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Airway clearance, mucoactive therapies and pulmonary rehabilitation in bronchiectasis

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Abstract:
This paper aims to provide physiological rationale for airway clearance, mucoactive therapy and pulmonary rehabilitation (PR) (or exercise interventions) in bronchiectasis.

There is increasing emphasis on the role of Airway clearance techniques (ACTs) in the management of bronchiectasis. No single ACT has currently shown superior effect over another. Given the large range of different techniques available, consideration of the physiological effects underpinning a technique including expiratory flow, ventilation and oscillation, are essential to effectively personalise ACTs.

Key clinical trials of mucoactives in bronchiectasis are underway and will provide clarity on the role of these agents in the management of patients with bronchiectasis. Prescription of mucoactive therapies should be done in conjunction with ACTs and therefore the mechanism of action of mucoactive drugs and their timing with ACTs should be taken into consideration.

PR and/or exercise training are recommended in all current bronchiectasis guidelines. There is a clear physiologic rationale that muscle weakness and physical inactivity may play a role in disease progression as well as impacting on health related quality of life, frequency of pulmonary exacerbations and ability to mobilize sputum. However, there are residual unanswered questions surrounding the delivery and accessibility to PR. This review summarises the physiological principles and supporting evidence for airway clearance, mucoactive medication and PR, which are key components in the management of bronchiectasis.

Keywords:
Bronchiectasis, airway clearance, mucoactives, pulmonary rehabilitation
1. Introduction

Chronic cough, sputum production as well as decreased exercise capacity and inactivity are some of the main clinical manifestations reported in people with bronchiectasis (1)(2,3). These symptoms worsen during exacerbations and impact negatively on health-related quality of life (HRQoL) (4). This paper summarises the physiological rationale for airway clearance including mucoactive therapy as well as pulmonary rehabilitation (PR) (or exercise interventions) in bronchiectasis.

2. Airway clearance in bronchiectasis

Airway clearance techniques (ACTs) are non-pharmacological strategies to improve symptoms and HRQoL and reduce exacerbation frequency (5,6). Short-term goals are to provide more effective sputum clearance that improves ventilation and reduces cough impact and breathlessness. Longer-term goals are reducing further airway damage by halting the vicious cycle of bacterial colonisation and subsequent inflammation, reducing the number of pulmonary exacerbations and hospitalisations and improving HRQoL (7-9).

Published guidelines agree that ACTs are a key component in the management of bronchiectasis and that all patients with bronchiectasis should be screened for symptoms that may benefit from ACTs i.e. chronic productive cough or difficulty expectorating sputum (7,8). ACTs which can be performed independently are recommended in these guidelines. In practice, ACTs remain significantly underutilized. Data from the European Bronchiectasis Data Registry (EMBARC) reports that only 45% of data registrants perform an ACT regularly (10). Furthermore, airway clearance has very low rates of adherence (11).

ACTs rely on two overriding physiological principles. First, a mechanism to allow air to move behind the obstruction and ventilate the regions distally and second, modulation of
expiratory airflow to propel secretions proximally up the airways. In vitro flow models suggest two conditions that improve airway clearance: i) the peak expiratory flow rate should be greater than the peak inspiratory flow rate (at least 10%) for mucus to move proximally; ii) and a peak expiratory flow rate of 30-60 L/min is required to break the adhesive bonds generated between the mucus layer and the airway epithelial surface (12). Both are essential for enhancing mucus clearance.

Recommendations and the evidence to support the use of ACTs are based on a limited number of clinical trials, many of which are single treatment studies. Two Cochrane reviews have summarised data from 16 randomized controlled trials (RCTs) (13 of which were cross-over design) concluding that airways clearance is safe and may account for improvements in sputum expectoration, some measures of lung function, symptoms and HRQoL(5,6). One of the reviews concluded that positive expiratory pressure (PEP) was as effective as other ACTs (5).

Considering studies with interventions longer than single treatments, Patterson et al demonstrated that there was no difference in lung function and sputum weight with Active Cycle of Breathing Techniques (ACBT) vs. Acapella (oscillating PEP device) over a 10-14 day treatment period in 20 stable patients (13). In 17 patients, Thompson et al reported that there was no significant difference between ACBT and the Flutter (oscillating PEP device) after a 4 week treatment period, in any of the outcomes used (HRQoL, lung function and sputum) (14). Over 3 treatment sessions, the techniques of autogenic drainage (AD) and ELTGOL (an active technique where the subject carries out slow expiration with the glottis open in a lateral decubitus position) have been compared to a control group of 31 patients performing temporary PEP in a study by Herrero-Cortina and colleagues. Both AD and ELTGOL resulted in significantly greater sputum compared to the control group (15). Munoz et al. compared the ELTGOL technique to placebo exercises twice daily in 44 patients over a 1 year period and reported fewer exacerbations, reduced cough impact and improved HRQoL in the ELTGOL group (16).
In terms of the supporting evidence for oscillating PEP, Murray et al. compared Acapella to no treatment in 20 stable adult bronchiectasis patients over a 3-month period (17). There was no change in pulmonary exacerbation frequency or pulmonary function. There was significant increases in HRQoL, sputum volume and exercise capacity for the patients performing Acapella compared to the control. Tambascio et al. compared Flutter to control (flutter-sham) in 17 stable adult bronchiectasis patients over a 4 week period and reported an improvement in sputum transport and a reduction in inflammatory cells in respiratory secretions using flutter (18).

These studies with interventions longer than a single treatment demonstrate some proof of concept on the effectiveness of ACTs in bronchiectasis and support the general consensus that currently no one ACT is superior in terms of clinical outcomes (6).

Selection of ACTs should be targeted according to the patient's individual characteristics i.e. personalized to that patient (19,20). McIlwaine et al highlighted that key to personalizing ACTs is considering the physiological principles underpinning the technique. ACTs rely on two main physiological premises: the ability to ventilate behind obstructed regions of the lung and the capacity to achieve the minimum expiratory airflow bias necessary to mobilise secretions. The authors advocate that understanding how each ACT incorporates these proposed physiological effects could inform clinical decision-making and drive personalization of ACTs, for example, use of a forced expiration may need to be adapted to a patient with collapsible airways (19). We now describe how a range of additional techniques utilise the physiological principles of ventilation and expiratory airflow (Table 1). These additional techniques have been used in studies of bronchiectasis and/or reported by the manufacturers to be of benefit in bronchiectasis for airway clearance. Albeit, many of these techniques have not been subject to clinical trials. Table 1 provides a description of the technique and how they perform considering these key physiological principles (Table 1).
For children with bronchiectasis, the principles of ACTs in current practice follow what has been described in adults, given the paucity of research which exists (21). Questions remain around how airways clearance relates to key clinical outcomes in bronchiectasis in both adults and children (6,21). Crucially, there is no strong evidence to inform choice, frequency or duration of ACTs in bronchiectasis. Tailoring of ACT to the individual patient is recommended across the age range (19,22) and physiotherapists must consider how to optimally personalize ACTs. Tailoring includes physiology, symptoms, evidence base and patient factors as well as age related factors when treating children such as; levels of understanding, maturity and the parent-child relationship, all of which may influence adherence to ACTs. There are recognised challenges performing traditional, longer term RCTs of ACTs due to the huge challenge of blinding and random allocation of such treatments as well as the influence of patient preference. Exploration of different study designs has been suggested in cystic fibrosis (CF) (23). In bronchiectasis, future research using novel designs and long-term observational data from large datasets as well as the exploration of delivering ACT personalization will both contribute to the current evidence base and support the delivery of personalized ACT.

3. Mucoactive therapy in bronchiectasis

ACTs should be coordinated with mucoactive medications to ensure the overall effect is optimised.

Mucoactive drugs potentially increase the ability to expectorate sputum and/or decrease mucous hypersecretion (24). They can broadly be characterised into several major groups based on their potential mechanism of action:

- Expectorants: drugs that induce discharge or expulsion of mucous from the respiratory tract. Typically this requires coughing action to loosen and bring up the mucous from the lungs or upper respiratory tract. Examples include hypertonic saline (HTS), guaifenesin.
- Mucoregulators: drugs that regulate mucous secretion or interfere with the DNA/F-actin network. Examples include carbocisteine, anticholinergic agents.
- Mucolytics: drugs that decrease mucous viscosity. Examples include N-acetylcysteine, erdosteine, DNase.
- Mucokinetics: drugs that increase mucociliary clearance by acting on the cilia. Also referred to as cough clearance promoters. Examples include bronchodilators, surfactants. (24).

The ERS guidelines (7) summarise the findings of three systematic reviews which have comprehensively examined the current evidence for mucoactives (25-27). None of the mucoactive agents significantly reduced the number of exacerbations, and the exacerbation rate was higher in the recombinant human DNase (rhDNase) group compared with placebo (28). The Wilkinson systematic review focused on the evidence for bromhexine and DNase. Due to methodological differences in studies, a meta-analysis could not be performed. One trial with 88 participants showed that high doses of bromhexine with antibiotics significantly eased difficulty in expectoration and sputum production days compared to placebo; however the quality of the evidence was rated as low (29). In a single small, blinded but not placebo-controlled trial of older (> 55 years) participants with stable bronchiectasis and mucus hypersecretion, erdosteine combined with physiotherapy over a 15-day period significantly improved spirometry and sputum purulence more effectively compared with physiotherapy alone (30). Further long-term trials are needed to fully understand if these mucoactives are beneficial in bronchiectasis. The remaining two studies in this review (with a combined total of 410 participants) compared RhDNase versus placebo (28,31). The larger and longer of these studies showed a significant negative effect on forced expiratory volume in one second (FEV₁) and an increase in exacerbations (28). Based on this evidence synthesis of proprietary patented mucolytics such as DNase, the ERS guidelines recommend that DNase should not be offered to patients with bronchiectasis. Similarly for
oral carbocisteine, the evidence base in bronchiectasis is poor and there is insufficient
evidence to recommend (7).

With regard to mannitol, current systematic reviews (25,27) as well as studies subsequent
to the reviews (32) provide insufficient evidence to draw firm conclusions on its effect. Bilton
and colleagues found that inhaled mannitol at 400 mg twice daily for 12 months in patients
with non-CF bronchiectasis did not reduce exacerbation rates, thus supporting the findings
in the Hart review (32).

The Hart systematic review concluded that inhaled HTS had no significant benefit over
isotonic saline (25). This review highlighted that there was only 1 long term (1 year)
randomised parallel group study exploring the efficacy of HTS (6%) versus placebo in
bronchiectasis and the study demonstrated that there was no difference between treatment
and placebo in hospital admissions (33). The findings in this study contrasts to other
respiratory conditions where the evidence base for HTS is stronger (34) as well as the more
positive results seen in other single intervention/ cross over studies exploring the use of
HTS in bronchiectasis (35,36). There may be a number of issues that contributed to the
findings in the Nicolson study, including the different methodologies used for the collection
of exacerbation data(37). Both groups experienced benefit, which may be linked to the
frequent medical review obtained by participating in the study and the potential for
increased self-awareness related to the disease process. A third potential contributing
factor is that isotonic saline is not a true placebo in this context and may have benefits by
increasing airway hydration, with further benefit possibly conferred by the respiratory
manoeuvres that participants were instructed to undertake during nebulisation. The
Nicolson trial may also have been underpowered based on exacerbation from recent trials
(RESPIRE trials) (38,39). In this trial, as well as many of the current trials on mucoactives,
the inclusion criteria may not have been specific enough to recruit patients to which
mucoactives should be targeted and this is an important consideration for future trials.
These issues contribute to uncertainty regarding whether the “no effect” observed by Nicolson was due to study design or a true lack of effect of HTS (37).

In a recent double-blind randomized crossover trial in patients with bronchiectasis and chronic sputum, three solutions (7% HTS; 0.1% Hyaluronic acid, (HA) +7%HTS; and 0.9% isotonic saline, (IS) were compared (35). It was hypothesized that the hyaluronic acid (HA) would mitigate bronchospasm caused by HTS. Participants inhaled each solution across four consecutive sessions separated by a 7-day washout period. Both HTS and HA+HS promoted greater sputum weight during sessions than IS with HA+HTS being associated with less side effects. 24-hour sputum volumes were higher for IS, than HTS. This study highlights that HTS has short-term efficacy likely linked to HTS immediate effects on airway surface liquid volume biophysical sputum properties and stimulation of cough (35).

In children, whilst 7% hypertonic saline is likely the most commonly used clinically and is probably safe and effective, there is no RCT evidence to support the use of mucolytics (22).

Many of the trials exploring inhaled mucoactives incorporated a drug response assessment (DRA) (formally known as a challenge test or a bronchoconstriction trial) to exclude hyper-responsiveness to airway pharmacotherapy and/or the need for using bronchodilators prior to mucoactive therapies. Some studies have used a bronchodilator with all patients prior to HTS inhalation. Whilst a short acting bronchodilator should be considered prior to HTS inhalation (especially in patients that exhibit some bronchoconstriction on DRA) there is no evidence to support this if the patient passed the DRA and this could be an additional burden to treatment. If the patient normally uses a short acting bronchodilator, then it is reasonable to take this prior to HTS inhalation to minimise bronchoconstriction. The Association of Chartered Physiotherapists in CF have published a comprehensive Standard Operating Procedure (SOP) for DRAs directed at patients with CF upon a new nebulised or inhaled medication e.g. inhaled antibiotic, anti-
fungal or mucolytic drug. These SOPs are recommended for use in CF but have broad applicability for inhaled medications in other respiratory diseases including bronchiectasis (40). For mannitol, a specific drug response assessment template should be used.

Prescription of mucoactive therapies should be done in conjunction with ACTs and therefore it is important that the mechanism of action of mucoactive drugs and their timing with ACTs are taken into consideration. For example, HTS has a short term/immediate effect (41), therefore ACTs should be done immediately after HTS inhalation. All trials of HTS have delivered HTS immediately prior to ACTs. If adherence to treatment is a major barrier, consider delivering HTS during ACTs if technology allows. In fact, considering the devices described in Table 1, six can facilitate nebulisation during ACTs i.e. PEP mask, Acapella, Aerobika, RCCornet® PLUS, Vibralung, and Frequencer. The type of nebuliser can impact on the time required to nebulise the mucoactive drug (42). Although traditional jet-nebulisers are still in use (e.g. Pari LC jet nebuliser or equivalent), the use of “intelligent nebulisers” (I-neb/ eFlow devices) may be preferred by patients because they are more portable and can reduce nebulisation times.

There are two active clinical trials exploring the efficacy of commonly used mucoactives (HTS and carbocisteine) in bronchiectasis. The results of these trials are likely to have an important impact on future practice, not least because of the differential cost of these mucoactive medications (43,44). Data from the BTS audit (45) and more recently, a European database (46) indicates that HTS (7%) and carbocisteine are the two mucoactive agents used in bronchiectasis by up to 20% of patients. Despite current guidelines indicating there is insufficient evidence to recommend their use, it is probable that the stronger evidence base for carbocisteine and HTS in other respiratory conditions (47) justifies the current audit data which suggest that carbocisteine and HTS are the most commonly used mucoactives in bronchiectasis (46). These trials will be key to ascertaining
the role of these agents in the management of patients. If ineffective, then up to 20% of patients are on ineffective treatments; if they are effective then up to 80% of patients currently do not have access to effective treatments. Until these definitive trials are completed, a pragmatic approach is to consider stopping the use of mucoactives in patients if there is no benefit after a 4-week trial.

4. Pulmonary rehabilitation in bronchiectasis

All of the current guidelines and clinical reviews in bronchiectasis recommend incorporating PR and/or exercise training (ET) into treatment protocols (7,8,48-50). PR and ET programs exist in many parts of the world but the content and duration of the programs vary. In general, PR incorporates several exercise modalities (treadmill walking, cycle ergometry, weight lifting, arm ergometry) and patient education. ET programs are comprised of the exercise modalities without an educational component. PR and ET programs are generally aimed at improving both upper limb and lower limb endurance and are tailored to the needs of the individual patient. The exercise is supervised by trained staff; depending upon the location of the program these staff may include exercise physiologists, respiratory care practitioners, physiotherapists and nurses. Patients participating in PR or ET are generally monitored with oximetry and occasionally cardiac monitoring. The location of these programs vary: some are incorporated into hospital based Physical Medicine and Rehabilitation Medicine facilities; others are free standing and may even be in a community centre or in an outpatient physiotherapy department. Home based programs have also been developed. The duration of the programs vary: in the United States these programs generally are comprised of an initial intensive phase which includes 36 one hour sessions over 12 weeks followed by a self-guided maintenance phase. In other parts of the world the patients may receive shorter or longer periods of supervision (51). Almost all programs obtain a baseline patient assessment of exercise capacity and HRQoL and then measure those parameters again at the end of the rehabilitation period. Incorporation of disease
specific education as well as general respiratory health and overall wellness training (including nutrition education and psychosocial support) varies. A challenge in many parts of the world is that PR programs are primarily aimed at patients with chronic obstructive pulmonary disease (COPD); patients with bronchiectasis also need additional focused training in airway clearance modalities and other disease specific education (52).

A recent systematic review confirmed the short-term benefits that patients achieve from participating in supervised PR and ET, but noted that sustaining benefit is challenging (53). The physiologic rationale for PR and ET in bronchiectasis is that muscle weakness and physical inactivity may play a role in disease progression as well as impacting HRQoL, frequency of infectious exacerbations and ability to mobilize secretions (54). One observational study of 41 patients with bronchiectasis showed that 36 sessions of PR significantly improved forced vital capacity and residual volume measurements (55). A retrospective study of 95 patients from two tertiary institutions in Australia where subjects received 6 to 8 weeks of PR demonstrated improvement in 6 minute walk distance and HRQoL measured by the Chronic Respiratory Disease Questionnaire (56). An Italian cohort of 108 bronchiectasis subjects who enrolled in a 3 week PR program showed similar results; Multivariate analysis revealed that male gender, baseline FEV1/vital capacity less than 70% and greater than two exacerbations in the previous year were independent predictors of PR efficacy (57). A prospective randomized trial done in Scotland compared PR and chest physiotherapy versus chest physiotherapy alone in 30 patients with bronchiectasis: the PR/physiotherapy group showed significant improvement over the control group in walking distance and HRQoL measures (58). Another randomized study done in Australia comparing ET with airway clearance training to standard care also showed improvement in exercise capacity, dyspnea and fatigue as well as fewer exacerbations over 12 months (59). All of these programs included lower and upper limb exercise and strengthening exercises and were tailored to the individual patient's capabilities. In children,
exercise (especially endurance exercise) is helpful and some experts have also suggested that singing may have a salutatory effect in children (21,22).

Though the evidence base and anecdotal experience suggest that PR or ET are beneficial for patients with bronchiectasis, there are residual unanswered questions. Indeed, exercise as an ACT is an unanswered question in this patient group. Further research questions include the timing of referral for PR; it is unclear at what stage of disease patients might get the most benefit. Additionally, there are potential risks associated with PR and ET in the bronchiectasis population including the potential for unrecognized cardiac co-morbidities, exercise induced hypoxemia, and hemoptysis (54). Many patients with bronchiectasis are elderly and frail with orthopaedic risks (60). Finally, the potential for spread of infectious respiratory pathogens from patient to patient is a concern in this population. More study is needed on home-based PR (61) and tele-rehabilitation programs (62). Finally, access to rehabilitation programs is a problem worldwide and ways to maintain benefit must also be further evaluated.

Summary

Airway clearance, mucoactive medication and PR are key components in the management of bronchiectasis. The stepwise approach to the management of bronchiectasis in line with disease severity is advocated in a key review with the inclusion of airway clearance and PR for patients at all stages of disease severity and the escalation of therapy and inclusion of mucoactive medication in patients with persistent symptoms or exacerbations despite standard care (63). There are few RCTs assessing treatments in children with bronchiectasis. Future research is needed to drive personalisation of ACT, inform clinical decision making on mucoactive medication and improve accessibility to PR in children and adults.
Disclosure statement:

AOE has acted as paid scientific consultant to Electromed Inc.

The authors:

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Table 1. Physiological effects of Airway clearance techniques (ACTs) (adapted with permission from McIlwaine et al. Grey sections denote content from the original paper) (19).

<table>
<thead>
<tr>
<th>Technique title and description</th>
<th>Interdependence</th>
<th>Collateral Ventilation (CV)</th>
<th>Breath hold</th>
<th>Huffing</th>
<th>PEFR/PIFR &gt;1.1</th>
<th>PEFR &gt; 30 – 60 L/min</th>
<th>Oscillation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACBT^</td>
<td>Thoracic expansion exercises utilise interdependence.</td>
<td>Thoracic expansion exercises utilise CV.</td>
<td>Sometimes used with this technique if hypo- ventilating.</td>
<td>Uses forced expirations at different levels.</td>
<td>Yes</td>
<td>Ratio = 2.8.</td>
<td>Average 302 L/min with huffing.</td>
</tr>
<tr>
<td>Autogenic Drainage (AD)^</td>
<td>No.</td>
<td>Yes with breath hold.</td>
<td>Uses 3 second breath hold with each breath.</td>
<td>No.</td>
<td>Yes, emphasis is on slow inspiration and increased velocity on expiration.</td>
<td>40 – 70 L/min. Depends on level of breathing and degree of airway obstruction.</td>
<td>No.</td>
</tr>
<tr>
<td>ELTGOL</td>
<td>No.</td>
<td>No. Tidal breathing during inspiration.</td>
<td>No. Tidal breathing during inspiration.</td>
<td>No.</td>
<td>Yes.</td>
<td>Emphasis is on slow, prolonged expiration from functional residual capacity to residual volume.</td>
<td>Yes. Airflow may be increased with the application of slow abdominal and thoracic compression during expiration.</td>
</tr>
</tbody>
</table>

Positive expiratory Pressure (PEP) devices

<table>
<thead>
<tr>
<th>Technique title and description</th>
<th>Interdependence</th>
<th>Collateral Ventilation (CV)</th>
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<th>Huffing</th>
<th>PEFR/PIFR &gt;1.1</th>
<th>PEFR &gt; 30 – 60 L/min</th>
<th>Oscillation</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEP mask^</td>
<td>No.</td>
<td>As PEP is maintained within the airways during 12 – 15 breaths.</td>
<td>Not necessary as PEP is maintained within the airways during 12 – 15 breaths.</td>
<td>Used at end of each cycle of 12 -15 breaths.</td>
<td>No</td>
<td>Ratio = 0.47.</td>
<td>Average 26 L/min</td>
</tr>
<tr>
<td>Oscillating PEP devices</td>
<td>Technique title and description</td>
<td>Interdependence</td>
<td>Collateral Ventilation (CV)</td>
<td>Breath hold</td>
<td>Huffing</td>
<td>PEFR/PIFR &gt;1.1</td>
<td>PEFR &gt; 30 – 60 L/min</td>
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<tr>
<td>Oscillating PEP with Flutter^ (65)</td>
<td>Oscillations between 3-5 Hz may play a role, but frequency used in Flutter is &gt; 5 Hz.</td>
<td>Yes with breath hold.</td>
<td>Uses 3-second breath hold with each breath.</td>
<td>Used at end of each cycle of 8 -10 breaths.</td>
<td>Ratio = 1.15.</td>
<td>Average 68 L/min.</td>
<td>2 – 32 Hz. Most often uses 6 - 26 Hz.</td>
</tr>
<tr>
<td>Oscillating PEP with Acapella^ (65)</td>
<td>Oscillations between 3-5 Hz may play a role, but frequency used in Acapella is &gt; 5 Hz.</td>
<td>As a PEP (10.31-19.41 cmH₂O) is maintained within the airways during 12 – 15 breaths, use of CV is maximised.</td>
<td>Not necessary.</td>
<td>Used at end of each cycle of 12 -15 breaths.</td>
<td>No. Ratio = 0.64.</td>
<td>Average 35.4 L/min</td>
<td>10 - 18 Hz.</td>
</tr>
<tr>
<td>Oscillating PEP with Aerobika^ (66-68)</td>
<td>Oscillations between 3-5 Hz may play a role, but frequency used in Aerobika is &gt; 5 Hz. Thoracic expansion exercises utilise interdependence</td>
<td>Uses 2-3 second breath hold with each breath.</td>
<td>Used at end of each cycle of 10-20 breaths.</td>
<td>Yes Ratio &gt;1.1.</td>
<td>PEFR can range from 15 to 40 L/min depending on breath volume and resistance settings.</td>
<td>9-20 Hz (depending on resistance settings and PEFR).</td>
<td></td>
</tr>
<tr>
<td>Oscillating PEP with Shaker* (69,70)</td>
<td>Oscillations between 3-5 Hz may play a role, but frequency</td>
<td>Thoracic expansion exercises utilise CV.</td>
<td>No.</td>
<td>Used at end of each cycle of 8-10 breaths.</td>
<td>Emphasis is on slow inspiration and increased</td>
<td>5-32 L/min depending on breath volume and angle of device.</td>
<td>10-28.5 Hz (depending on angle of device).</td>
</tr>
<tr>
<td>Oscillating PEP with REVITIVE Aerosure Medic* (71)</td>
<td>Oscillations between 3-5 Hz may play a role, but frequency used in REVITIVE Aerosure Medic is &gt; 5 Hz.</td>
<td>As a PEP of 4-25cmH₂O is maintained within the airways during 15-20 breaths, the use of CV is maximised.</td>
<td>No.</td>
<td>Used at end of each cycle of 15-20 breaths</td>
<td>No.</td>
<td>Unknown.</td>
<td>15 Hz with non IMT mode. 25 Hz with IMT mode.</td>
</tr>
</tbody>
</table>
| Oscillating PEP with RC-Cornet® device or RC-Cornet® PLUS device^ (72-75) | Oscillations between 3-5 Hz may play a role, but frequency used in RC-Cornet® is > 5 Hz. Thoracic expansion exercises utilise interdependence. | Thoracic expansion exercises utilise CV. As a PEP of 10-28 cmH₂O is maintained within the airways the use of CV is maximised. | No. | Used at end of each cycle of 10 breaths. | No. | RC-Cornet® device: 90 L/min – 177 L/min.  
RC-Cornet® PLUS device: Setting 1 resistance 37.2 –149 L/min  
Setting 2 resistance 43.2 –236 L/min. | RC-Cornet® PLUS device: 8-160 Hz (depending on resistance settings).  
RC-Cornet® PLUS device: 12-14 Hz. |
| Oscillating PEP with Lung flute* (76) | No. Tidal breathing during treatment. | No. A PEP of 2.5 cm H₂O is maintained in the airways | No. | Used at end of 5 sets of 2 blows. | Emphasis is on expiratory flow rate higher than inspiratory flow rate. | Minimal flow rate required 128.4 L/min. | 16-25 Hz. |
Oscillations between 3-5 Hz may play a role, but frequency used in Lung flute is > 5 Hz. during a single breath. Tidal breathing during treatment.

<table>
<thead>
<tr>
<th>Percussion devices</th>
<th>Technique title and description</th>
<th>Interdependence</th>
<th>Collateral Ventilation (CV)</th>
<th>Breath hold</th>
<th>Huffing</th>
<th>PEFR/PIFR &gt;1.1</th>
<th>PEFR &gt; 30 – 60 L/min</th>
<th>Oscillation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vibralung Acoustical Percussor (Intrapulmonary Acoustical Airway Clearance). (When used independently with no active component).* (77)</td>
<td>Tidal breathing during treatment but oscillations between 3-5 Hz may play a role. When using the PEP resistor, a PEP in the airways 4-20 cmH₂O therefore CV can be maximised.</td>
<td>No.</td>
<td>No.</td>
<td>No.</td>
<td>No.</td>
<td>Frequency range 5-1200 Hz depending on setting.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequencer (Acoustic sound waves). (When used independently with no active component).* (78)</td>
<td>No. Tidal breathing during treatment. Oscillations between 3-5 Hz may play a role, but frequency used in Frequencer is &gt; 5 Hz.</td>
<td>No.</td>
<td>No.</td>
<td>No.</td>
<td>No.</td>
<td>20-65 Hz.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

High Frequency Chest Wall Oscillation (HFCWO) devices

<table>
<thead>
<tr>
<th>Technique title and description</th>
<th>Interdependence</th>
<th>Collateral Ventilation (CV)</th>
<th>Breath hold</th>
<th>Huffing</th>
<th>PEFR/PIFR &gt;1.1</th>
<th>PEFR &gt; 30 – 60 L/min</th>
<th>Oscillation frequency</th>
</tr>
</thead>
</table>

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**HFCWO**

Oscillations between 3-5 Hz may play a role, but frequency used in HFCWO is > 5 Hz.

No. | No. | Interspersed with HFCWO. | Yes, expiratory flow rate is much higher than inspiratory flow rate. | Average 120 L/min. | 5-25 Hz.
---|---|---|---|---|---


*See references for a further description of how this technique works and the application of the technique*

**Further description of how this technique works and the application of the technique available at [https://www.cff.org/Life-With-CF/Treatments-and-Therapies/Airway-Clearance/High-Frequency-Chest-Wall-Oscillation/](https://www.cff.org/Life-With-CF/Treatments-and-Therapies/Airway-Clearance/High-Frequency-Chest-Wall-Oscillation/)*
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