

define the effects of obesity on oscillometric parameters in overweight and obese children. In both adults and children, it remains unclear how oscillometry data in obesity will contribute to clinical diagnosis and management.

### Restrictive diseases

The clinical application of oscillometry in restrictive lung disease is less established in comparison to obstructive disease. Most oscillometric studies of restrictive lung diseases have investigated interstitial lung disease (ILD). Although ILD and obstructive lung diseases are clinically distinct, their corresponding  $Z_{rs}$  spectra demonstrate similar patterns of abnormalities, perhaps due to the higher airway resistance found at lower lung volume in ILD. For example, a patient with ILD may demonstrate elevated  $R_{rs}$ , enhanced frequency dependence of  $R_{rs}$ , and more negative  $X_{rs}$  at low frequencies consistent with increased elastance [159–162]. Such findings correlate with the severity of the restriction assessed by either TLC or vital capacity and with the severity of radiographic abnormalities [162–165]. Recent work has shown that while oscillometric parameters in both patients with ILD and COPD correlate well with ventilation unevenness and  $R_{rs}$ , correlations were poor with alterations in static compliance due to emphysema or pulmonary fibrosis [166]. The longitudinal change of  $Z_{rs}$  measured by oscillometry in ILD has not been studied.

Oscillometry has also been used to study lung function in pulmonary restriction caused by neuromuscular disease. Conventional physiological studies document diminished vital capacity due to both reduced lung compliance and reduced outward pull of the chest wall in children and adults with neuromuscular disease [167, 168]. While it has been suggested that oscillometry may be useful for the evaluation of neuromuscular disease [169], the data are limited. Technical difficulties in establishing an adequate mouth seal in patients with bulbar weakness may limit applicability in this group. However, oscillometry would appear to have a major advantage over spirometry in detecting lung disease in patients with neuromuscular weakness in general because it does not require muscle force to generate the deep inspiration involved in spirometry.

### Vocal cord dysfunction

Paradoxical inspiratory adduction of the vocal cords or reduction in subglottal cross-sectional area induces acute symptoms that is often mistaken for (or associated with) asthma [170]. Detection of inspiratory flow limitation is not widely assessed in clinic and is poorly tolerated, particularly in children. Model analysis has indicated the potential of oscillometry for assessing vocal cord dysfunction (VCD) [171, 172]. It is recommended to carefully examine intratidal changes in  $Z_{rs}$  for large positive swings during inspiration [173], especially when tidal inspiratory flow limitation may be suspected [174], and to identify markedly *positive* differences between inspiratory and expiratory  $R_{rs}$  [175]. Owing to expiratory glottal narrowing, these differences are usually negative in control subjects or stable asthmatics and may be enhanced further in acute bronchoconstriction [175–177]. Large case-control studies are necessary to establish the sensitivity and specificity in VCD.

### Sleep apnoea

Obstructive sleep apnoea (OSA) is a very prevalent disease in adults, characterised by recurrent upper airway collapse and obstruction, resulting in nocturnal apnoea and hypopnoea. Given that increase in upper airway resistance is a landmark of OSA, oscillometry is particularly suited for detecting such airway obstruction [178] and hence for application in this disease [179, 180]. Initially, oscillometry was applied to help diagnose OSA in awake patients, since increased susceptibility to airway collapse can be detected by measuring changes in  $R_{rs}$  during continuous negative airway pressure [181]. The effect of posture on oscillometric measures is also enhanced in supine patients with OSA compared to supine patients without OSA, increasing the sensitivity of oscillometry in OSA [182]. Although initial data showed that oscillometry was able to distinguish OSA patients from healthy adults [181], its application for simplified diagnosis has not yet been implemented in routine clinical practice. However, oscillometry is useful for monitoring upper airway collapse during sleep [183–185]. Oscillometry also provides insight into how airway resistance is normalised by application of continuous positive airway pressure (CPAP) [186], and how sleep apnoea and asthma may interact to worsen airway obstruction [187]. Further information on the use of oscillometry in the setting of CPAP is found in the supplementary material.

### Environmental and occupational exposures

Oscillometry has been used in monitoring and detection of lung function among people exposed to various environmental or occupational irritants or hazards. Firefighters and those exposed to asbestos have been shown to have abnormalities in oscillometry parameters even with normal spirometric indices [188]. Similar findings are seen in symptomatic people exposed to World Trade Center dust during the 9/11 attacks and suggest the detection of distal airway dysfunction even when spirometry is normal [189, 190]. Exposures to specific inhaled contaminants have been shown to result in changes in  $Z_{rs}$  that often but not

invariably correlate with changes in spirometry; hence, the two measures may be complementary [191]. Oscillometry has the potential to detect changes years after an environmental exposure. For example, infants exposed to poor air quality from a coal mine fire for a 6-week episode when less than 2 years old had worse AX 3 years after the fire [192]. Furthermore, a study in adolescents showed that exposure to air pollution from local traffic during infancy was associated with abnormal oscillometry parameters suggesting distal airways disease, especially in those with asthma [193]. These studies all suggest that oscillometry may be useful for monitoring lung function in occupational settings and in detecting early changes in lung function in association with environmental exposures.

Of unique concern at the time of this writing is the prevention of spreading contaminated aerosols during lung function testing during the current coronavirus disease 2019 pandemic. Although no data are available, oscillometry is thought to be safer than spirometry in this regard, given that deep inhalation and forced exhalation are not required [194].

### Critical care

The measurement of  $Z_{rs}$  in critically ill patients receiving ventilatory support poses many unique challenges to the clinician, especially regarding technique and safety [195–200], including managing the interface between the oscillometric generator and the patient's airway [201–203], and the influence of the ventilator circuit on the excitation waveform [204–215]. Further details related to the technical issues of applying oscillometry through the ventilatory circuit are discussed in the supplementary material. Despite technical challenges, the use of oscillometry in ventilated and critically ill patients has yielded tremendous information on the mechanical derangements and pathophysiological processes associated with various respiratory diseases [198, 200, 216–220], such as lung derecruitment [221], parenchymal overdistention [222] and EFL<sub>T</sub> [124, 223, 224]. In the paediatric patients, oscillometry may be useful for monitoring the effects of positional changes and adjustment of PEEP [220, 225–228] and for improving prediction of respiratory outcomes in extremely preterm newborns receiving invasive ventilation [229]. A recent American Thoracic Society/European Respiratory Society workshop report on the evaluation of respiratory function, including oscillometry in the neonatal and paediatric intensive care units, has recently been published [230]. Oscillometry thus has the potential not only to optimise ventilator settings [226, 231–235], but also to enhance our understanding of the immediate impact of various surgical interventions on lung function [204, 205, 216, 236].

### Summary and future research

In summary, oscillometry has shown to be of value for the diagnosing lung disease in our youngest patients and throughout life, and monitoring disease progression, acute exacerbations and treatment effects. While many gaps in our understanding are closing, many still need to be filled in order to ensure a smooth transition of oscillometry from a research tool to a reliable, robust, clinical tool (table 2). In undertaking this review of clinical literature using oscillometry, we have identified several areas where more evidence is required before oscillometry may be used routinely in clinical practice. Looking to the future, we envision many opportunities to develop oscillometry for a wide range of clinical applications [1].

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