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Review article

What can we learn about COPD from impulse oscillometry?

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ABSTRACT

Impulse oscillometry (IOS) is the most commonly used type of forced oscillation technique in clinical practice, although relatively little is known about its application in COPD. Resistance at 20 Hz (R20) is unrelated to COPD severity and does not improve with bronchodilatation or bronchoconstriction, inferring a lack of large airway involvement in COPD. Peripheral airway resistance expressed as frequency dependent heterogeneity between 5 Hz and 20 Hz (R5-R20), and peripheral airway compliance as area under the reactance curve (AX), are both closely related to COPD severity and exacerbations. Both R5-R20 and AX markedly improve in response to long acting bronchodilators, while AX appears to be more sensitive than R5-R20 in response to bronchoconstriction.

Future studies may be directed to assess if IOS in combination with spirometry is more sensitive at predicting future exacerbations. Perhaps AX might also be useful as a screening tool in early stage disease or to monitor long term decline in COPD.

1. Background

Current COPD guidelines advocate using spirometry to assess airflow limitation in conjunction with symptoms and exacerbation history [1]. Spirometry involves a forced expiratory manoeuvre to measure dynamic lung volumes and expiratory flow. It has no comparable manoeuvre in real life, and hence is an artificial action. Cooperation may be difficult especially in patients who are breathless or susceptible to coughing. The forced expiratory flow between 25 and 75% (FEF25-75) of forced vital capacity (FVC) is thought to represent dynamic volume dependent small airway closure, but has marked inherent variability. Hence there is an unmet need for an alternative more patient friendly method to assess lung function in patients with COPD.

The forced mono-frequency oscillation technique (FOT) was first described in 1956 by Dubois [2]. Since then several FOT methods have been developed, of which impulse oscillometry (IOS) is most commonly used in every day clinical practice. The application of IOS has been extensively described in asthma [3]. The purpose of this article is to critically appraise the potential role of IOS in COPD, where much less is known. It will focus on the more clinical applications of IOS, as this appertains to the general pulmonologist. This review will therefore not detail the physics of IOS or other FOT methods which have been covered elsewhere [4–6].

2. Basic principles of impulse oscillometry

The currently used method of IOS was originally detailed in 1976 by Michaelson [7] and was then commercialised in 1998 [8], available as the Jaeger Masterscreen IOS (Hoechberg,Germany). It has been widely adopted in paediatric pulmonology, but less so for adults, aside as a research tool. IOS propagates a train of bi-directional, harmonic sound waves along the bronchial tree, from a source such as a loudspeaker. The oscillations are applied at a fixed square wave frequency of 5 Hz, from which all other frequencies of interest are derived, typically multiples of 5 Hz (between 5 and 35Hz) [9], each impulse lasting between 30 and 40 ms. Measurements are made via a conducting tube to a mouthpiece with the cheeks held to obviate upper airway shunting. Forced oscillations are superimposed on top of tidal breathing to assess the frequency (Hz) dependence of the pressure/flow (as kPa/L/s or $cmH_2O/L/s$) relationship of respiratory impedance (Z), as in phase resistance (R) and out of phase reactance (X) components. A transducer attached to a pneumotachograph measures inspiratory and expiratory flow and pressure with signal filtering used to separate breathing patterns from pressure and flow. It is performed using normal tidal breathing over a period of around 30–40s, and being effort independent is more physiological than spirometry. Conventionally the mean of whole breath values are used rather than separate inspiratory and expiratory moieties. As in spirometry three technically acceptable IOS manoeuvres are used.

In essence, IOS can be considered as bronchial sonar. Higher frequency waves travel shorter distances typically reflecting larger airways. Thus the resistance at 20 Hz (R20) represents proximal resistance. Lower frequency waves travel further reaching the smaller airways < 2 mm in diameter after the eighth generation. Hence the

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Abbreviations

AX	Area under reactance curve between 5 Hz and resonant frequency
COPD	Chronic obstructive pulmonary disease
FEF25-75	Forced expiratory flow between 25 and 75%
FEV1	Forced expiratory volume in 1 s
FVC	Forced vital capacity
FOT	Forced oscillation technique
Fres	Resonant Frequency
GOLD	Global Initiative for Chronic Obstructive Lung Disease
HRCT	High resolution CT scanning
IOS	Impulse oscillometry
R	Resistance
R5	Resistance at 5 Hz
R20	Resistance at 20 Hz
R5-R20	Heterogeneity of resistance
SRM	Standardised response mean
X	Reactance
X5	Reactance at 5 Hz
Z	Impedance

resistance at 5 Hz (R5) represents the total lung resistance. COPD and asthma will increase total resistance (R5) to a relatively greater degree than proximal resistance (R20). This is known as a frequency dependent change or heterogeneity of resistance evident as raised peripheral resistance (R5-R20). Nonetheless, further validation is required to characterise heterogeneity of resistance and its relationship to the calibre of small and large airways.

Reactance can be considered as the out of phase component of respiratory impedance (with flow, but not volume), reflecting the balance between inertial and elastic properties of distensible airways. Typically this is measured at 5 Hz (X5) or as the area under the reactance curve (AX) between 5 Hz and the resonant frequency (RF), the latter representing the point at which opposing inertial and capacitive components cancel each other out. Conventionally AX is reported as a positive value for the area under the curve, even though in reality reactance per se becomes more negative (Fig. 1). AX represents low frequency reactance in smaller airways where elastance exceeds inertance, with increased values reflecting reduced lung compliance and stiffer lungs (Table 1). In asthma resistance and reactance tend to change in proportionate fashion, while in COPD reactance usually alters to a relatively greater degree than resistance.

IOS therefore provides more detailed information than spirometry on regional lung function and should be considered as being complementary to spirometry to comprehensively assess lung function in COPD. For example in patients with persistent asthma who had a preserved FEV1, the combined use of R5-R20 with FEF25-75 is more predictive of impaired long term asthma control than either parameter used alone [10]. Although there are no defined reference values for COPD, we would propose pragmatic IOS cut offs for R5 > 0.5 kPa/L/s (> 5.1 $cmH_2O/L/s$), R5-20 > 0.10 kPa/L/s (1.02 $cmH_2O/L/s$), AX > 1.0 kPa/L (> 10.2 cmH_2O/L) as being pathologically abnormal [11,12]. Further cohort based studies are required to define proper reference values for COPD and asthma.

3. Relationship of IOS to disease severity

The largest database involving IOS was the ECLIPSE cohort comprising 2054 patients with COPD (GOLD stage 2–4) and 233 healthy controls, in whom high resolution CT scanning (HRCT) was also performed [11]. R20 values were similar across GOLD stages 2–4 (0.29, 0.31, 0.31 kPa/L/s), but higher than controls (0.26 kPa/L/s). In contrast R5-R20 increased proportionately from GOLD stage 2–4 (0.15, 0.20, 0.24 kPa/L/s), compared to controls (0.07 kPa/L/s). This, in turn, suggests that smaller rather than larger airways are the main determinant of increased lung resistance.

For AX there were increasing values across GOLD stages 2–4 (1.37, 2.25, 3.23 kPa/L) which were also higher than controls (0.38 kPa/L) along with a similar pattern for X5. Comparing GOLD 2 versus 4, equated to a 136% difference in AX and 60% in R5-20. Hence increased reactance (i.e. reduced compliance) predominates over increased resistance in relation to increasing COPD severity. There was a poor degree of correlation between R5-R20 or AX and HRCT low attenuation, inferring that the degree of emphysema is not closely related to either resistance or compliance.

In a cohort of 215 patients GOLD stages 1–4, values for AX (0.66,1.43,2.07, 2.5 kPa/L) mirrored the ratio of residual volume to total lung capacity (RV/TLC) (45.7,51.2,58.1,66.0%), inferring the degree of air trapping is related to reduced lung compliance [12]. Studies have also shown a relationship between increasing AX and exacerbation frequency in COPD [11,12]. A cross sectional evaluation of 94 COPD patients with moderate COPD revealed the strongest relationships for X5 in relation to FEV1 and specific airway conductance [13]. Multiple regression analysis of 75 patients with moderate COPD found that R5-R20 and X5 but not R20 were more closely related to health status and symptoms than either FEV1 or HRCT low attenuation [14]. In a screening study to detect early COPD, among 124 subjects who had positive spirometry criteria, the presence of self reported symptoms was associated with higher values of R5-R20, X5 and AX [15].

A comparison of 36 asthma patients, 24 COPD patients and 24 healthy subjects showed values for R5-R20 and X5 in severe asthma of 0.13 kPa/L/s and −0.18 kPa/L/s respectively; in moderate COPD 0.22 kPa/L/s and X5 -0.27 kPa/L; and in controls 0.01 kPa/L/s and −0.12 kPa/L/s [16]. Thus, patients with COPD have a relatively higher level of peripheral airway dysfunction compared to those with asthma in respect of both resistance and reactance. This is in keeping with pathological and radiological changes seen in small airways associated with disease progression in COPD [17,18].

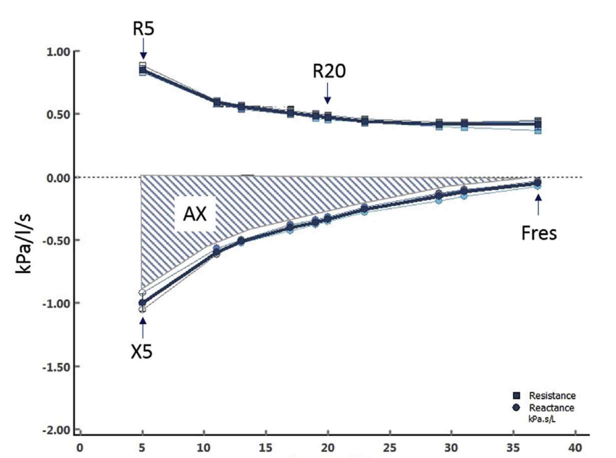

Fig. 1. 67 year old female, ex-smoker; COPD; BMI 23, FEV1 0.56L (31% predicted). Values are as follows: Resistance at 5Hz (R5) 0.85 kPa/l/s; Resistance at 20Hz (R20) 0.47 kPa/l/s; Heterogeneity of resistance between 5 and 20Hz (R5-R20) 0.38 kPa/l/s; Reactance at 5Hz (X5) -1.00 kPa/l/s; Area under the curve reactance (AX) 11.71 kPa/l; Resonant frequency (Fres) 37.5Hz .Measured with airwave oscillometry (Thorasys Tremoflo, Monteral, Canada).