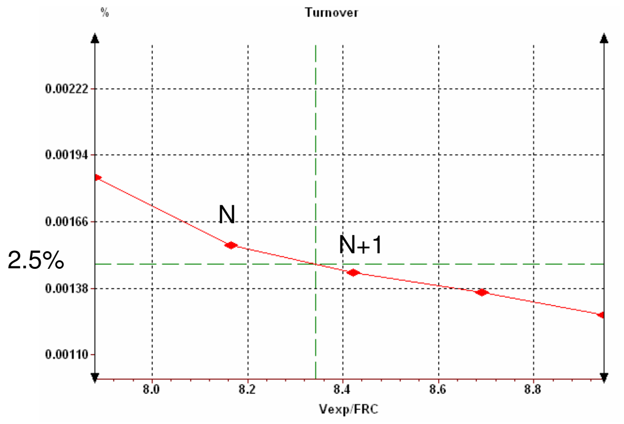
where V_{CE} is the cumulative *net* volume expired during the multi -breath washout – see below.

V_{CE} is the cumulative *net* (i.e. corrected for equipment dead space) volume expired (i.e. the sum of tidal volumes) during the multi-breath washout.
The V_{CE} is calculated as:

$$V_{CE} = \sum_{n=1}^{N} (V_T(n) - V_{DS}) + \frac{\text{Cet(N)}/\text{Cet(Start)} - 1/40}{\text{Cet(N)}/\text{Cet(Start)} - \text{Cet(N+1)}/\text{Cet(Start)}} (V_T(N+1) - V_{DS})$$

where

n = breath after start of multi-breath washout.
N = last breath where end tidal inert marker gas is above 1/40th of the starting concentration Cet(start).
N+1 = first breath where end tidal inert marker gas is below 1/40th of the starting concentration. (Cet(N+2) and Cet(N+3) must also be below 1/40th).
$V_T(n)$ = tidal volume of breath n.
V_{DS} = equipment dead space.
Cet(n) = End tidal concentration of breath n



Example:

FRC(BTPS) = 3.16 l

VCE(BTPS) = 25.9 l

$$\text{LCI} = \frac{25.9}{3.16} = 8.20$$

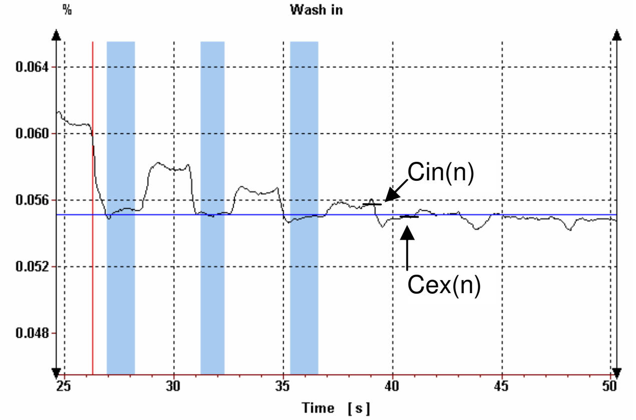
1.6 LCI EVALUATION AND RESULTS

1.6.1 LCI test acceptance

A manoeuvre is correctly performed when:

- The deviation (x) between the inspiratory and expiratory concentration of the inert marker gas is less than 2% relative at the end of the wash-in.

$$X = \frac{\text{Cin}(n) - \text{Cex}(n)}{(\text{Cin}(n) + \text{Cex}(n)) \bullet ½}$$



- The end tidal concentration of the inert marker gas is below 1/40th of the starting concentration over three subsequent breaths.

Based on minimum 2 correctly performed manoeuvres, an acceptable repeatability is achieved when the difference between two FRC determinations is less than 10% (in relation to the lower).

As default all manoeuvres with FRC within ±4.88% (which corresponds to 10% in relation to the lower) are marked as acceptable.

1.6.2 LCI results

The results are summarised as:

- The average FRC found in the accepted manoeuvres is recorded.
- The average LCI found in the accepted manoeuvres is recorded.

1.6.3 Conversion between ATP, STPD and BTPS

The volume of a number of moles (n) of gas molecules depends on the thermodynamic temperature (T) and the ambient pressure (P). The following relationship holds for dry gas:

$$V = n \cdot R \cdot T/P$$

where R = gas constant, and T is expressed in Kelvin (T(K) = 273.2 + t(ºC)).
Air and expired gas are made up of gas molecules and water vapour. In a gas mixture saturated with water vapour and in contact with water (such as occurs in the lung) the number of water molecules in the gas phase varies with temperature and pressure. As the number of molecules is not constant, the above gas law should be applied to dry gas. This also holds outside the lung when gas saturated with water vapour is compressed or cools down.

BTPS:	In respiratory physiology lung volumes and flows are standardised to barometric pressure at sea level, body temperature, saturated with water vapour: body temperature and pressure, saturated.
ATPS:	Measured at ambient temperature, pressure, saturated with water vapour (e.g. expired gas, which has cooled down): ambient temperature and pressure, saturated.
ATP:	Like ATPS, but not saturated with water vapour (e.g. room air).
ATPD:	Like ATPS, but dry (e.g. from a gas bottle).
STPD:	Oxygen consumption and carbon dioxide excretion are standardised to standard temperature (0 ºC), barometric pressure at sea level (101.3 kPa / 760 mmHg) and dry gas: standard temperature and pressure, dry.

Correction from ATP to STPD. Multiply the ATP-value by:

$$C_1 = \frac{273}{273 + t_a} \cdot \frac{P_B - \frac{RH}{100} \cdot P_{H2O}(t_a)}{760}$$

Correction from BTPS to STPD. Multiply the BTPS-value by:

$$C_2 = \frac{273}{273 + 37} \cdot \frac{P_B - 47}{760}$$

where

t_a = ambient temperature in °C
P_B = barometric pressure in mmHg
RH = relative humidity in %
$P_{H2O}(t_a)$ = saturated water vapour pressure in mmHg at temperature t_a, see table below

Temperature [°C]	Water vapour pressure [mmHg]
0	4.7
1	5.2
2	5.6
3	6.1
4	6.5
5	7.0
6	7.4
7	7.9
8	8.3
9	8.8
10	9.2
11	9.8
12	10.5
13	11.2
14	12.0
15	12.8
16	13.6
17	14.5
18	15.5
19	16.5
20	17.5
21	18.7
22	19.8
23	21.1
24	22.4
25	23.8
26	25.2
27	26.7
28	28.3
29	30.0
30	31.8
31	33.7
32	35.7
33	37.7
34	39.9
35	42.2
36	44.6
37	47.1
38	49.7
39	52.4
40	55.3