EFFECTS OF PURSED LIPS BREATHING WITH FORCED EXPIRATION TECHNIQUES AND ACTIVE CYCLE OF BREATHING TECHNIQUE ON AIRWAY CLEARANCE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

SAOWANEE WORAVUTRANGKUL

A THESIS SUBMITTED IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR
THE DEGREE OF DOCTOR OF PHILOSOPHY
(PHYSICAL THERAPY)
FACULTY OF GRADUATE STUDIES
MAHIDOL UNIVERSITY
2009

Thesis
entitled

EFFECTS OF PURSED LIPS BREATHING WITH FORCED EXPIRATION TECHNIQUES AND ACTIVE CYCLE OF BREATHING TECHNIQUE ON AIRWAY CLEARANCE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

……..……
Ms. Saowanee Woravutrangkul
Candidate

……..……
Assoc. Prof. Suwannee Jarungjitaree, M.Sc.
Major-advisor

……..……
Assoc. Prof. Roongtiwa Vachalathiti, Ph.D.
Co-advisor

……..……
Asst. Prof. Benjamas Chuaychoo, M.D.,Ph.D.
Co-advisor

……..……
Asst. Prof. Chanika Sritara, M.D.
Co-advisor

……..…
Prof. Banchong Mahaisavariya, M.D.
Dean
Faculty of Graduate Studies
Mahidol University

……..……
Asst. Prof. Jarugool Tretriluxana, Ph.D.
Chair
Doctor of Philosophy Program in Physical Therapy
Faculty of Physical Therapy
Mahidol University

Thesis
entitled

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was submitted to the Faculty of Graduate Studies, Mahidol University
for the degree of Doctor of Philosophy (Physical Therapy)
on
August 11, 2009

……
Ms. Saowanee Woravutrangkul
Candidate

……
Asst. Prof. Jatuporn Wongsathikun, Ph.D.
Chair

……
Asst. Prof Benjamas Chuaychoo, M.D., Ph.D.
Member

……
Assoc. Prof. Suwannee Jarungjitaree, M.Sc.
Member

……
Asst. Prof. Chanika Sritara, M.D.
Member

……
Assoc. Prof. Roongtiwa Vachalathiti, Ph.D.
Member

……
Prof. Banchong Mahaisavariya, M.D.
Dean
Faculty of Graduate Studies
Mahidol University

……
Assoc. Prof. Roongtiwa Vachalathiti, Ph.D.
Dean
Faculty of Physical Therapy
Mahidol University

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude and deep appreciation to Associate Professor Suwannee Jarungjitaree my major advisor for her excellent guidance, worthy suggestion and discussion. She always teaches me useful things both directly and indirectly pertaining to academic and clinical knowledge.

My sincere gratefulness and appreciation are given to Associate Professor Dr. Roongtiwa Vachalathiti, my co-advisor for her invaluable advice, supervision and encouragement throughout this study.

Deep gratefulness also reaches upon Assistant Professor Dr. Benjamas Chuaychoo, MD, my co-advisor. She always supervises me the excellent clinical and non-clinical knowledge with full of graciousness.

I am specially grateful to Assistant Professor Dr. Chanika Sritara, MD, my co-advisor for her intellectual guidance and her support during data collection of radioaerosol technique. She always gives me good knowledge and challenging ideas of the study.

Special thanks are extended to my subjects for their nice co-operation and good assistance. As well as all staffs in COPD clinic, Division of Respiratory Disease and Tuberculosis, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University and Outpatient Unit of Respiratory Disease, Chest Disease institute, Department of Medical Services, Ministry of Public Health, they are very nice assistances that made the data collection period ran smoothly. Also, I would like to thank all radiotechnologists and officers, Division of Nuclear Medicine, Department of Radiology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University for the assistances.

I would like to especial thank Miss Putthiporn Charoenthun and Miss Nattha Titthasiri for their sincere assistance, suggestions and encouragement.

Finally, I would like to express my deepest gratitude to my family and friends for their support, entirely care and love. The usefulness of this thesis, I dedicate to my father, my mother and all the teachers who have taught me since my childhood.

Saowanee Woravutrangkul

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SAOWANEE WORAVUTRANGKUL 4836611 PTPT/D

Ph.D. (PHYSICAL THERAPY)

THESIS ADVISORY COMMITTEE: SUWANNEE JARUNGJITAREE, M.Sc. (PHYSIOTHERAPY), ROONGTIWA VACHALATHITI, Ph.D. (PHYSIOTHERAPY), BENJAMAS CHUAYCHOO, M.D., Ph.D., CHANIKA SRITARA, M.D.

ABSTRACT

This study investigated the efficacy of pursed lips breathing with forced expiration techniques (PLB&FETs) and active cycle of breathing technique (ACBT) on pulmonary mucus clearance in healthy subjects and the effectiveness of both techniques in persons with chronic obstructive pulmonary disease (COPD). In the first study, pulmonary mucus clearance of three healthy male volunteers was measured over a 70-minute period on three different days by using a radioaerosol tracer technique. The efficacy of both airway clearance techniques was similar, but better than that of the normal breathing. In the central lung zone, the PLB&FETs demonstrated a slight enhancement of mucus clearance as compared to the ACBT and normal breathing. In the intermediate and peripheral zone, the PLB&FETs and ACBT resulted in a relatively high mucus clearance as compared to the normal breathing. Overall mucus clearance of normal lungs was remarkable improved by the PLB&FETs and ACBT.

In the second study, twenty-two persons with mild to severe COPD were recruited. Each patient was tested for the following: a) pulmonary function test, b) modified patient evaluation questionnaire, c) self-reported daily log book including peak expiratory flow rate (PEFR), sputum volume, modified Borg score, and d) modified patient satisfaction questionnaire. Participants were then randomly assigned into two intervention groups: PLB&FETs and ACBT group. The training lasted for two weeks. Between-group comparisons demonstrated no significant differences in all variables of interest. However, within-group comparisons demonstrated significant differences in PEFR, sputum volume, and peak expiratory flow between time duration. In the PLB&FETs group, the total mean PEFR was significantly increased and the sputum volume was significantly decreased between the first and second week. In the ACBT group, the peak expiratory flow was significantly increased between baseline and day 14^{th}. In both groups, total scores of modified patient evaluation questionnaire were significantly decreased, indicating improvement symptoms, between baseline and day 14^{th}. The effectiveness of airway clearance and pulmonary function in persons with mild to severe COPD was similar between the two airway clearance techniques.

KEY WORDS: PURSED LIPS BREATHING WITH FORCED EXPIRATION TECHNIQUES/ ACTIVE CYCLE OF BREATHING TECHNIQUE/ CHRONIC OBSTRUCTIVE PULMONARY DISEASE/ AIRWAY CLEARANCE TECHNIQUE/ RADIOAEROSOL TECHNIQUE

231 pages

ผลของเทคนิคการหายใจแบบห่อริมฝีปากร่วมกับการหายใจออกอย่างแรงและเทคนิคการหายใจแบบวงจรด้วยตนเองต่อการขจัดเสมหะของทางเดินหายใจในผู้ป่วยโรคปอดอุดกั้นเรื้อรัง
EFFECTS OF PURSED LIPS BREATHING WITH FORCED EXPIRATION TECHNIQUES AND ACTIVE CYCLE OF BREATHING TECHNIQUE ON AIRWAY CLEARANCE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

เสาวณีย์ วรวุฒางกูร 4836611 PTPT/D

ปร.ด. (กายภาพบำบัด)

คณะกรรมการที่ปรึกษาวิทยานิพนธ์: สวรรณี จรุงจิตรอารี,M.Sc. (กายภาพบำบัด),รุ่งทิวา วัจฉละฐิติ, Ph.D. (Physiotherapy), เบญจมาศ ช่วยชู, M.D., Ph.D., ชนิกา ศรีธรา, M.D.

บทคัดย่อ

การศึกษานี้ มีวัตถุประสงค์เพื่อศึกษาประสิทธิผลของเทคนิคการหายใจแบบห่อริมฝีปากร่วมกับการหายใจออกอย่างแรง และเทคนิคการหายใจแบบวงจรด้วยตนเองต่อการระบายเสมหะในทางเดินหายใจของคนสุขภาพดี และศึกษาประสิทธิภาพของเทคนิคทั้งสองในผู้ป่วยโรคปอดอุดกั้นเรื้อรังในการศึกษาที่ 1 ผู้เข้าร่วมการศึกษาเป็นชายสุขภาพดี 3 คน ได้รับการตรวจวัดเทคนิคละอองสารเภสัชรังสีต่อการเคลื่อนของเสมหะในทางเดินหายใจภายในเวลา 70 นาที ตลอด 3 วันศึกษาด้วยเทคนิคการรักษาที่ต่างกัน ผลพบว่าทั้งสองเทคนิคมีประสิทธิผลใกล้เคียงกันแต่ดีกว่าการหายใจปกติในการศึกษาควบคุม โดยเทคนิคการหายใจแบบห่อริมฝีปากร่วมกับการหายใจออกอย่างแรงมีการเคลื่อนระบายเสมหะในทางเดินหายใจส่วนต้นได้ดีกว่าเล็กน้อย ส่วนทางเดินหายใจส่วนกลางและทางเดินหายใจส่วนปลายนั้น ทั้งสองเทคนิคจะได้ผลดีชัดเจนเมื่อเทียบกับการหายใจปกติ ดังนั้นการระบายเสมหะในปอดปกติโดยรวมจะเกิดขึ้นได้ดีด้วยเทคนิคการหายใจแบบห่อริมฝีปากร่วมกับการหายใจออกอย่างแรงและเทคนิคการหายใจแบบวงจรด้วยตนเอง

การศึกษาที่ 2 ผู้ป่วยโรคปอดอุดกั้นเรื้อรังระดับรุนแรงน้อย-ปานกลาง จำนวน 22 ราย เข้าร่วมการศึกษาและได้รับการตรวจประเมิน ประกอบด้วย 1) การวัดค่าสมรรถภาพปอด, 2) แบบสอบถามการประเมินอาการด้วยตนเอง, 3) ใบบันทึกประจำวันด้วยตนเองเกี่ยวกับค่าอัตราการไหลสูงสุดของอากาศขณะหายใจออก, ปริมาณเสมหะ, ค่าคะแนนความรู้สึกเหนื่อยด้วยบอร์ก และ4) แบบสอบถามความพอใจต่อเทคนิครักษาของผู้ป่วย ผู้ป่วยถูกสุ่มคัดเลือกเข้ากลุ่มศึกษา คือ กลุ่มที่ได้รับการรักษาด้วยเทคนิคการหายใจแบบห่อริมฝีปากร่วมกับการหายใจออกอย่างแรง (กลุ่ม 1) และกลุ่มที่ได้รับการรักษาด้วยเทคนิคการหายใจแบบวงจรด้วยตนเอง (กลุ่มที่ 2) ตลอดระยะเวลา 2 สัปดาห์ ผลการศึกษาพบว่า ตัวแปรการศึกษาต่างๆ ไม่พบความแตกต่างระหว่างกลุ่มในช่วงเวลาศึกษา ส่วนภายในกลุ่ม 1 ค่าเฉลี่ยรวมของอัตราการไหลสูงสุดของอากาศขณะหายใจออกสูงขึ้นและปริมาณเสมหะลดลงอย่างมีนัยสำคัญทางสถิติระหว่างสัปดาห์แรกและสอง ในกลุ่มที่ 2 พบว่า ค่าความเร็วลมหายใจออกสูงสุดของสมรรถภาพปอดมีค่าสูงขึ้นอย่างมีนัยสำคัญในวันที่ 14 เทียบกับเมื่อแรกเข้า นอกจากนี้ทั้งสองกลุ่มมีค่าคะแนนแบบสอบถามการประเมินอาการด้วยตนเองลดลง นั่นคือ อาการโดยรวมของผู้ป่วยดีขึ้นในวันที่ 14 เทียบกับวันแรกของการศึกษา การศึกษานี้ ชี้ให้เห็นถึงผลของทั้งสองเทคนิคต่อเพิ่มการระบายเสมหะและสมรรถภาพปอดดีขึ้นในผู้ป่วยโรคปอดอุดกั้นเรื้อรังและทั้งสองเทคนิคมีประสิทธิภาพดีพอกัน

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LIST OF ABBREVIATIONS

ACBT	=	Active Cycle of Breathing Technique
ACTs	=	Airway Clearance Techniques
AD	=	Autogenic Drainage
ATS	=	American Thoracic Society
BC	=	Breathing Control
BPM	=	Beat per Minute
CBFs	=	Ciliary Beating Frequencies
cm	=	Centimeter
COPD	=	Chronic Obstructive Pulmonary Disease
EPP	=	Equal Pressure Point
ERS	=	European Respiratory Society
ERV	=	Expiratory Reserve Volume
$FEF_{25-75\%}$	=	Forced Expiratory Flow between 25% - 75% of FVC
FET	=	Forced Expiratory Technique
FEV_1	=	Forced expiratory Flow in one second
FVC	=	Forced Vital Capacity
GOLD	=	Global Initiative for Chronic Obstructive Lung Disease
HFCWO	=	High Frequency Chest Wall Oscillation
HR	=	Heart Rate
IPV	=	Intrapulmonary Percussion Ventilation
IRV	=	Inspiratory Reserve Volume

LIST OF ABBREVIATIONS (cont.)

kg	=	Kilogram
L/min	=	Liter per minute
Lt	=	Left, Left side
MCC	=	Mucociliary Clearance
MH	=	Manuel Hyperinflation
min	=	Minute
PEF	=	Peak Expiratory Flow
PEFR	=	Peak Expiratory Flow Rate
PEP	=	Positive Expiratory Pressure
PLB	=	Pursed Lips Breathing
PLB&FETs	=	Pursed Lips Breathing with Forced Expiratory Techniques
RAT	=	Radioaerosol Tracer Technique
RIM	=	Resistive Inspiratory Manoeuvres
Rt	=	Right, Right side
SpO2	=	Oxygen Pulse Saturation
TEE	=	Thoracic Expansion Exercise
TIRE	=	The Test of Incremental Respiratory Endurance
TPGLF	=	Two-phase Gas Liquid Flow
wk	=	Week
yr	=	Year

CHAPTER I
INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is defined as "a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases" (1). COPD is a major public health problem. Its prevalence and mortality are increased throughout the world. COPD is expected to increase in prevalence and mortality over the coming decades. There is also projected to be the fifth greatest cause of worldwide burden of disease in 2020 and the third most common cause of death internationally (1, 2). Chronic cough and sputum production are key features of COPD (1, 3). Pathological changes that affect on chronic cough and excessive mucous production are mainly found in the large and small airways. There are increase in the size of the tracheobronchial mucous glands, goblet cell hyperplasia, reduction in ciliated cells with results in its replacement with stratified squamous epithelium in the airway. Large volume of airway mucus becomes to affect mucociliary clearance. Changes of mucus depth, mucus viscoelasticity and interaction between cilia and mucus could lead to mucociliary dysfunction. Chemical and physical alterations render such mucus thicker, more tenacious and therefore less easily cleared by either ciliary action or cough. For this reason, chronic cough and sputum production play an important role in the clinical course of COPD (3-6). They are predictive of frequent COPD exacerbations and those patients who have frequent exacerbations have worse health-related quality of life and a more rapid rate of deterioration in health status (7). In COPD patients with impaired mucociliary transport, airway clearance techniques (ACTs) play an essential role in removing mucus from the lung.

ACTs involve the external application of forces to enhance removal of sputum from the airway (7). In recent years, a variety of techniques for secretion clearance have become available. New modalities include autogenic drainage (AD), active cycle of breathing technique (ACBT), positive expiratory pressure methods, high-frequency airway oscillation (Flutter), high-frequency chest wall oscillation (The Vest), intrapulmonary percussive ventilation (IPV), and mechanical insufflation-exsufflation (the "in-exsufflator") (8-10). Goals of treatment with all airway clearance methods are to improve the clearance of airway secretions, to decrease airway obstruction with improve the homogeneity of ventilation and gas exchange (8, 11, 12). Desirable features of any ACTs relate to its effectiveness in the clinical application. Techniques should also be easy to teach to patients and should be easy for patients to perform independently or with assistance, depending on the patient's age and physical condition. Techniques should not fatigue the patient but should rather be comfortable and time-efficient whenever possible. Cost-effective treatments that rely upon patient participation rather than expensive equipment are even more important in health management (11). Therefore, the possibility of modifying the active form of techniques to facilitate airway clearance is likely to be a topic of great interest.

Different ACTs have developed independently in different parts of the world. The evidence in support of these techniques is variable. Literature is confusing and conflicting (8, 13). However, the results of different studies indicated that active forms of forced expiratory manoeuvres of a "huff" are the most effective part of physiotherapy intervention (7, 8, 10, 14). Therefore, many of the regimens now include the forced expiratory manoeuvres and this has probably increased the effectiveness of airway clearance (8, 14). Physiologically, the concepts of the equal pressure point (EPP) explains the mechanism of the effectiveness of huffing in airway clearance. During a forced expiratory manoeuvre, there are forces which tend to collapse or compress the airways downstream (towards the mouth) of the EPP. This dynamic compression is an essential part of the mechanism of a huff, which are therefore only effective at the compression points ("choke point") downstream of the EPP (14, 15). In addition, the shear forces generated during huffing should reduce mucus viscosity. This together with the high flows generated during a forced

expiratory manoeuvre would be expected to aid mucus clearance and the expectoration of sputum (7, 8, 10).

In 1979, the forced expiration technique (FET) was defined. It typically consists of one or two huffs followed by a period of relaxed, controlled breathing. Breathing control is an essential part of the forced expiration technique to allow relaxation of the bronchial muscles after the forced expiratory manoeuvre of the huff. This combination will bring the secretions further up the bronchial tree without the distress of paroxysmal coughing. Also, the FET may change the position of the equal pressure point in the airways allowing for greater clearance of mucus from further down the airways (9, 11, 15). In 1992, The FET was renamed the active cycle of breathing technique (ACBT) as a mean of emphasizing that the forced exhalations or huffs are to be performed in conjunction with breathing exercises. There are three essential components in a set of cycle; 1) breathing control (BC), 2) thoracic expansion exercises (TEE) and 3) FET (9-11). ACBT begins with BC, which is gentle, relaxed breathing at the patient's own tidal volume and resting respiratory rate. BC is also interspersed throughout the cycle to allow recovery and prevent any increase in airflow obstruction. TEE are deep, slow, relaxed inspirations to inspiratory reserve volume, with or without breath-holds, with quiet, unforced exhalations. These respiration help maximize ventilation via collateral channels. This portion of the cycle aids the problems of asynchronous ventilation and blocked airways. The FET is a series of huffs, usually starting from mid lung volume, slightly above the tidal volume, with an easy active exhalation into the expiratory reserve volume (ERV). The following huffs may start at higher lung volumes (further into the inspiratory reserve volume) and again move into the ERV (10, 16). The theory behind the ACBT includes the benefit of the FET and the improvement of alveolar aeration, which decreases inhomogeneity and improves the driving pressure in alveoli behind blocked airways (9-11). The fluidity of the ACBT allows easy adaptation to patients with different disease states. The cycle is adjusted for each individual patient (10, 16, 17). However, from the various components of the ACBT, only the FET has been systematically evaluated. No controlled data are available to assess the relative contribution of the components of the ACBT (7, 10). To date, the literature of ACBT remains rely heavily

on basic airway physiology of EPP concepts and collateral ventilation to enhance the airway clearance.

One of the concerns regarding the use of breathing techniques is important facets of airway clearance. There are a wide variety of breathing techniques that may be useful adjusts with FET to enhance the movement and expectoration of mucus. Moreover, breathing techniques should also minimize the effort, aid the re-expansion of lung tissue and depend on the patient's condition. The physiotherapy management of stable chronic obstructive pulmonary disease has traditionally focused on a variety of chest clearance techniques and breathing control. Interestingly, breathing retraining has received relatively little attention from the literature search (18). Breathing techniques in COPD patients aim to relieve symptoms and ameliorate adverse physiological effects by: 1) increasing strength and endurance of the respiratory muscles, 2) optimizing the pattern of thoracoabdominal motion and 3) reducing dynamic hyperinflation of the rib cage and improving gas exchange (19). Pursed-lips breathing (PLB) is considered to be the cornerstone of breathing retraining in pulmonary rehabilitation. It works to improve expiration, both by requiring active and prolonged expiration and by preventing airway collapse. It may contribute to alleviating the phenomenon of airway closure and decrease in transpulmonary resistance in COPD patients (19-22). By adjusting the size of the orifice created by their lips, patients can vary the degree to which they can retard expiration. Retarding expiration slows their respiratory rate, reduces the work of breathing, creates a back pressure that prevents collapse of the smaller airways, lessens the probability of air trapping, promotes more effective ventilation and improves exercise tolerance (12, 19, 23). Several investigators had examined the effect of PLB on ventilatory parameters and arterial blood gases in people with COPD (19-21). They uniformly reported that the technique decreased respiratory rate, minute ventilation, and partial pressure of carbon dioxide in arterial blood and increased tidal volume. It was also documented to increase partial pressure of oxygen in arterial blood and the percentage of hemoglobin sites that were bound to oxygen in arterial blood. PLB was reported to decrease dyspnea and may improve exercise tolerance and reduce limitations in activities of daily living (21). Indeed, PLB represents a functional predecessor to many of modern

strategies of applying positive expiratory pressure to the airway. It is believed that the resistance at the mouth during a pursed-lips exhalation transmits back pressure that splints the airways open, preventing compression and premature closure, which is the same principle of operation as the fixed-orifice resistor of positive airway pressure techniques (12, 24). The subject performs a moderately active expiration through the half-opened lips, inducing expiratory mouth pressures of about 5 cmH_2O (19, 20, 24). Thus, the positive expiratory pressure of PLB may be an important additional effect to apply for airway clearance.

Recently, clinical trials of airway clearance techniques in COPD have shown little evidence (7). There has been no evidence that a single airway clearance regimen is effective in COPD. It seems likely that a more complex approach is required into account the heterogeneity of COPD and the specific mechanisms of different ACTs. The selection of an optimal ACTs should take into account its effects on lung volumes, expiratory flow and dynamic airway compression. Therefore, future research should focus on more appropriate matching of the physiological effects of ACTs to the pathophysiological of lung disease in COPD (7). Pursed lip breathing that increase pressure at the mouth could be used to splint open the airways and enhance prolonged expiration. It may facilitate a secondary clearance mechanism known as two-phase gas liquid flow (TPGLF) through the splinting of collapsible airways. This physiological basis of mucus clearance plays an essential role in removing mucus from the lung. Moreover, PLB is expected to reduce dynamic hyperinflation. This will presumably result in the inspiratory muscles working over a more advantageous part of their length-tension relationship, to decrease the elastic work of breathing and to increase alveolar gas refreshment. These changes might have contribute to the decrease in dyspnea sensation. Nevertheless, there are no studies of COPD patients using PLB combined with FET (PLB&FETs) focus on the improvement of airway clearance. It is unknown whether effects on secretion clearance from airways or whether effects on associated symptoms in patients with COPD. This idea of study is based on the assumption that the combinations of PLB&FETs may be an effective pattern of airway clearance and that benefits may extend to relieve dyspnea symptoms in COPD patients. Therefore, this study aims to investigate the efficacy of PLB&FETs and

ACBT for the removal of pulmonary mucus clearance in healthy subjects and investigate the effective of both techniques in COPD patients.

Purposes of the Study

General Objective

The purposes of this study are to compare the efficacy of pursed lips breathing with forced expiration techniques (PLB&FETs) and active cycle of breathing technique (ACBT) on pulmonary mucus clearances in healthy subjects and to investigate the effectiveness of PLB&FETs and ACBT in patients with chronic obstructive pulmonary disease.

Specific Objectives for the First Study

1. To compare the percentage retention of radioactivity in the central, intermediate, peripheral and whole zone of the right lung among the control (normal breathing), PLB&FETs and ACBT during the experimental period
2. To compare heart rate, percentage of oxygen pulse saturation among the control (normal breathing), PLB&FETs and ACBT during the experimental period
3. To compare the percent change of peak expiratory flow rate and Modified Borg scores of dyspnea among the control (normal breathing), PLB&FETs and ACBT at before and immediate after the experimental period

Specific Objectives for the Second Study

1. To compare pulmonary function test parameters; forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), ratio of FEV1/FVC, forced expiratory flow between 25% and 75% of the FVC ($FEF_{25-75\%}$) and peak expiratory flow (PEF) between PLB&FETs and ACBT group on the 1^{st}, 7^{th}, 14^{th} day of the study
2. To compare peak expiratory flow rate (PEFR), sputum volume and Modified Borg score of dyspnea between PLB&FETs and ACBT group at the 1^{st}, 2^{nd} week of the study
3. To compare total score of Modified patient evaluation questionnaire between PLB&FETs and ACBT group on the 1^{st}, 7^{th}, 14^{th} day of the study

4. To compare total scores of Modified patient satisfaction questionnaire between PLB&FETs and ACBT group at the 14th day of the study

Parameters in the Study

The First Study

1. The percentage retention of radioactivity in the right lung
2. Heart rate (HR)
3. Percentage of oxygen pulse saturation (% SpO_2)
4. Peak expiratory flow rate (PEFR) by peak flow meter
5. Modified Borg score of dyspnea

The Second Study

1. Pulmonary function test parameters :
   - forced vital capacity (FVC)
   - forced expiratory volume in 1 second (FEV_1)
   - ratio of FEV_1/ FVC
   - Mean forced expiratory flow between 25% and 75%of FVC($FEF_{25-75\%}$)
   - Peak expiratory flow rate (PEF)
2. Peak expiratory flow rate (PEFR) by peak flow meter
3. Sputum volume
4. Modified Borg score of dyspnea
5. Modified patients evaluation questionnaire
6. Modified patients satisfaction questionnaire

Scope of the Study

In the first study, all subjects who participated in the study are healthy subject with no previous history of chronic respiratory disease. Each subject attends three separate occasions within three days and undergo an identical experimental procedure with the three treatment protocols with control (normal breathing), PLB&FETs and ACBT.

The second study focused on stable COPD of stage I- stage III according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) updated 2006 criteria. Each patient is randomly assigned to one of the two treatment groups. One group of patients received PLB&FETs, while the other group underwent ACBT. They performed ACTs in 30 minute per session, twice-daily session for 14 consecutive days. The effects of both ACTs are examined on 1^{st}, 7^{th}, 14^{th} day of the study.

The study protocol was approved by the Ethics Committee of Faculty of Medicine Siriraj Hospital, Mahidol University, Committee on Human Rights Related to Researches Involving Human Subjects, Faculty of Medicine Ramathibodi Hospital, Mahidol University and the Ethics Committee of Chest Disease institute, Department of Medical Services, Ministry of Public Health .

Hypotheses of the Study

The First Study

1. The percentage retention of radioactivity in the central, intermediate, peripheral and whole zones of the right lung would be significantly different among the control (normal breathing), PLB&FETs and ACBT during the experimental period
2. Heart rate, percentage of oxygen pulse saturation would be significantly different among the control (normal breathing), PLB&FETs and ACBT during the experimental period
3. The percent change of peak expiratory flow rate and Modified Borg scores of dyspnea would be significantly different among the control (normal breathing), PLB&FETs and ACBT at before and immediately after the experimental period.

The Second Study

1. Pulmonary function test parameters; FVC, FEV_1, ratio of FEV1/FVC, $FEF_{25-75\%}$ and PEF in patients who receive PLB&FETs would be significantly different from those who obtain ACBT on the 1^{st}, 7^{th}, 14^{th} day of the study
2. Peak expiratory flow rate, sputum volume and Modified Borg scores of dyspnea in patients who receive PLB&FETs would be significantly different from those who obtain ACBT at 1^{st}, 2^{nd} week of the study
3. Total scores of Modified patient evaluation questionnaire in patients who receive PLB&FETs would be significantly different from those who obtain ACBT at the 1^{st}, 7^{th}, 14^{th} day of the study
4. Total scores of Modified patient satisfaction questionnaire in patients who receive PLB&FETs would be significantly different from those who obtain ACBT at the end of the study

Advantages of the Study

1. The results of the first study could be the ideal efficacy of normal breathing, PLB&FETs and ACBT on the alteration of pulmonary mucus clearance in healthy subjects and might be evidence support the effects of PLB&FETs and ACBT on mucus clearance.
2. The results of the second study could be used as a guideline for airway clearance management of chronic obstructive pulmonary disease patients.
3. This study might support the effectiveness of PLB&FETs and ACBT as an adjunctive therapy to chest physical therapy program in chronic obstructive pulmonary disease

CHAPTER II
LITERATURE REVIEW

2.1 Chronic Obstructive Pulmonary Disease

2.1.1 Prevalence of Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (COPD) is a major public health problem throughout the world. A World Health Organization (WHO) /World Bank Study estimated the worldwide prevalence of COPD in 1990 to be 9.33/1000 in men and 7.33/1000 in women. COPD was estimated to be the sixth most common cause of death globally, and the twelfth most common cause of burden of disease worldwide. Furthermore, COPD is expected to increase in prevalence and mortality over the coming decades. For example, of the four leading causes of death in the USA, COPD is the only one that continues to increase in prevalence. COPD is also projected to be the fifth greatest cause of worldwide burden of disease in 2020, and the third most common cause of death internationally (25, 26). Regional COPD working groups in 2003 used a COPD prevalence model to estimate the prevalence of COPD in 12 Asia-Pacific countries and regions. The results shown that the total number of moderate to severe COPD cases among individuals 30 years and older within all the 12 identified countries, is 56.6 million. This translates to a mean COPD prevalence rate of 6.3% for the region. Table 2.1 shows the data for each country. The COPD prevalence rates vary twofold between the 12 Asian countries and range from a minimum of 3.5% (Hong Kong & Singapore) to a maximum of 6.7% (Vietnam) (27).

A recent study in Thailand estimate the prevalence of COPD in 1998 to be 2075 per 100000 people at risk (smoker aged $\geq$ 40 years), but this estimate is based on the number of people hospitalized with COPD and represents only the prevalence of moderate to severe disease (27, 28).

Table 2.1 Model projections of the prevalence of moderate to severe COPD in those 30 years and older for 12 countries in the Asia-Pacific region

Country	Moderate/ severe COPD cases	Prevalence
1. Australia	553,000	4.7 %
2. China	38,160,000	6.5 %
3. Hong Kong	139,000	3.5 %
4. Indonesia	4,806,000	5.6 %
5. Japan	5,014,000	6.1 %
6. South Korea	1,467,000	5.9 %
7. Malaysia	443,000	4.7 %
8. Philippines	1,691,000	6.3 %
9. Singapore	64,000	3.5 %
10. Taiwan	638,000	5.4 %
11. Thailand	1,502,000	5.0 %
12. Vietnam	2,063,000	6.7 %
Total	56,553,000	6.3 %

References : COPD prevalence in 12 Asia-Pacific countries and regions: Projections based on the COPD prevalence estimation model.Regional COPD working group. Respirology 2003;8:192-8 (27).

2.1.2 Definition

Chronic obstructive pulmonary disease (COPD),sometimes also called chronic obstructive lung disease (COLD), is a group of common chronic respiratory disorders that are characterized by progressive tissue degeneration and obstruction in the airways of the lungs (5, 29). COPD is characterized by airflow obstruction with breathing-related symptoms such as chronic cough, exertional dyspnea, expectoration and wheeze (29).

Several different definitions exist for COPD. The American Thoracic Society (ATS) defined COPD as “a disease state characterized by the presence of airflow limitation due to chronic bronchitis or emphysema; the airflow obstruction is generally progressive, may be accompanied by airway hyperreactivity and may be partially reversible”. The European Respiratory Society (ERS) defined COPD as“ reduced maximum expiratory flow and slow forced emptying of the lungs, which is slowly progressive and mostly irreversible to present medical treatment” (29). In the

Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines, COPD is defined as "a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases"(1). The National Collaborating Centre for Chronic Conditions in UK defined COPD as "a disease is characterised by airflow obstruction. The airflow obstruction is usually progressive, not fully reversible and does not change markedly over several months" (30).

2.1.3 Diagnosis

A clinical diagnosis of COPD should be considered in any patient who has dyspnea, chronic cough or sputum production and/or a history of exposure to risk factors for the disease. The diagnosis should be confirmed by spirometry. The presence of a post- bronchodilator $FEV_1 < 80\%$ of the predicted value in combination with an $FEV_1/FVC < 70\%$ confirms the presence of airflow limitation that is not fully reversible. Where spirometry is unavailable, the diagnosis of COPD should be made using all available tools. Clinical symptoms and signs, such as abnormal shortness of breath and increased forced expiratory time, can be used to help with diagnosis (1, 30).

The overall guideline recommendations (2006 Update) of Global Initiative for Chronic Obstructive Lung Disease (GOLD) reported the key points of the component of assess and monitor disease following (1):

- A clinical diagnosis of COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease. The diagnosis should be confirmed by spirometry.
- For the diagnosis and assessment of COPD, spirometry is the gold standard as it is the most reproducible, standardized, and objective way of measuring airflow limitation. A post-bronchodilator $FEV_1/FVC < 0.70$ confirms the presence of airflow limitation that is not fully reversible.

- Health care workers involved in the diagnosis and management of COPD patients should have access to spirometry.
- Assessment of COPD severity is based on the patient's level of symptoms, the severity of the spirometric abnormality, and the presence of complications.
- Measurement of arterial blood gas tensions should be considered in all patients with $FEV_1 < 50\%$ predicted or clinical signs suggestive of respiratory failure or right heart failure.
- COPD is usually a progressive disease and lung function can be expected to worsen over time, even with the best available care. Symptoms and objective measures of airflow limitation should be monitored to determine when to modify therapy and to identify any complications that may develop.
- Comorbidities are common in COPD and should be actively identified. Comorbidities often complicate the management of COPD, and vice versa.

Key indicators for considering a diagnosis of COPD (1):

Consider COPD, and perform spirometry, if any of these indicators are present in an individual over age 40. These indicators are not diagnostic themselves, but the presence of multiple key indicators increases the probability of a diagnosis of COPD. Spirometry is needed to establish a diagnosis of COPD.

- Dyspnea that is: progressive (worsens over time), usually worse with exercise, persistent (present every day), described by the patient as an "increased effort to breathe," "heaviness," "air hunger," or "gasping".
- Chronic cough: may be intermittent and may be unproductive.
- Chronic sputum production: Any pattern of chronic sputum production may indicate COPD.
- History of exposure to risk factors, especially: tobacco smoke, occupational dusts and chemicals, smoke from home cooking and heating fuels.

2.1.4 Spirometric Classification of Severity and Stages of COPD

For educational reasons, a simple spirometric classification of disease severity into four stages is recommended (see Table 2.2). Spirometry is essential for diagnosis and provides a useful description of the severity of pathological changes in COPD. Specific spirometric cut-points (e.g,post-bronchodilator FEV_1/FVC ration < 0.70 or FEV_1 <80, 50 ,or 30% predicted) are used for purposed of simplicity: these cut-points have not been clinically validated (1).

Table 2.2 Spirometric classification of COPD severity based on post-bronchodilator FEV_1

Stage I : Mild	$FEV_1/FVC < 0.70$
	$FEV_1 \geq 80\%$ predicted
Stage II : Moderate	$FEV_1/FVC < 0.70$
	$50\% \leq FEV_1 < 80\%$ predicted
Stage III : Severe	$FEV_1/FVC < 0.70$
	$30\% \leq FEV_1 < 50\%$ predicted
Stage IV :Very Severe	$FEV_1/FVC < 0.70$
	$FEV_1 < 30\%$ predicted or FEV_1 <50% predicted plus chronic respiratory failure

Reference: Global Initiative for Chronic Obstructive Lung Disease (GOLD). Executive summary: Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease- updated 2006. Update of the Management Sections, GOLD website (www.goldcopd.com). Date updated: Aug 2007 (1).

Stage I: Mild COPD – Characterized by mild airflow limitation ($FEV_1/FVC < 0.70$; $FEV_1 \geq 80\%$ predicted). Symptoms of chronic cough and sputum production may be present, but not always. At this stage, the individual is usually unaware that his or her lung function is abnormal.

Stage II: Moderate COPD – Characterized by worsening airflow limitation ($FEV_1/FVC < 0.70$; $50\% \leq FEV_1 < 80\%$ predicted), with shortness of breath typically developing on exertion and cough and sputum production sometimes also

present. This is the stage at which patients typically seek medical attention because of chronic respiratory symptoms or an exacerbation of their disease.

Stage III: Severe COPD – Characterized by further worsening of airflow limitation (FEV_1/FVC <0.70; 30% ≤ FEV_1 < 50% predicted, greater shortness of breath, reduced exercise capacity, fatigue, and repeated exacerbations that almost always have an impact on patients'quality of life.

Stage IV: Very Severe COPD – Characterized by severe airflow limitation (FEV_1/FVC <0.70; FEV_1 < 30% predicted or FEV_1 < 50% predicted plus the presence of chronic respiratory failure). Respiratory failure is defined as an arterial partial pressure of O_2 (PaO_2) less than 8.0 kPa (60 mmHg) with or without arterial partial pressure of CO_2 ($PaCO_2$) greater than 6.7 kPa (50 mmHg) while breathing air at sea level. Respiratory failure may also lead to effects on the heart such as cor pulmonale (right heart failure). Clinical signs of cor pulmonale include elevation of the jugular venous pressure and pitting ankle edema. Patients may have Stage IV even if the FEV_1 is > 30% predicted, whenever these complications are present. At this stage, quality of life is very appreciably impaired and exacerbation may be life threatening (1).

2.1.5 Pathogenesis of COPD

COPD is characterized by chronic inflammation throughout the airways, parenchyma, and pulmonary vasculature. Macrophages,T lymphocytes (predominately $CD8^+$), and neutrophils are increased in various parts of the lung. Activated inflammatory cells release a variety of mediators-including leukotriene B_4 (LTB_4) ,interleukin-8 (IL-8), tumor necrosis factor-α, (TNF- α), and others- capable of damaging lung structures or sustaining neutrophilic inflammation. In addition to inflammation, two other processes thought to be important in the pathogenesis of COPD are an imbalance of proteinases and antiproteinases in the lung, and oxidative stress. Inflammation of the lungs is caused by exposure to inhaled noxious particles and gases. Cigarette smoke can induce inflammation and directly damage the lungs (3, 26).

2.1.6 Pathology of COPD

Pathologic changes characteristic of COPD are found in the central airways, peripheral airways, lung parenchyma and pulmonary vasculature. In the central airways- the trachea, bronchi, and bronchioles greater than 2 to 4 mm in internal diameter-inflammatory cells infiltrate the surface epithelium. Enlarged mucus-secreting glands and an increase in the number of goblet cells are associated with mucus hypersecretion. In the peripheral airways- small bronchi and bronchioles that have an internal diameter of less than 2 mm-chronic inflammation leads to repeated cycles of injury and repair of the airway wall. The repair process results in a structural remodeling of the airway wall, with increasing collagen content and scar tissue formation, that narrows the lumen and produced fixed airway obstruction.

Destruction of the lung parenchyma in patients with COPD typically occurs as centrilobular emphysema. This involves dilatation and destruction of the respiratory bronchioles. These lesions occur more frequently in the upper lung regions in milder cases, but in advanced disease they may appear diffusely throughout the entire lung and also involve destruction of the pulmonary capillary bed. An imbalance of endogenous proteinases and antiproteinases in the lung resulting from genetic factors or the action of inflammatory cells and mediators, is thought to be a major mechanism behind emphysematous lung destruction. Oxidative stress, another consequence of inflammation, may also contribute.

Pulmonary vascular changes in COPD are characterized by a thickening of the vessel wall that begins early in the natural history of the disease. Thickening of the intima is the first structural change, followed by an increase in smooth muscle and the infiltration of the vessel wall by inflammatory cells. As COPD worsens, greater amounts of smooth muscle, proteoglycans, and collagen further thicken the vessel wall (3, 26).

2.1.7 Pathophysiology of COPD

Pathologic changes in the lungs lead to corresponding physiologic changes characteristic of the disease, including mucus hypersecretion, ciliary dysfunction, airflow limitation, pulmonary hyperinflation, gas exchange abnormalities, pulmonary hypertension, and cor pulmonale. They usually develop in this order over the course of the disease. Mucus hypersecretion and ciliary dysfunction lead to chronic cough and sputum production. These symptoms can be present for many years before other symptoms or physiologic abnormalities develop. Expiratory airflow limitation, best measured through spirometry, is the hallmark physiologic change of COPD and the key to diagnosis of the disease. It is primarily caused by fixed airway obstruction and the consequent increase in airway resistance. Destruction of alveolar attachments, which inhibits the ability of the small airways to maintain patency, plays a smaller role. In advanced COPD, peripheral airway obstruction, parenchymal destruction, and pulmonary vascular abnormalities reduce the lung's capacity for gas exchange, producing hypoxemia and ,later on, hypercapnia. Pulmonary hypertension,which develops late in the course of COPD, is the major cardiovascular complication of COPD and is associated with the development of cor pulmonale and a poor diagnosis (3, 26).

COPD is a nonspecific term referring to a set conditions that develop progressively as a result of various disease processes, COPD most commonly refers to chronic bronchitis, emphysema and a subset of patients with asthma, and these conditions can be present with or without substantial impairment. Emphysema and chronic bronchitis are often clinically grouped together and referred to as COPD, since many patient have overlapping features of damage at both the acinar level (emphysema) and bronchial level (bronchitis), almost certainly because one extrinsic trigger-cigarette smoking-is common to both. Although asthma (reversible airway hyperreactivity) is a distinct disorder, it may be a component of COPD in some patients (3, 26, 29).

2.1.8 Emphysema

Emphysema is a condition of the lung characterized by abnormal permanent enlargement of the airspaces distal to the terminal bronchiole, accompanied by destruction of their walls and without obvious fibrosis (3). The ensuing loss of lung elastic recoil and intraluminal pressure in the terminal airways causes small airways to lose their patency, especially during forced expiratory maneuvers. The collapse of these airways causes airflow limitation independent of exertion (29). Emphysema is classified according to its anatomic distribution within the lobule. There are four major types:1) centriacinar, 2) panacinar, 3) paraseptal, 4) irregular. Centriacinar emphysema is far more common than the panacinar form, constituting more than 95% of cases. Clinical management does not rely on precise anatomic diagnosis and classification (3).

Pathogenesis & Pathophysiology : The genesis of the emphysema, the most plausible hypothesis to account for the destruction of alveolar walls is the protease-antiprotease mechanism, aided and abetted by oxidant-antioxidant imbalance (Figure 2.1) (3). The protease-antiprotease theory holds that alveolar wall destruction results from an imbalance between proteases (mainly elastase) and antiproteases in the lung, which is an enzyme that digests elastin, are released from polymorphonuclear leukocytes (i.e.,neutrophils), alveolar macrophages, and other inflammatory cells. Normally,the lung is protected by antiprotease enzymes including α_1-antitrypsin. α_1–AT (which is synthesized in the liver and is present in serum, tissue fluids, and macrophages) is a major inhibitor of proteases secreted by neutrophils during inflammation. In smoker in whom COPD develops, antiprotease production and release may be inadequate to neutralize the excess protease production such that the process of elastic tissue destruction goes unchecked. A hereditary deficiency in α_1–antitrypsin accounts for approximately 1% of all cases of COPD and is more common in young persons with emphysema. An α_1–antitrypsin deficiency is inherited as an autosomal recessive disorder. Smoking and repeated respiratory tract infections, which also decrease α_1–antitrypsin levels contribute to the risk of emphysema in persons with an α_1–antitrypsin deficiency. Thus, emphysema is seen to result from the destructive effect of high protease activity in subjects with low antiprotease activity. Smoking also

plays a seminal role in perpetuating the oxidant-antioxidant imbalance in the pathogenesis of emphysema. Normally, the lung contains a healthy complement of antioxidants (superoxide dismutase, glutathione) that keep oxidative damage to a minimum. Tobacco smoke contains abundant reactive oxygen species (free radicals), which deplete these antioxidant mechanisms, thereby inciting tissue damage (3, 5, 31).

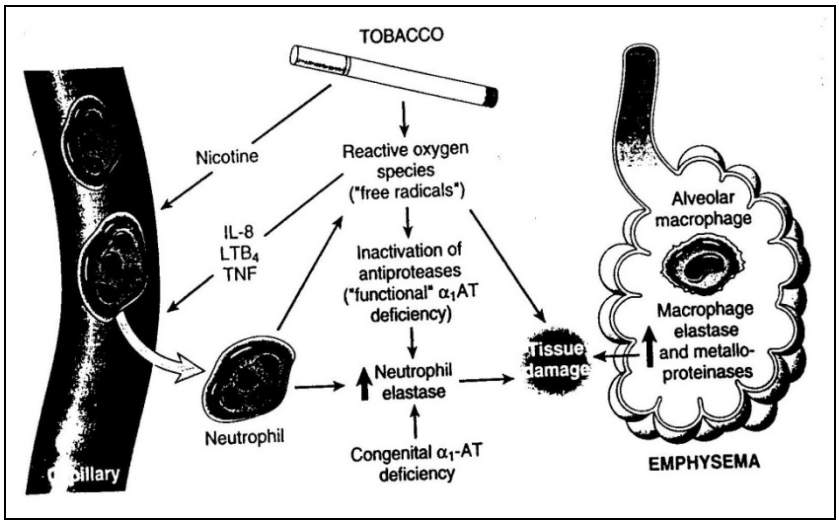

Figure 2.1 Pathogenesis of emphysema. The protease-antiprotease imbalance and oxidant-antioxidant imbalance are additive in their effects and contribute to tissue damage. α_1–antitrypsin (α_1–AT) deficiency can be either congenital or "functional" as a result of oxidative inactivation. [From : Kumar V,Abbas AK,Fausto N. Robbins and Cotran: Pathologic basis of disease. International ed. Philadelphia. Elsevier Saunders, 2005. P720 (3)]

The changes in the lung tissue have many effects on lung function (5):

- The breakdown of the alveolar wall results in :
  - loss of surface area for gas exchange
  - loss of pulmonary capillaries, affecting perfusion and the diffusion of gases.
  - loss of elastic fibers, affecting the ability of the lung to recoil on expiration
  - altered ventilation-perfusion ratio as various changes occur in the alveoli
  - decreased support for other structures such as the small bronchi, which often leads to collapse of the walls and additional obstruction of airflow during expiration

- Fibrosis and thickening of the bronchial walls have resulted from chronic irritation and the frequent infections associated with smoking and increased mucus production. These conditions lead to narrowed airways, weakened walls, and interference with passive expiratory air flow.
- Progressive difficulty with expiration leads to :
  - air trapping and increased residual volume
  - overinflation of the lungs
  - fixation of the ribs in an inspiratory position, and an increased anterior posterior diameter of the thorax (barrel chest)
  - diaphragm appears flattened on x-rays
- With advance emphysema, and significant loss of tissue :
  - adjacent damaged alveoli coalesce, and the lung appears full of large holes called blebs or bullae
  - large blebs near the surface of the lung may rupture, resulting in pneumothorax
  - hypercapnia becomes marked
  - hypoxic drive for inspiration develops as the patient's respiratory control adapts to a chronic elevation of carbon dioxide levels and hypoxia become the driving force for respiration
  - infections develop frequently because secretions are more difficult to remove past obstructions, and airway defenses are impaired
  - pulmonary hypertension and cor pulmonale may develop in a late stage as the pulmonary blood vessels are destroyed and hypoxia causes pulmonary vasoconstriction. The increased pressure in the pulmonary circulation increases resistance to the right ventricles, and eventually the ventricle fails. Many patients with respiratory disease manifest signs of heart failure.

Signs and symptoms : The onset of emphysema is insidious (5).

- Dyspnea occurs first on exertion and then progresses until it is marked even at rest.
- Hyperventilation with a prolonged expiratory phase, use of the accessory muscles, and hyperinflation leading to development of a "barrel chest" mark the ventilation difficulty. Typical posture is a sitting position, leaning forward, to facilitate

breathing. The chest is hyperresonant on percussion. Hyperventilation maintains adequate oxygen levels until later stages.

- Anorexia and fatigue contribute to weight loss.
- Clubbed fingers and secondary polycythemia may develop as compensations.

2.1.9 Chronic Bronchitis

Chronic bronchitis, which is defined in clinical terms, is the presence of a chronic productive cough for 3 months in each of 2 successive years. Airway obstruction is caused by inflammation of the major and small airways and nonspecific bronchial hyperreactivity associated with chronic bronchitis (29, 31).

Pathogenesis & Pathophysiology : The primary or initiating factor in the genesis of chronic bronchitis appears to be chronic irritation by inhaled substances such as tobacco smoke (90% of patients are smokers) and grain, cotton, and silica dust. Bacterial and viral infections are important in triggering acute exacerbation of the disease. Both sexes and all ages may be affected, but chronic bronchitis is most frequent in middle-aged men. Chronic bronchitis is 4 to 10 times more common in heavy smokers regardless of age, sex, occupation and place of dwelling (Figure 2.2) (3).

The earliest feature of chronic bronchitis is hypersecretion of mucus in the large airways, associated with hypertrophy of the submucosal glands in the trachea and bronchi. Proteases released from neutrophils, such as neutrophil elastase, cathepsin, matrix metalloproteinases, stimulate this mucus hypersecretion. There is also a marked increase in goblet cells of small airways-small bronchi and bronchioles-leading to excessive mucus production. Both the submucosal gland hypertrophy and the increase in goblet cells are a protective metaplastic reaction against tobacco smoke or other pollutants. Inflammation and obstruction, repeated infections and chronic coughing characterize bronchitis as the following occur (3, 5, 31) :

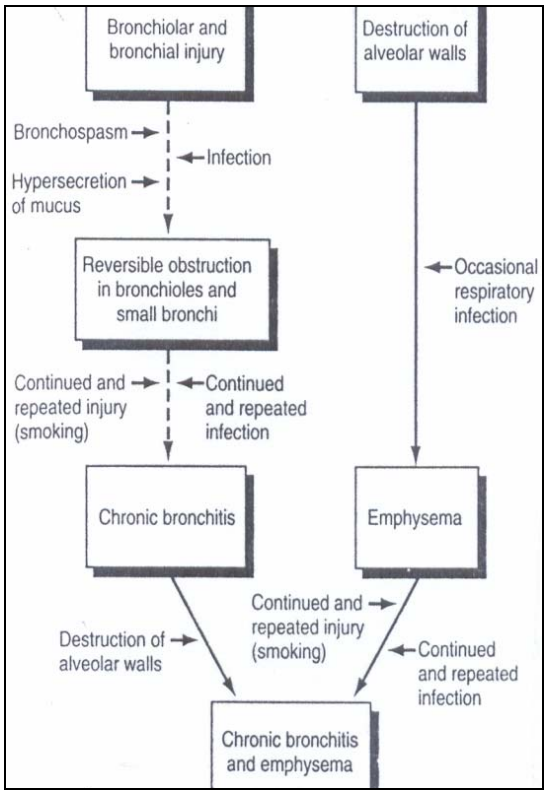

Figure 2.2 Schematic representation of evoluation of chronic bronchitis (left) and emphysema (right). Although both can culminate in chronic bronchitis and emphysema, the pathways are different, and either one may predominate. The dashes arrows on the left indicate that in the natural history of chronic bronchitis, it is not known whether there is a predictable progression from obstruction in small airways to chronic (obstructive) bronchitis. [From: Kumar V, Abbas AK,Fausto N. Robbins and Cotran: Pathologic basis of disease.International ed. Philadelphia. Elsevier Saunders,2005.P723 (3)]

- The mucosa is inflamed and swollen.
- There is hypertrophy and hyperplasia of the mucous glands, and increased secretions are produced. The number of goblet cells is increased, and there is decreased ciliated epithelium.
- Chronic irritation and inflammation lead to fibrosis and thickening of the bronchial wall and further obstruction. Secretions pool distal to obstructions and are difficult to remove.
- Oxygen levels are low. The typical clinical presentation of lower oxygen levels, cyanosis and edema, the “blue bloater” of bronchitis.
- Severe dyspnea and fatique interfere with nutrition, communication, and daily activities, leading to general debilitation.
- Pulmonary hypertension and cor pulmonale are common.

Signs and symptoms : Constant productive cough is the significant indicator of chronic bronchitis, as is tachypnea and shortness of breath. Frequently secretions are thick and purulent. Cough and rhonchi are usually more severe in the morning because the secretions have pooled during sleep. Airway obstruction leads to hypoxia and eventually to cyanosis as well as to hypercapnia. Secondary polycythemia, severe weight loss and signs of cor pulmonale often develop as the vascular damage and pulmonary hypertension progresses (see Table 2.3) (3, 5, 31).

Table 2.3 Characteristics of chronic bronchitis and emphysematous types of chronic Obstructive lung disease

Characteristic	**Type A Pulmonary Emphysema ("Pink Puffer")**	**Type B Chronic Bronchitis ("Blue Bloaters")**
Smoking history	Usual	Usual
Age of onset	40 to 50 years of age	30 to 40 years of age; disability in middle age
Clinical features		
Barrel chest	Often dramatic	May be present
Weight loss	May be severe in advanced dis.	Infrequent
Shortness of breath	May be absent early in disease	Predominate early symptom, insidious in onset, exertional
Decreased breath sound	Characteristic	Variable
Wheezing	Usually absent	Variable
Rhonchi	Usually absent or minimal	Often prominent
Sputum infections	May be absent or may develop late in the course	Frequent early manifestation, frequent aburdant purulent sputum
Cyanosis	Often absent, even late in the disease when there is low PO_2	Often dramatic
Blood gases	Relatively normal until late in the disease process	Hypercapnia may be present Hypoxemia may be present
Cor pulmonale	Only in advanced cases	Frequent peripheral edema
Polycythemia	Only in advanced cases	Frequent
Prognosis	Slowly debilitating disease	Numerous life-threatening episode due to acute exacerbations

Reference: Porth CM, Kunert MP. Pathophysiology: Concepts of altered health states. 6nd ed. Philadelphia. Lippincott Williams &Wilkins,2002. P648 (31).

2.2 Airway Mucus Clearance

Ventilation of between 12,000 and 24,000 L/day exposes the lungs to a large amount of potential damaging agents, including pollutants, viruses and bacteria, organic agents. The body has developed reflex responses, such as coughing, sneezing, bronchoconstriction, altered breathing patterns and increased mucous production, to counteract the effects of these possible damaging agents. Another important defense mechanism that uses cellular strategies is the mucociliary apparatus of the tracheobronchial tree (Fig 2.3) (32).

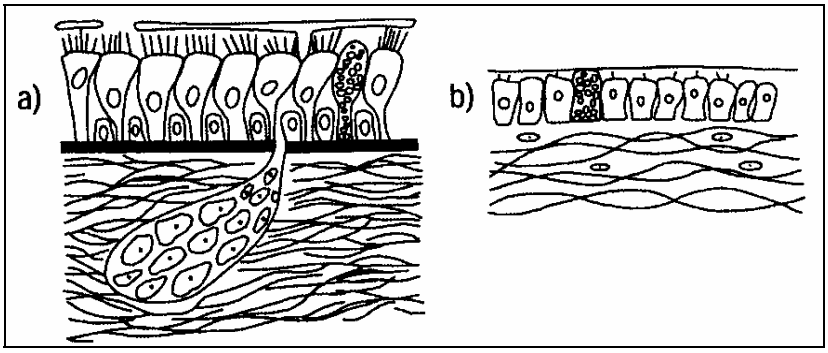

Figure 2.3 –Schematic representation of the normal adult mucociliary apparatus in: a) central (e.g. trachea), b) peripheral (e.g. terminal bronchioles) airways. The components of the apparatus in the central airway are, from top to bottom, the mucus layer (gel), periciliary fluid layer (sol), surface epithelial layer consisting of ciliated and nonciliated (basal and secretory granule containing goblet) cells and submucosal gland. By contrast, in the peripheral airways, there is no mucus layer gland, the epithelium is flat and less densely ciliated and mucus-producing cells are replaced with other secretory (Clara) cells.

Mucus secretion and clearance are extremely important for airway integrity and pulmonary defense. It has been estimated that mucus secretion volume is between 10 and 100 ml per day in health. Respiratory tract secretions consist of mucus, surfactant, and periciliary fluid (33). The airway surface fluid is present as a bilayer, with a superficial gel or mucous layer and a layer of periciliary fluid interposed between the mucous layer and the epithelium. A thin layer of surfactant separates the mucous and periciliary fluid layers. The mucous layer extends from the intermediate airway to the upper airway and is approximately 2-10 micro gmm thick in the trachea. Airway mucus is the secretory product of the goblet cells and the submucosal glands.

Mucus is transported from the lower respiratory tract into the pharynx by air flow and mucociliary clearance (16, 33, 34).

2.2.1 Air Flow

Mucus is moved by 3 mechanisms of air flow. First, slug flow describes the means by which a semi-solid mucus plug obstructing or partially obstructing an airway can be pushed from behind by air flow. Second, annular flow describes mucus moving along the walls of the airway, either being pulled along by expiratory air flow or transported by cilia. Third, mist flow describes aerosolized mucus that is exhaled as suspended droplets. Slug and annular flow account for the majority of airway secretion clearance (16, 34).

2.2.2 Mucociliary Clearance

Mucociliary clearance (MCC) comprises the cephalad movement of mucus caused by the cilia lining the conducting airways until it can be expectorated or swallowed. MCC is a very complex process in which many variables are involved. The structure, number, movement and co-ordination of the cilia present in the airways as well as the amount, composition and rheological properties of the periciliary and mucus layer are determinants of MCC (34, 35).

Structure of the cilia

The two human lungs contain ~ 0.5 m^2 of ciliated epithelia, with a total number of cilia in the order of $3x10^{12}$. The tracheobronchial tree is formed by a pseudostratified columnar epithelium, on which surface cilia are found down to about the sixteenth bronchial division. The ciliated cells, characterized by their long cytoplasmic projections and numerous microvilli, have about 200 cilia/cell. Each cilium has a length of 5-7 μm in the trachea and 2-3 μm in the seventh airway generation and a diameter of 0.25-0.33 μm. Cilia have a 9+2 ciliary axoneme (Figure 2.4), which comprises nine interconnected doublet microtubules surrounding and joined by cross-bridges to two centrally positioned microtubules. Each doublet is formed by an A-subfibre and a B-subfibre or microtubule. Subfibre A is a complete microtubule whereas subfibre B has a smaller number of protofilaments, but shares

part of the A subfibre as well. Paired adenosine triphosphatase (ATPase) or dynein arms are located on subfibre A. Adjacent to these dynein arms, subfibre A also has radial links or spokes. These structures join the outer doublets to the so-called sheath which surrounds the two central microtubues. Each radial link terminates in a head near the surface of the central sheath. Interdoublet links or nexin links appear to connect the terminal portion of the inner arm to the adjacent B-subfibre (32, 33, 35).

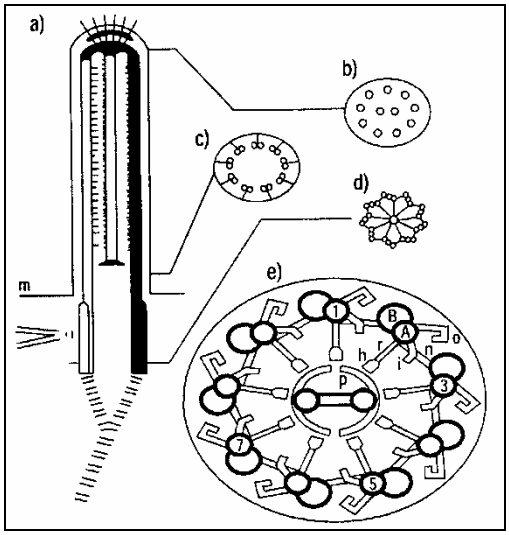

Figure 2.4 – a) Longitudinal; and b-e) cross-sectional views of the structure of a cilium from the respiratory tract. The ciliary shaft, which is surrounded by a membrane continuous with that around the cell (m), terminates in a crown of "claws" attached to a dense cap at the tipe of the longitudinal microtubules of the axoneme (a). The cross-sectional arrangement of a cilium (e) including the arrangement and conventional numbering of 9 doublets. The doublets are connected by nexin links (n). The A-subfibre (A) of each doublet bears outer (o)and inner (i) dynein arms, projecting towards the next doublet. Radial spokes (r) with dilated heads (h) can attach to projections (p) associated with the central microtubules. B: B-subfibre. Changes in microtubules pattern at different levels are shown b-d. (33)

Movement and co-ordination of the cilia in the respiratory tract

Mucus is propelled by ciliary movement. Cilia start moving from the rest position by bending sideways and backwards. This is called the recovery stroke. During this recovery stroke, ciliary movement takes place near the cell surface (Figure 2.5). The recovery phase amounts to three-quarters of the cycle time. This is followed by an effective stroke during which the cilia move in a plane perpendicular to the cell surface. This phase ends with the cilium bent over in its rest

position and with its tip pointing in the direction of propulsion. The normal beating of cilia results from active sliding movements between adjacent doublets of the axoneme. This sliding is powered by an adenosine triphosphate (ATP)-driven mechanochemical cycle in which the dynein arms of doublet interact with successive binding sites along B-microtubule of an adjacent doublet. When many cilia interfere with their neighbors in such a way, their beating will become organized into coordinated metachronal waves for propagation. A wide range of ciliary beating frequencies (CBFs) in the central airways of mammals, including humans, have been reported. For example, CBF in rabbit tracheal explants to be 11 Hz, rat tracheal explants varied between 18.3-22.4 Hz, mean CBF in hamster tracheal rings was 16.1 Hz, CBF in healthy subjects (in vivo) with a range of 12-15 Hz. (33, 35)

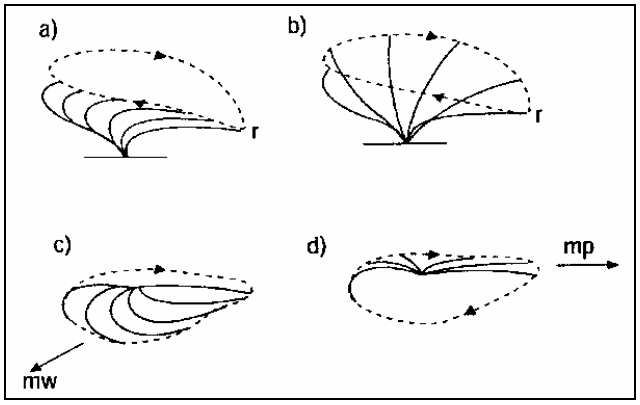

Figure 2.5 – Schematic representation of the beat cycle of a rabbit tracheal cilium as seen: a,b) from the side; and c,d from above. In the recovery stroke (a,c), the cilium starts moving from the resting position (r) and unrolls clockwise (a) to the left. In the effective stroke (b,d), it remains extended and bends over to reach the resting position, to the right. Mucus is propelled (mp) towards the right, and the metachronal wave (mw) is propagated backwards and towards the left (33)

Respiratory mucus

Composition of respiratory mucus

Mucus is composed of ~ 1% by weight of salts and other dialyzable components, 0.5-1 % free protein, a similar proportion of carbohydrate-rich glycoproteins (also called mucins or mucoproteins) and $\geq$ 95% water. Mucus behaves as a viscoelastic gel, consisted of water and high relative molecular mass cross-linked glycoproteins mixed with serum and cellular proteins, including albumin, enzymes and

immunoglobulins and lipids. Mucus glycoproteins are composed of protein and carbohydrate components. A high density of oligosaccharide units attached to a long polypeptide chain is a predominant feature of most mucus glycoproteins and might be expected to contribute greatly to the biological properties of these molecules. Airway mucus is a mixure of products from several sources: 1) alveolar liquid, 2) secretory products from a variety of cells along the surface of the conducting airways, 3) submucosal gland secretory cell products, and 4) serum transudate. Epithelial cell turnover may also add membrance and cytoplasmic components to these secretions (33-35).

The role of respiratory mucus

MCC is the most widely studied function of respiratory mucus. A traditional and an alternative model have been proposed for the MCC mechanism. The traditional concept of the anatomy of the mucociliary apparatus in the airways. The mucus blanket is usually thought to consist of a sol layer, which bathes the cilia, and a gel layer, which lies on top of the sol (or periciliary) fluid, in the proximal airways. Clearly there is an equilibrium between these two layers and it may be argued that the sol layer, which is thin and watery, allows the cilia to beat and sweep the overlying gel in a cephalic direction on the lubricant-like sol. More recently, an alternative model has been proposed in which mucins form a tangled network that is concentrated at the air-liquid interface but extends to the epithelial surface. There are studies showing a wide range of MCC values within a group of healthy persons. For instance, Yeates et al 1975 reported mucus flow in the trachea of 42 healthy nonsmoking adults to average 3.6 mm/ min, Foster et al 1980 showed that the mucus velocity in the main bronchi average 2.4 mm/min and tracheal mucus velocity 5.5 mm/min (33, 35).

Rheological and physical properties of mucus and their effect on MCC

The respiratory mucus is a viscoelastic material characterized by nonlinear (non-Newtonian viscosity) and time-dependent flow (thixotropic) properties. Spinability is also a property common to respiratory mucus. Besides these rheological properties, the respiratory mucus possesses surface

properties, such as adhesivity and wettability. There are probably almost as important or even more important than the rheological properties.

As a viscoelastic gel, mucus exhibits a response to stress that is neither solid-like nor liquid-like, but some combination of the two. A true solid responds to stress with a finite deformation from which it totally recovers after the stress is removed. A true liquid responds to the same stress by deforming or flowing continuously for the time that the stress is applied. After the removal of the stress, the flow ceases and there is no recovery of the strain. Owing to the recently proposed alternative model of the mucociliary apparatus in which the mucin network has a tangled rather than a cross-linked topology, the rheological properties of mucus are believed to be physiologically regulated by hydration via control of the transepithelial movement of water, ions and soluble protein rather than by variations in the degree of covalent crosslinking between glycoprotein chains.

Mucus is non-Newtonian and behaves as a pseudoplastic liquid in which viscosity decreases as the applied force is increased. This implies that the more forcefully the cilia beat, the more easily the mucus moves. Mucus exhibits shear thinning, it show a decrease viscosity at lower shear forces. Spinability is the thread-forming capacity of mucus under the influence of large amplitude elastic deformation. An important feature of spinability is that it gives information on the internal cohesive forces of mucus as well as on its elasticity. It has been reported that the spinability of normal respiratory mucus ranges between 40 and 100 mm and decreases in pathological conditions as its purulence increases. Adhesiveness is the ability of mucus to bind to a solid surface. It is dependent on mucus surface tension, hydration, wettability and contact time. The wettability of a biological fluid characterizes its ability to spread when deposited onto a solid planar surface. The degree of wettability is characterized by the contact angle between the solid and the liquid at equilibrium; the lower the contact angle, the greater the wettability (33, 35).

Factors affecting mucociliary clearance

Age

Yager et al in 1978 measured the ciliary beat frequency (CBF) of human respiratory epithelium in vitro. Their results indicate that CBF decreases with increasing age. Goodman, et al in 1978 showed that the mean tracheal movement velocity in a group of 10 young nonsmoking subject was 10.1 mm/min and in a group of seven elderly nonsmokers 5.8 mm/min (33)

Ho and coworkers in 2001 studies the nasal mucociliary clearance (NMCC) time, ciliary beat frequency (CBF) and ultrastructure of respiratory cilia in a cohort of healthy volunters. There was a correlation of CBF and NMCC time with increase age. Subjects older than 40 yr of age had significantly slower ciliary beat frequency, high percent of ciliary cross-sections displaying single tubules, and longer NMCC time than their younger counterparts. These finding may help explain the frequent occurrence of respiratory infection in the elderly (36).

Gender

Svartengren et al in 1986 studied mucociliary clearance in relation to clinical features in patients with bronchiectasis. The subjects inhaled 6 microns Teflon particles labeled with 99mTc and radioactivity was measured externally. The average retention of the Teflon particles at 2 h was significantly higher than in 21 patients than in healthy nonsmokers. The percentage retention (an indication of the rate of MCC, with a higher percentage retention indicating slower MCC) in healthy nonsmoking females and males was significantly different $26 \pm 17\%$ for the female and $41 \pm 23\%$ for the male subjects respectively). This study indicated that MCC was faster in females than in males (33, 37).

Hasani et al 1994 studied 41 healthy, non-smoking subjects had their lung mucociliary clearance measured using an objective, non-invasive radioaerosol technique. There was no statistically significant difference between young healthy males and females in the rate of clearance of inhaled radioaerosol over a 6 hour observation period (38).

Mortensen et al 1994 showed that mucociliary clearance was significantly faster when the radioaerosol was deposited in the central airway than in the peripheral airway, and faster in life-long non-smoker than in ex-smorkers. There was no influence of age, no convincing association with sex (39).

Posture

Wong et al 1977 studied a noninvasive, radionuclide imaging technique for measuring the rate of mucus clearance in the trachea to gravitational effects on mucus clearance in patients with cystic fibrosis (CF), upper respiratory tract infection (URTI) and normal subject. The normal subjects and two of the CF patients showed no significant difference in the RT measured in the upright and head down position. The results of the study indicate that the force of gravity can be a major influence on tracheal mucus clearance in CF and URTI subjects. This conclusion supports the use of postural drainage as an effective form of therapy in cystic fibrosis patients (40).

Gatto et al 1989 . This study centered on changes in airway length under physiological conditions in the rat. Following extension of the head, the length of the trachea increased 50% without change in diameter. The rate of mucociliary clearance did not change with head position. Extension of the head caused surface epithelial cell to elongate longitudinally and to decrease in height (41).

Isawa et al 1991 studied 11 normal subjects on effect of gravity and respiratory phase on mucociliary transport with inhaling 99mTc-human serum albumin aerosol. Each subject was positioned in right lateral decubitus and then supine position before a scintillation camera. Neither respiratory phases nor gravity had any significant effect on mucociliary transport (42).

Dolovich et al 1998 studied the effect of continuous lateral rotational therapy (CLRT) on lung mucus transport in mechanically ventilated patients with a radiolabeled aerosol. This study resulted that 1) the mucous clearance was slower than that reported in normal subjects and in ambulatory patients with

COPD; 2) there was a slight, but not significant, increase in clearance during CLRT; 3) clearance reverted to pre-oscillation levels following therapy. Lack of significant effect may be attributed to too shallow an angle for rotation or too short an intervention period. Positional drainage effected by short duration CLRT did not appear to stimulate significant mucous removal from the lung in critically ill patients but also did not cause any adverse effects (43).

Tobacco smoke

Vastag et al 1985 studied mucociliary clearance and airways obstruction in smoker, ex-smokers and normal subjects who never smoked with 99mTc tagged monodisperse erythrocyted. The ex-smoker without chronic bronchitis showed the same mucociliary clearance rate (mC) as the control subjects who never smoked. The subjects who never smoked showed less airway obstruction. The smokers without chronic bronchitis showed normal ventilatory function tests but a lower mC rate than the healthy ex-smokers and control subjects. The ex-smokers and smokers with chronic bronchitis had a lower mC rate and more airway obstruction than the subjects who did not report any symptoms of chronic bronchitis. The ex-smoker with persistent symptoms of chronic bronchitis showed the severest degree of airway obstruction. The smokers with chronic bronchitis showed the most delayed central mC rate. The smoking habits correlated with the decreased mC rate and the degree of airway obstruction (44).

Drannik et al 2004 was to investigate the impact of cigarette smoke on bacterial clearance and immune inflammatory parameters after infection with Pseudomonas aerudinosa in mice. They observed a delay rate of bacterial clearance in smoke-exposed compared with sham-exposed mice. This was associated with increased inflammation characterized by greater numbers of neutrophils and mononuclear cells in the bronchoalveolar lavage. Delayed clearance was associated with increased morbidity and greater weight loss of smoke-exposed mice. Their finding suggest that cigarette smoke affects respiratory immune-inflammatory responses elicited by bacteria. They postulate that altered respiratory

host defense may be implicated in smoking-related diseases such as chronic obstructive pulmonary disease (45).

Drug

Houtmeyers et al 1999 focused on the effects of various drugs on mucus clearance.Tertiary ammonium compounds (anticholinergics), aspirin, anaesthetic agents and benzodiazepines have been shown to be capable of depressing the mucociliary transport system. Cholinergics, methylxanthines, sodium cronmoglycate, hypertonic saline, saline as well as water aerosol have been shown to increase MCC. Adrenergic antagonists, guaifensesin, S-carboxymethylcysteine, sodium 2-mercapto-ethane sulphonate and frusemide have been reported not to alter the mucociliary transport significantly. Amiloride, uridine 5-triphosphate (UTP), quaternary ammonium compounds (anticholinergics), adrenergic agonists, corticosteroids, recombinant human deoxyribonuclease (rhDNase), N-acetylcysteine, bromhexine and ambroxol have been reported either not to change or to augment MCC. Indirect data suggest that surfactant as well as antibiotics may improve the mucociliary transport system (46).

Disease

Asthma : The interrelated processes that are believed to be responsible for the clinical features of asthma include airway smooth muscle contraction and hyperresponsiveness, mucosal inflammation and edema, and the accumulation of secretions in the airway lumen. Recently published studies of bronchoscopic biopsies of patients with mild to moderate asthma have revealed marked mucosal inflammation of a severity that had not been previously suspected. The mucociliary dysfunction in asthma has been closely linked to the inflammation as detailed above in inflammatory mediators and drugs. MCC measurements using radioisotopes to label airway mucus suggest that clearance of secretions is impaired in asthma. MCC is determined by many factors- the quantity of sputum, the quality and viscosity of sputum, ciliary function, and epithelial integrity. All of these factors have been suggested as playing a role in the pathogenesis of asthma (33, 47).

Bronchiectasis: Bronchiectasis develops when mucus plugging and infection occur together in the absence of functioning cilia. In patients, the clearance of mucus varied from normal to extremely slow. Indeed , the more impaired the clearance was, the more generalized the airway symptoms were (affecting upper as well as lower airways), the more continuous they were and the earlier in life they had started. An impairment of clearance is usually generalized in patients with bronchiectasis, regardless of the localization of the bronchiectasis. In fact, for most bronchiectatic patients, local damage to the respiratory tract epithelium or bronchial wall along with a local clearance defect (e.g. due to infection) might be the cause of the mucociliary transport dysfunction (33).

Cystic fibrosis (CF): CF is a common lethal genetic disease that affects epithelia. Although different organs are affected, including the pulmonary airways, pancreas, sweat glands, intestine and male genital tract, lung disease is the major cause of morbidity and mortality. CF patients have defective epithelial Cl^- permeability and a reduced capacity for Cl^- secretion, an increased rate of Na^+ absorption, which may generate dehydrated respiratory tract fluid. Abnormal amounts of viscous mucus are thus produced. As a result, the efficiency of the normal MCC defence mechanism may be impaired and the lungs may become more susceptible to bacterial infection.*Staphylococcus aureus* and *Pseudomonas aeruginosa* are the most common sources of bacterial colonization,resulting the bronchiectasis and chronic airway obstruction (33).

Chronic bronchitis (CB): CB is characterized by the presence of persistent mucus hypersecretion and is associated with varying degrees of airway obstruction. CB is usually caused by cigarette smoking. The histologic findings in the airways of patients with CB and of asymptomatic smokers are similar: hypertrophy and hyperplasia in smaller airways, atrophy of columnar epithelium, squamous metaplasia, and a reduction in the number of ciliated cells. Various studies agree that MCC is impaired in patients with simple as well as obstructive CB. Simple CB is defined as chronic expectoration of mucoid secretions without major airway obstruction, whereas in obstructive CB airway obstruction is present. Ericsson et al in

1987 found a slight impairment of MCC in the tracheobronchial tract of patients with mainly simple CB. Goodman et al in 1978 reported a markedly decreased TMV in patients with simple as well as obstructive CB. Ericson et al in 1995 suggested that, in patients with CB, coughing may compensate for decrease MCC. This would lead to a fairly effective overall tracheobronchial clearance (33).

2.2.3 Airway Physiology of Mucus Clearance

All airway clearance techniques must interact with lung physiology to enhance secretion movement. A clear and thorough understanding of a few physiologic concepts and hypotheses will help the respiratory practitioner understand how each airway clearance technique works and it may also aid in deciding which modality to use for which disease state (16).

Equal Pressure Point Concept

The equal pressure point (EPP) concept is integral to understanding the airflow limitation that is so important in many aspects of pulmonary medicine, from pulmonary function test (PFT) to airway clearance techniques. EPP is the point at which the pressure within the airways exactly equal to the pleural pressure. By this concept, alveolar pressure, Palv, is the driving pressure which causes gas to flow through the airways. To a close approximation it exceeds the pleural pressure, Ppl, by an amount equal to the recoil pressure of the lungs, Pst (l). This may be expressed: Palv =Ppl + Pst (l) (all pressures are expressed relative to atmospheric). Thus, the driving pressure may be thought of as being made up of two parts (16, 48, 49). Add the influence of pressure outside the airways, transmural pressure,Ptm, expresses pressure at the inside wall of a structure relative to that outside. By definition of concept, all pressures at inside walls upstream from EPP exceed Ppl and since all pressures at outside walls are equal to or less than Ppl, it follows that all Ptm at points upstream from EPP are positive. All pressures at inside walls downstream from EPP must be less than Ppl. So, EPP is defined as the point at which transmural pressure become zero. Beyond this EPP, the airway is subject to compressive forces

and collapses. It follows that any compression of airways that occurs during forced expirations must take place downstream from EPP (50, 51).

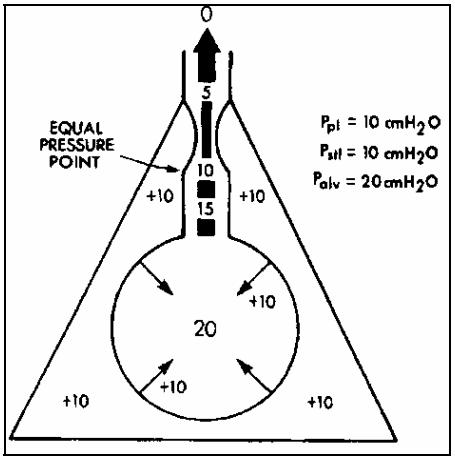

Figure.2.6 The equal pressure point concept. Pressure is dissipated as air flows towards the mouth. The point at which the pressures inside and outside the wall are the same is the equal pressure point (EPP). Downstream (toward the mouth) from the EPP, the airway is compressed because the pressure surrounding it is greater than the pressure in the lumen. Ppl = expiratory force, Pstl = static elastic recoil, Palv = intraluminal (alveolar) pressure (16)

During a forced exhalation, the pressure in the airway (intraluminal) gradually decreases from the peripheral airways to the mouth because of frictional pressure loss and convective acceleration pressure loss. The extraluminal (pleural) pressure remains relatively constant. Therefore, there is a wave of equal pressure points moving deeper (more peripherally) into the airways as exhalation proceeds and intraluminal pressures fall. The site of the EPP is determined by the amount of expiratory force and the elastic recoil (16, 48). Likewise, if the forced exhalation is initiated at a lower lung volume, the pressure from the static elastic recoil will be less, as will the intraluminal pressure, and the resulting EPP will again be more peripheral. Initiated at normal lung volumes or with normal-to-high expiratory pressure, the EPP is estimated to lie at the carina or larger bronchi, which are reinforced by cartilage and thus resist collapse (16).

Cough is the body's natural backup mechanism for airway clearance. Usually a deeper inspiration is followed by closure of the glottis, high intrapulmonary pressures are built up behind the glottis, and when the glottis opens, supra-maximal, expiratory, turbulent air flows are generated. The EPP plays an extremely important role in the effectiveness of cough, because a substantial jump in airflow velocity occurs at points of narrowing (choke points). High linear airflow

velocity provides the turbulent flow, high shearing forces at the airway wall, and high kinetic energy that move secretions cephalad. However, a cough is generated by the build-up of extremely high intraluminal and extraluminal pressure, so with cough there is more potential for substantial airway collapse at the EPP, especially if airway stability is lacking. It may compress the airways too much to allow effective clearance (16).

During forced expirations, there are forces tending to collapse and compress the airways downstream of the EPP. This dynamic compression is an essential part of the mechanism to move secretions from airways. A substantial jump in airflow velocity occurs at points of narrowing. The high airflows velocity and the shearing forces at the airway walls generate that move secretions cephalad. In addition, the shear forces at the airway walls should reduce mucus viscosity (10, 15, 16, 48, 52). Therefore, the location and magnitude of the compression can be varied by expiratory force and lung volume to allow effective clearance. The EPP concepts seems to play an important role to understanding the airway clearance.

Collateral Ventilation

The phenomenon of collateral ventilation in the human lung is defined as " the ventilation of alveolar structures through passages or channels that bypass the normal airways". Collateral ventilation channels (the canals of Lambert, channels of Martin, and pores of Kohn) (Figure 2.7) between adjacent contiguous lobules and adjacent alveoli are probably not important in normal ventilation, but may be important when there is airway obstruction. The major physiologic factors in collateral ventilation are collateral resistance and respiratory frequency relative to regional time constants. Increasing lung volume substantially decreases collateral resistance, probably as a result of outward forces of interdependence on the obstructed region and increased segmental volume. At an increased respiratory rate and flow, an unobstructed region will fill more rapidly than a partially or completely obstructed one, because the pressure drop across the obstruction is less and flow is less impeded. As the time constants of the connected pathways shift, the more slowly ventilating unit will receive part of its inspired volume

via collateral channels from the more rapidly ventilating unit (this is known as *pendelluft flow).* Lower respiratory frequency and larger tidal volume should increase the degree of collateral ventilation (16).

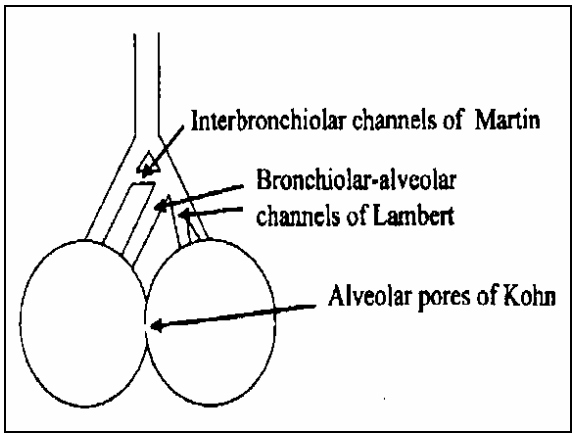

Figure 2.7 Collateral ventilation channels. From Lapin CD. Airway physiology, autogenic drainage and active cycle of breathing. Respir Care 2002;47:p781 (16)

For airway clearance techniques, the collateral ventilatory system aims to improve the aeration of alveoli and assist the movement of air distal to mucus plugs in the peripheral airway for loosen secretion. It is improve the driving pressure in alveolar behind blocked airways that related to airflow in EPP concept and to encourage optimal filling of all lung segments, including the obstructed ones by collateral filling. Optimal filling by collateral airways is necessary for the alveolar pressure will be the same in most lung part that minor paradoximal airflow during expiration (15, 17, 53).

Two-Phase Gas-Liquid Flow Mechanism (TPGLF)

A simultaneous flow of gas and liquid, so called two-phase gas-liquid flow, has been treated extensively in some engineering fields. This particular flow phenomenon has a fundamental resemblance to an airflow in the mucus lined respiratory airways (54, 55). Therefore, when mucociliary transport is impaired, a secondary clearance mechanism known as two-phase gas liquid flow (TPGLF) plays an essential role in removing mucus from the lung (7, 56).

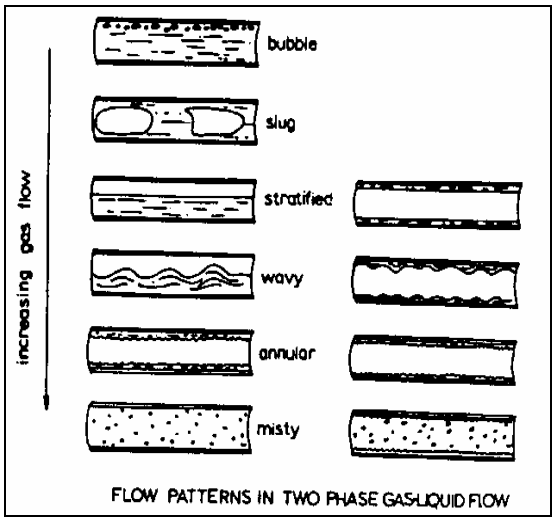

Figure 2.8 Diagrammatic representation of the effect of increasing gas flow through a tube containing liquid. *left:* tubes are initially filled with liquid; *right:* liquid is initially distributed uniformly on wall of the tube (54)

When a mixture of gas and liquid flows through a tube, the gas-liquid mixture may flow in a variety of different patterns (Figure 2.8). At low gas flow rate, bubbles of gas may be dispersed in the liquid (bubble flow), but as the gas flow rate is increased, the bubbles become larger and fill most of the tube cross section; these gas "slugs" alternate with volumes of liquid and are displaced toward the top of the tube during horizontal tube flow (slug flow). Further increase of gas flow-rate causes the gas slugs to merge randomly after which the liquid may occupy the lower part of the tube with a fairly smooth surface (stratified flow) and with even faster flows marked surface roll waves appear (wavy flow). At still higher flow rates the tube orientation becomes less important and the film of liquid is covered by a dense array of small waves which may cause the surface to appear smoother although there is extreme agitation of the liquid (annular flow). The difference between the gas and liquid velocities becomes very large and the liquid holdup becomes much higher than would be expected on the basis of the relative flow rates. At these gas flow rates the presence of the liquid phase has a great influence on the pressure drop in the gas stream. With wave formation there is a marked increase in pressure drop in the gas phase. The high pressure loss is believed to result both from energy losses in liquid due to gas-liquid interaction and energy losses in the gas due to liquid surface

roughness consequent upon the gas-liquid interaction. It has been suggested that viscous energy losses in the liquid must be the main cause of the pressure drop. For extreme gas velocities the liquid waves are entrained and blow through the tube in the form of droplets (mist flow). The liquid viscosity and shear elasticity will modify the flow pattern and pressure gradient (54).

The two-phase gas-liquid flow in the airways may be divided into two categories (55) :

1) airflow through the mucus-plugged airways

In this category, when airflow rate is low, air may flow through the mucus-plug as small bubbles (bubble flow). As the airflow rate increases, the bubbles grow in size, combine together (plug flow) and eventually from a continuous channel through the mucus plug (annular flow). At an extreme airflow rate the mucous layer may be peeled off from the surface of the airways and blown away as in the case of a cough. However, this sequence of flow may not occur in reality because airflow through a mucus plug requires a tremendous pressure, which may not be generated by a normal tidal breathing maneuver. Therefore, cough may be the only mechanism to open up or expel the mucus plug unless the mucus is very watery.

2) airflow through the open airways but thickly lined with mucus

The mucous lining, either uniform or nonuniform, may initially remain calm at a low airflow rate (stratified flow). As air velocity increases, the mucous layer becomes unstable, forms ripples and waves (wave flow) and may move in the direction of the airflow (annular flow). A further increase of airflow would then accelerate the mucus movement. The essential factors affecting this type of liquid transport have been identified as the air velocity, liquid layer thickness and viscosity of liquid among others.

Clarke et al in 1970 was to investigate the conditions under which two-phase gas-liquid flow could occur in airway such as those of the human bronchial tree and whether in bronchial disease. The results support the view that both the thickness and

the viscoelastic properties of the liquid layer are important in the determination not only of the overall flow resistance, but also of the critical velocity of gas flow at which wave formation occurs. The relevance of the results to the case of flow in human airways is discussed in some detail. The thin liquid layers present in healthy lungs probably have a negligible effect on flow resistance, but in endobronchial disease a large proportion of the total flow resistance is likely to stem from the presence of disturbed liquid layers (54).

Kim et al in 1986 investigate critical conditions for mucus transport by two-phase gas-liquid flow mechanism at non-cough flow situations. The critical airflow rate and critical liquid layer thickness required for the upward transport of the liquids were determined. The results indicate that the critical airflow rate lies within the range that can be achieved during normal tidal breathing. The difference in velocity profiles between the inspiratory and expiratory airflow, a positive mucus transport could occur during normal tidal breathing and conditions for effective mucus transport may occur throughout the smaller airways. The critical liquid layer thickness relative to the tube diameter ranged from 3 to 15% of the respective tube diameter and depend on rheological properties of liquid. Therefore, the mucous layer in the normal lungs (< 5 μm) is very thin, the two-phase flow mechanism may not be effective in the normal lung. Once the mucous layer reaches this critical thickness, then it can be transported by the two-phase flow mechanism. The results indicate that the critical conditions for the mucus transport by two-phase gas-liquid flow mechanism are within the range that can be achieved in patients with bronchial hypersecretions during normal breathing. In vertical flow study, expiratory airflow during tidal breathing is more effective in clearing mucus when there is an increased thickness of the mucus layer (55).

Kim et al in 1986 investigated conditions for the mucus transport by two-phase gas-liquid flow mechanism in the continuous two-phase annular flow tube model. The mucous layer transport speed showed increased with increasing airflow rate and decreased with increasing viscosity of mucus. There are two forced promoting liquid transport; the interfacial shear force which is proportional to the square of airflow velocity and the pressure force resulted from difference in static pressure

across the tube. These forces are opposed by the gravitational force and viscous shear force of liquid layer on the tube wall. Elasticity influence was remarkable in pressure drop. The highly elastic solutions might be able to produce the low pressure drop by quickly readjusting the wave pattern in such a way to minimize the flow resistance. This indicated that more elastic mucus can be transported easily with a much reduced work load. The mean mucous layer thickness decreased rapidly with increasing airflow rate and decreasing viscosity of mucus. This study shown that the critical airflow rate required for the mucus transport decreases rapidly with decreasing airway diameter and that the critical conditions can be met in the 10^{th} generation airways during normal breathing. This study results clearly demonstrate that conditions for the mucus transport by two-phase gas-liquid flow mechanism can be met in vivo and suggest that effective mucus transport may actually occur by the two-phase gas-liquid flow mechanism alone or together with mucociliary action in patients with excessive bronchial secretions (57).

Kim et al 1987. With theoretically, when air flows over a thickly lined mucus layer, a shear force is developed on the interface of a mucus layer in proportion to the square of the airflow velocity. Therefore, if the airflow velocity is maintained above a certain level at which the shear force on the mucus layer exceeds the resistive force in the mucus layer, the mucus layer starts to move in the direction of airflow. Despite the complexities, an effective mucus clearance can be expected by a certain extent the inspiratory flow velocity, subsequently producing a net shear force high enough to push the mucus layer in the direction of expiratory flow. In this study, they investigated systematically conditions for effective mucus transport in vitro flow models. The liquid layer transport speed (LLTS) increased with increasing peak expiratory flow rate, increasing the ratio of the peak expiratory –to-inspiratory flow rate (PEIFR). LLTS was always higher with viscoelastic than with viscous liquid. Relevance to in vivo situation, Once the mucus lining exceeds the critical thickness, the mucus may then by transported by maintaining a breathing pattern in such a way that the expiratory flow velocity is higher than the inspiratory flow velocity. This results indicate that the required airflow velocity for mucus transport is within the range of normal tidal breathing and that the expiratory flow bias required is as low as

10% of the inspiratory flow rate, the kind of breathing pattern necessary for mucus transport may not be difficult to achieve with the patient's own effort. The resulting increased expiratory flow velocity is a great contributing factor for mucus clearance by two-phase flow mechanism(56). Therefore, the flow pattern in the lung is not one-way but two-way periodic flow, the cephalad mucus transport could be achieved by keeping the expiratory flow higher than the inspiratory flow rate. The ratio of the expiratory to the inspiratory flow rate of 1.5, with a tidal volume of 500 ml, was sufficient to transport the mucus in a vertical tube model (56, 57).

2.3 Physiotherapy for Airway Clearance

Techniques for augmenting the normal mucociliary and cough clearance mechanisms of the lungs are not new. Over the past 35 years a multitude of airway clearance techniques have been developed, introduced, refined, researched and used in patient populations to help assist normal mucus clearance mechanisms. Postural drainage with chest clapping and chest shaking has been replaced by the more effective techniques of the active cycle of breathing, autogenic drainage, R-C Cornet®, Flutter®, positive expiratory pressure mask, high frequency chest wall oscillation and intrapulmonary percussive ventilation in most parts of the world. Glossophargyngeal breathing is being considered again and is often a useful technique for increasing the effectiveness of cough in patients with tetraplegia or neuromuscular disorders. Different airway clearance techniques have developed independently in different parts of the world. Each is claimed to be effective at mucus clearance and to provide independence for the patient. The impetus for this explosion in airway clearance options has been the continued search for improved efficacy and adherence to a prescribed therapy (8, 17).

When prescribing airway clearance techniques, many factors should be considered including the severity of disease, the patient's lifestyle and factors affecting adherence (Table 2.4). These goals may be obtained by performing the airway clearance interventions and described in the following section (58).

Table 2.4 Decision making for airway clearance techniques

Considerations When Recommending	Airway Clearance Techniques
History of esophageal reflux	Cost of device or technique
Osteopenia or osteoporosis	Lifestyle
Hemoptysis	Energy cost
Pulmonary function	Portability/space constraints
Severity of exacerbation	Energy source
Bronchospasm	Time constraints
Claustrophobia	Available assistance
Age	Comprehension
Patient preference (ease to learn, ease to teach)	

References: Down AM, Lindsay KLB. Physical therapy associated with airway clearance dysfunction. In DeTurk WE, Cahaling LP. Cardiovascular and pulmonary physical therapy: an evidence-based approach. New York; McGraw-Hill, 2004:478. (58)

There are various techniques and several methods that have been effective at assisting the clearance of secretions from the airways. Breathing techniques using controlled flow at varying lung volumes, improve sputum production. Devices augment these techniques, such as by providing expiratory retard, which is beneficial for patients with early airway collapse. The following descriptions of these techniques and devices.

2.3.1 Postural Drainage or Bronchial Drainage

Postural drainage, also known as bronchial drainage, is a passive technique in which the patient is placed in positions that allow gravity to assist with the drainage of secretions from the bronchopulmonary tree. It usually understood to be the use of gravity-assisted positions in various positions so that gravity assist in the flow of mucus. The positions are based upon the anatomy of the tracheobronchial tree (8, 17, 59, 60). The benefits of postural drainage appear technique-dependent, requiring sufficient drainage time (3-15 min) for each position drained. The key concepts of PD are posture, time, breathing and cough. Percussion and vibration are some components of the therapy (60).

Knowledge of the anatomy of the tracheobronchial tree is vital to effective treatment. Each lobe to be drained must be aligned so that gravity can mobilize the secretions from the peripheral to the larger, more central airway. The mechanism of postural drainage is considered to be a direct effect of gravity on bronchial secretion (8, 17, 59, 60). Close to the vertical position of segmental bronchi as possible assuming that liquid flows fastest through a vertically inclined tube under the force of gravity. Gravity has a key role in maintaining lung health, with body position impacting depth and patterns of ventilation, perfusion and lymphatic drainage, each of which impact the ability to effectively clear secretions from the lung and improve oxygenation (8, 17, 60).

2.3.2 Percussion

Percussion, sometimes referred to as manual chest clapping, is a traditional approach to secretion clearance. A rhythmic force is applied with cupped hand with extension action of the wrist on the patient's thorax over the involved lung segment, with the aim of dislodging or loosening bronchial secretion. This technique is performed with the patient in postural drainage position. The percussion should be applied rhythmically and vigorously throughout inspiratory and expiratory for 3-5 minutes continuously in each of the position utilized (12). There is no evidence that alteration in the rate of chest clapping increases or decreases the mobilization of bronchial secretions (8, 17, 59). The proposed mechanism of action of percussion is the cupped hand must be formed in a manner that will trap a cushion of air, which can be compressed and then transmit a wave of mechanical energy through the chest wall and into the lung parenchyma. The resulting motion loosens secretions from the bronchial wall and moves them proximally, where ciliary motion and cough (or suction) can remove them. Chest clapping (manual chest percussion) and mechanical chest percussion will increase intrathoracic pressure, but the relationship between this increase in pressure and airway clearance is yet to be determined. In infants, small children patients with neuromuscular weakness or paralysis, chest clapping or mechanical percussion may be a useful technique to stimulate coughing probably by the mobilization of secretions (12, 17, 59).

2.3.3 Vibration, Shaking, Rib Springing

Vibration is applied by placing both hands on the chest wall (or one hand on top of the other), gently compressing and rapidly vibrating to chest wall. It is a sustained co-contraction of the upper extremities of a caregiver to produce a vibratory force that is transmitted to the thorax over the involved lung segment. Vibration is applied throughout exhalation in the same direction as that in which the chest is moving. The technique is used in conjunction with percussion in postural drainage (61).

Shaking is a slower form of vibration that applied to the chest wall with wide movement of the therapist's hand. Rib springing is a more vigorous form of vibration with greater pressure to the chest wall and applied to the chest wall several times during exhalation. Shaking consists of a bouncing maneuver, sometimes referred to as "rib springing", against the thoracic wall in a rhythmic fashion throughout exhalation. A concurrent pressure is given to the chest wall, compressing the thorax. Shaking is similar in application to vibration, with shaking being on one end of the spectrum in application of force and vibration being on the opposite end, supplying a gentle pressure. Many variation exist throughout the continuum between these techniques (8, 12, 17, 59).

With vibration, the hands are placed on the chest wall and during expiration, a vibratory action in the direction of the normal movement of the ribs is transmitted through the chest using body weight. The vibratory action may be either a coarse movement (chest shaking) or a fine movement (chest vibrations). This action augments the expiratory flow and may help to mobilize secretions. Rhythmical comfortable rate for both patient and physiotherapist is probably the most appropriate.

Shaking is assumed to work in the same manner as vibration, mobilizing secretions to the central airways. Because the compressive force to the thorax is greater, producing increased chest wall displacement, the stretch of the respiratory muscles may produce an increased inspiratory effort and lung volume (8, 12, 17, 59).

2.3.4 Cough/ Assisted Cough Technique/ Mechanical In-Exsufflator

An effective cough is a primary method of clearing airway mucus for all persons. A cough consists of three phases: 1) a maximal inspiratory effort raising lung volume to near total lung capacity, 2) generation of increased intrathoracic pressure by closure of the glottis and activation of expiratory muscles and 3) explosive exhalation by sudden opening pf the glottis resulting in very high airflow causing high shear in forced to the mucus (9, 59). The effectiveness of a cough is dependent upon the flow-limiting segment of the airways. Directed cough is a technique that mimics the attributes of an effective spontaneuos cough. The cough can be assisted by application of external pressure to the epigastric region or thoracic cage during the expiratory phase (62).

Assisted cough technique, it is modify and develop additional techniques based on the manually assisted cough technique or self-assisted technique for improve a cough in patient. The manual consists of applying pressure with both hands to the upper abdomen following an inspiratory effort and glottis closure. Self-assisted techniques are start out as physically assisted techniques, they are more active and require greater gross motor movement (9, 11, 63).

A Cough Assist Machine, previously known as mechanical In-Exsufflation (MI-E) is a noninvasive machine used for airway clearance. Application of a high positive-pressure phase (insufflation: 20 to 30 cmH_2O) is followed by rapid reversal negative pressure phase (exsufflation: -30 to -40 cmH_2O) to stimulate cough. This device can be used as a face mask or attacked to a universal adaptor for a tracheostomy tube (12, 17, 59, 62)

An effective cough is a primary method of clearing airway mucus for all. An effective cough depends on the ability to drive gas at high linear velocities through the airways and on an effective interaction between the flowing gas and mucus lining the airways (gas-mucus interaction). These events depend on the capacity of the respiratory muscle to increase intrathoracic pressure and dynamically compression the airway (64). The suggest mechanism of action of the cough assist

machine is to improve peak cough flow. However, the cough assist machine produced greater increase in cough pressure then other cough-assisted technique (17, 59, 63).

Assisted cough technique, manual compressing the lower thorax and abdomen or by binging the abdomen should theoretically improve cough efficiency. This maneuver was shown in an uncontrolled study to improve peak cough expiratory flow between 14-100 %. There are several applies technique to produce an effective cough in patients such as applied a quick manual stretch to facilitate a stronger respiratory muscle contraction based on PNF facilitation, effect of gravity and posture for the appropriateness of technique or compression assist.

Mechanical In-Exsufflator is applied rapid reversal of pressure to stimulate cough (17, 59, 62). Using this device, peak cough expiratory flows can be increased by more than fourfold (63).

2.3.5 Forced Expiration Technique (FET)

FET is a forced expiration or huff combined with periods of breathing control. One or two huffs from particular lung volume are followed by breathing control. A huff from mid-to low-lung volume with the glottis open will loosen and mobilize the more peripherally situated secretions. A huff from a high-lung volume will mobilize and often lead to expectoration of secretions from the upper airway (10, 15, 17, 59, 62, 63).

With physiology, a huff or cough is a forced expiratory manoeuvre which can be analysed using the concept of the equal pressure point (EPP). During a forced expiratory manoeuvre there is collapse and compression of the airways downstream (towards the mouth) of the EPP. The EPP, the regions of dynamic collapse and compression move in a peripheral direction with decreasing lung volume. The dynamic collapse and compression of the airways during a forced expiratory manoeuvre is effective from points, choke points, downstream of the EPP. As the lung volume decreases these choke points move upstream (towards the alveoli) and at low lung volumes the more peripheral parts of the airways can be cleared (15, 17, 48). In

addition, the intrathoracic pressures generated by huffing are less than those generated by coughing. The viscosity of mucus is shear dependent, and the shear forces generated during huffing should reduce mucus viscosity. This, together with the high flows generated during forced expiratory maneuver, would be expected to facilitate the movement of mucus in a proximal direction. There is also an inbuilt oscillatory movement of the airway walls during a forced expiratory maneuver and this should have an additional, mechanical loosening effect (10, 15, 16).

2.3.6 Active Cycle of Breathing Technique (ACBT)

ACBT is a cycle of techniques of breathing control (tidal breathing at the patient's own rate and depth, encouraging use of the lower chest with relaxation of the upper chest and shoulders), thoracic expansion exercises (deep breathing exercises emphasizing inspiration with or without a breath hold; expiration is quiet and relaxed) and the forced expiration technique (one or two huffs combined with periods of breathing control) (10, 17, 59, 60, 62, 63).

The period of breathing control between the other phases is essential so as to prevent bronchospasm, to minimize any increase in airflow obstruction and fatique. The thoracic expansion phase consists of deep inspiration and may be accompanied by percussion or vibration. This phase helps to loosen secretions. Thoracic expansion exercises recruit the collateral ventilatory system assisting, the movement of air distal to mucus plugs in the peripheral airways. Increasing tidal volume also utilizes the interdependence or mutual force of adjacent alveoli to re-expand collapsed alveoli. The forced expiration technique utilizes the physiology of the huff combined with a recovery phase to reduce the possibility of airway closure, desaturation or fatigue.

The physiological theory of equal pressure point (EPP) is the basis for the FET. A huff is a forced expiratory manouvre performed with an open glottis, resulting in lower intrathoracic pressures than a cough. These three steps are done in sequence to loosen and expel the mucous (9, 10, 15-17, 59)

2.3.7 Autogenic Drainage(AD)

Autogenic drainage is breathing at different lung volumes and expiration is used to move the mucus. The aim is to maximize expiratory flow. Breathing at low lung volumes is used to mobilize more peripherally situated mucus. Breathing around the individual's tidal volume is said to collect mucus in the middle range and with breathing around high lung volumes, expectoration of secretions from the central airways is promoted. When sufficient mucus has reached the upper airways, it may be cleared by a cough. The keys to this technique are airflow and volume control, suppression of cough until secretions are mobilized, inspiratory hold at the end of inhalation to equalize air across alveoli, and most importantly, patience (8, 10, 17, 53, 59, 62, 63, 65). Based on the theoretical physiology, utilization of expiratory airflow to mobilize secretions aim to reach the highest possible airflow in the different generations of bronchi by controlled breathing, to avoid compression of the airways by high flow peaks and to trying produce a mucus rattle rather than a wheeze. Thus, find a balance between expiratory forces and stability of the bronchial wall.

At breathing technique, inspiration is performed slowly through the nose to provide optimal humidification and warming of the inspired air. This helps to prevent coughing. At the end of inspiration, the glottis open with holds breath for two to three seconds is to encourage optimal filling of all lung segments, including the obstructed ones by collateral filling. Optimal filling by collateral airways is necessary to avoid an excessive rise of intrapleural pressure which could cause compression of a collapsible bronchial segment during expiration. To encourage narrowing of the bronchial lumen and a local increase in speed of airflow, expiration is performed through the open glottis and open mouth, without pursed lips.

For AD, the procedure consists of three phases, secretions from peripheral lung regions are mobilized by compression of peripheral alveolar ducts, a short breathing stop with open glottis to endure equal filling of all the lung segments by collateral filling. Increased airflow during expiration is necessary to achieve optimum loosening of mucus. The velocity of flow must be controlled to avoid high

flow peaks which result in spasm of the collapsible segments at the equal pressure point (EPP). The longer the expiration time, the greater the distance that the secretions will be transported (9, 10, 16, 53, 65).

2.3.8 Manual Hyperinflation (MH)

This is a technique to improve secretion clearance by use of a manual ventilation device (manual resuscitator). It is used in patients with an endotracheal or tracheostomy tube that can be attached to a manual ventilation bag. One caregiver uses the bag to hyperinflate the lung with a slow, deep inspiration and after a short inspiratory pause, provides a quick release to allow rapid exhalation. A second caregiver applies shaking or vibration starting at the beginning of exhalation so as to mobilize secretions. The timing of this sequence is important if the desired effect is to be achieved. It has been likened to simulating a cough-deep inspiration, pause, and forceful exhalation. Manual hyperventilation requires two competent caregivers and is performed while the patients is in a postural drainage (9, 12, 17, 59, 62, 66).

The inspiration provided by the manual ventilation bag, which is deeper than an inspiration the patient could generate, promotes aeration of the alveoli. The compression of the thorax augments the high expiratory flow rate from the bag, accelerating the movement of the secretions from the smaller airways to the larger bronchi. During MH, the high expiratory flows thought to be produced, together with dynamic change in airway diameter, may result in annular and mist flow, both within trachea and downstream from the equal pressure point. It is postulated that expiratory flow velocity needs to be higher than inspiratory for this clearance to occur. It seems possible that the mechanism of two-phase flow may contribute to clearance of secretions in intubated patients receiving MH treatment. Therefore, the use of MH is commonly employed by physiotherapists to assist in the removal of secretion and re-expand across of atelectasis (17, 59, 63, 66)

2.3.9 Positive Expiratory Pressure (PEP)/ Oscillating Positive Expiratory Pressure (Oscillating PEP)

With this technique, the patient exhales against a pressure of 10-20 cmH_2O. The application of PEP device involves a face mask or mouthpiece connected to a device that includes a one-way breathing valve and an adjustable level of expiratory resistance. A manometer is inserted into the system between the valve and the resistance to monitor the pressure. This results in positive pressure in the airways during exhalation. Tidal breathing with a slightly active expiration is used and lung volume is retained at a raised level by avoiding complete expiration with a ratio of I:E = 1:3, 1:4 (11). The forced expiration technique is used to clear the secretions that are mobilized. The duration and frequency of treatment are adapted for each individual, but treatment is usually performed for approximately 15 minutes, twice a day, in patients with stable chest disease and excess bronchial secretions (8-10, 17, 24, 59, 63).

In low-pressure PEP breathing, the resistance is regulated to achieve 10-20 cmH_2O during expiration. The pressure should be sustainable during only slightly active expiration. High-pressure PEP breathing requires the patient to perform forced vital capacity maneuvers through expiratory resistance with a mask connected to spirometer. The range of pressure is 50 to 120 cmH_2O. Low-pressure PEP breathing is used more often, as it offers equal effectiveness as a lower presumed risk of pneumothorax (8, 17, 24, 59).

Oscillating Positive Expiratory Pressure is a form of PEP breathing in combination with high frequency oscillation with available through a device (8, 9, 17, 59).

Flutter VRP1®; This device is pipe-shaped with a high-density stainless steel ball-bearing enclosed in a cone in the bowl of the “pipe”. During expiration through the Flutter VRP1®, the rise and fall of the ball and its movement along the surface of the cone created a positive expiratory pressure and oscillatory

vibration of the air within the airways. In addition, intermittent airflow accelerations are produced by the same ball movements.

RC-Cornet®; This is a curved plastic tube containing a flexible latex-free valve-hose. During expiration through the Cornet, a positive expiratory pressure and oscillatory vibration of the air within the airway are generated. It can be used in any position as it is independent of gravitational forces. The flow, pressure and frequency of the oscillations can be adjusted to suit the individual patient. Secretions mobilized to the central airways are cleared by coughing or huffing. When breathes out through the cornet, breath in with a pause 2 to 3 seconds at the end of inspiration, Initially, these interspersed with deeper and more forceful one. Again, the forced expiration technique is used to clear secretions that have been mobilized. It is recommended that the cornet be used for 10-15 minutes. The Cornet has been shown to be as effective as the Flutter® in airway clearance and to decrease the cohesiveness and viscoelasticity of sputum from patients with bronchiectasis .

Acapella®; this device is uses magnets to create the flutter effect,which allows the device to be used in any position. It is independent upon gravitational effects.

It is theorized that PEP breathing reinflate collapsed alveoli by allowing air to be redistributed through collateral channals-the pores of Kohn and the Lamber canals. Pressure is built up distal to an obstruction, promoting the movement of secretions toward the large airways. Airway stability is maintained with PEP breathing, which results in improved ventilation and gas exchange as well as in airway clearance. In additional effect of PEP during exhalation is the splinting of airway. The splinting acts oppose the premature collapse of airway. With the airway splinted open, the expiratory airflow can move secretions into larger airways. A fixed orifice resistance of device, created back pressure that splint airway open during expiration (8, 11, 12, 17, 24, 59, 63).

With oscillating PEP device, a positive expiratory pressure, oscillatory vibration of the air within the airways and intermittent airflow accelerations phenomena help to loosen secretions, which are mobilized to the central airways and cleared by deep exhalations through the device with the aid of subsequent coughing and/or huffing. Currently, the compression and oscillation applied during vibration are proposed to aid secretion clearance by a number of physiological mechanisms. These include: 1) increasing absolute peak expiratory flow rate (PEFR) to move secretions towards the oropharynx, 2) improving the expiratory bias of airflow to increase the annular flow of mucus towards the oropharynx, i.e. PEFR/PIFR ratio > 1.1, 3) increasing mucus transport by decreasing the viscosity of mucus and improving expiratory flow due to the effects of oscillation of airflow at frequencies ranging from 3-17 Hz and 4) eliciting spontaneous cough via the mechanical stimulation of the airway (67).

2.3.10 High Frequency Chest Wall Oscillation (HFCWO)

This technique uses an inflatable vest that attached by hoses to an air-pulse generator producing pressure to about 50 cmH_2O at frequency of 5 – 25 Hz (62). Efforts aimed at mucus clearance by creating a differential airflow rate (i.e., greater expiratory than inspiratory flow rate) led to the development of a high-frequency chest wall oscillation system. It designs a large-volume, variable-frequency air –pulse delivery system. HFCWO is the application of positive pressure air pulses to the chest wall by an inflatable vest (10, 12, 17, 59, 68).

The ThAIRapy Vest system consists of an inflatable fitted vest connects to an air-pulse generator by flexible tubing. This device provides oscillation of the entire thoracic cavity at varying frequencies (5 to 25 Hz) and is used while sitting upright. The lung volume expired tends to increase with lower frequencies (less that 10 to 12 Hz). A widely adopted protocol consists of three frequencies that vary the volume flow rate; each frequency is used for about 10 minutes. Continuous aerosolized medication or saline administered concurrently may assist with secretion mobilization (59, 68).

The Hayek Oscillator is an electrically powered, microprocessor-controlled, noninvasive oscillator ventilator that uses an external, flexible chest enclosure (cuirass) to apply negative and positive pressure to the chest wall to deliver noninvasive oscillation to the lung (12, 59, 68).

Two probable mechanisms of action have been offered to explain the significant increase in sputum mobilization that occurs with HFCWO. The first mechanism proposes that oscillatory airflow leads to changes in the consistency of mucus, which results in increased mobilization of secretions. Significant decreases in mucus viscoelasticity. The second mechanism proposes that the different between the expiratory and inspiratory velocities produced shear forces strong enough to move mucus. Each chest compression produces a transient flow pulse similar to that observed during coughing and by using the flows with the greatest rates and volumes, sufficient force is obtained to move mucus in the airway. It is hypothesized that increases in cough clearability may be due to an increase in mucus/airflow interaction and/or a shearing mechanism leading to a decrease in the viscoelasticity of mucus (11, 59, 63, 68).

2.3.11 Intrapulmonary Percussive Ventilation (IPV)

This technique uses a pneumatic pressure device that generates oscillations in range of 100-300 / min at pressure of 5 – 35 cmH_2O. IPV works in a manner similar to that of the HFCWO. However, the oscillation is delivered internally through a mouthpiece during inspiration. It results in an internal percussion. The subject's inspiratory effort initiates the flow of gas and the volume of gas released with each pulse and the pulsation frequency can be adjusted. IPV provides percussion at 6 to 14 Hz, with a positive expiratory pressure of 10-20 cmH_2O and simultaneous delivery of an aerosol. Two types of IPV are available: a hospital unit powered by 50 psi of gas and a home unit powered by a compressor (12, 17, 59, 62, 68).

IVP provides positive pressure to the airways in an oscillatory manner. This device uses small burst of air at 200 to 300 cycles per minute along with entranced aerosol delivered through a mouthpiece. The putative mechanisms for

efficacy include bronchodilation from increased airway pressure, increased airway humidification and cough stimulation (9, 63, 68). It is theorized that changes in the frequency and pressure of the airflow delivered through the IPV device assist in stabilizing the airways and decrease the viscosity of secretions. This results in increased sputum mobilization (9, 10, 12, 15-17, 59).

2.3.12 Exercise / Resistive Inspiratory Manoeuvres (RIM)/ The Test of Incremental Respiratory Endurance (TIRE)

The role of exercise has been widely studied both for its holistic effects on the patients and for its ability to assist with mobilization of secretion. All forms of exercise cause an increase in ventilation by an increase in both respiratory rate and tidal volume. The increase in breathing gets air "behind"mucus in the airways and propels the mucus toward the central airways, exercise has been shown to enhance mucociliary clearance in patients with chronic bronchitis (8, 11, 59). There were some studies of exercise that proposed as a methods of airway clearance. For instance, resistive inspiratory manoeuvres (RIM) is repeated maximum inspiratory vital capacity manoeuvre against a fixed resistance increased effective short-term sputum clearance (69). The test of incremental respiratory endurance (TIRE) is inspiratory muscle training that proposed as a method for airway clearance (70, 71).

From exercise, the increase in breathing gets air "behind"mucus in the airways and propels the mucus toward the central airways. In addition, many effects on health and well-being exercise has been shown to assist in secretion clearance. It has been suggested that exercise can replace all or part of a conventional chest physiotherapy routine in some patients. Exercise increases mucociliary transport in patients with chronic bronchitis. Higher transpulmonary pressure with aerobic exercise may open closed bronchi as well as increase collateral ventilation to allow mucus to be moved. It has also been shown that exercise-induced hyperventilation is more effective than eucapnic hyperventilation in mobilizing bronchial secretion. The contribution of expiratory flow and exercise-induced coughing are other factors in effective secretion removal (9, 11, 17, 59).

Resistive inspiratory manoeuvres (RIM) is increased effective short-term sputum clearance. The previously studies have described the use of a fixed-load method for assessing inspiratory muscle function, which can also be used for inspiratory muscle training. Some studies reported that RIM results in increased sputum expectoration. This effect may be similar to that seen in exercise, which has been associated with increased sputum clearance as a secondary effect (69).

The test of incremental respiratory endurance (TIRE) has been proposed as a method of airway clearance. The exact mechanism by which TIRE increases sputum clearance is unclear but in thought to be related to TIRE induced increases in respiratory pressure and flow out the range of inspiratory volume. The additional benefit of using TIRE as an ACT is its inspiratory muscle training properties. However, there are less studies in TIRE (70, 71).

2.4 The Studies of Forced Expiratory Techniques, Active Cycle of Breathing Technique and Pursed Lips Breathing

2.4.1 The Studies of Forced Expiratory Techniques

Thompson & Thompson in 1968 studied forced expiration exercises in asthma and their effect on FEV1. They have demonstrated the pattern of mucus movement by cine-radiography. Mucus was moved in the more peripheral bronchi, not by a blast of expired air, but by the squeezing action of the narrowing and shortening of the bronchial tree during forced expiration-the peripheral branches shortening towards the central bronchi. They find that even with an increasing programme of forced expiration activity, many patients dry out completely. The percentage of improvement in all cases ranges from 0% to 150% with an average of 33% . This results abundantly clear that in the vast majority of asthmatics in children group, bronchial obstruction was not increased, but in fact the airways were less obstructed (72).

Pryor et al in 1979 evaluated the use of the forced expiration technique (FET) as an adjunct to postural drainage in cystic fibrosis and asthmatic patients. From the results, more sputum was cleared in a shorter period of time using

self postural drainage with the FET than assisted postural drainage without the FET and neither method of treatment increased airway obstruction. The relationship between time and weight is a measurement of efficiency. Patients using the FET can treat themselves both effectively and efficiently (73).

Pryor et al in 1979 studied conventional physiotherapy aided by an assistant compared with physiotherapy using the forced expiration technique without an assistant. The results showed that the forced expiration technique cleared more sputum in less time than conventional physiotherapy and an assistant did not further improve the results obtained by the patient performing the forced expiration technique himself. These finding mean that patients with cystic fibrosis who have had to rely on the help of others for their home treatment may now perform more effective treatment without help. The forced expiration technique might also be helpful for patients with chronic bronchitis, asthma or bronchiectasis (52).

van der Schans et al 1990 investigated spontaneous mucus clearance and the effect of forced expirations and coughing on mucus clearance in chronic airflow obstruction and low elastic recoil pressure (emphysema group) and normal elastic recoil pressure (chronic bronchitis group). Spontaneous mucus clearance from the peripheral lung region was higher in the patients with emphysema than in those with chronic bronchitis. There was no difference in central mucus clearance between groups. Mucus clearance from the peripheral lung region increased significantly during forced expirations and coughing in the patients with chronic bronchitis but not in those with emphysema. It is concluded that in patients with chronic airflow obstruction and regular sputum production spontaneous peripheral mucus clearance is greater in those with decreased elastic recoil pressure. Physiotherapy that included forced expirations and coughing can enhance mucus clearance in such patients when elastic recoil pressure is normal but is unlikely to be effective when elastic recoil pressure is decreased (74).

van der Schans et al 1997 reviewed forced expiratory manoeuvres to increase transport of bronchial mucus. FET are probably the most effective part of

chest physiotherapy. Essential in the application of forced expiratory manoeuvres to improve mucus transport is whether airway compression should be used or prevented. The variables that influence the localization and degree of airway compression are expiratory force, lung volume and possibly mouth pressure. With these variables the patients should learn the most efficient form of forced expiration, according to the individual condition of the patient (14).

2.4.2 The Studies of Active Cycle of Breathing Technique

Miller et al 1995 was compared the active cycle of breathing (ACBT) together with postural drainage and autogenic drainage (AD) in cystic fibrosis. The result show that AD cleared mucus from the lungs faster than ACBT over the whole day. Both methods improved ventilation, as assessed by the xenon-133 ventilation studies. No overall differences were found in the pulmonary function test results, but more patients had an improved forced expiratory flow from 25% to 75% with AD, while more showed an improved forced vital capacity with ACBT. No differences were found in sputum weight and heart rate, nor in mean SaO_2 over the series, but four patients desaturated during ACBT. AD was found to be as good as ACBT at clearing mucus in patients with cystic fibrosis and is therefore an effective method of home physiotherapy. Patients with cystic fibrosis should be assessed as to which method suits them best (75).

Savci et al 2000 studied the effects of a long-term treatment of AD and ACBT in patients with chronic obstructive pulmonary disease (COPD). The results show that AD improved forced vital capacity, forced expiratory volume in 1 second, peak expiratory flow rate, forced expiratory volume from 25 to 75%, chronic hypercapnia, arterial oxygenation, exercise performance, and dyspnea perception during exercise. The ACBT increased forced vital capacity, peak expiratory flow rate, arterial oxygenation and exercise performance. Peak expiratory flow rate increased in AD more than in ACBT. In AD treatment, the increase in oxygen saturation was significantly higher than in ACBT treatment. Chronic hypercapnia improved significantly in AD treatment than in ACBT. No differences were found in other lung function parameters. AD is as effective as the ACBT in cleaning secretions and

improving lung functions. These techniques can be used in stable COPD patients according to the patients' and the physiotherapists' preferences (76).

Williams et al 2001 have investigated the comparison of two physiotherapy regimens, ACBT assisted by a physiotherapist and ACBT performed independently by the patient, during acute respiratory infection in cystic fibrosis patients. Energy expenditure was not significantly different between the two treatment regimens, though significant improvements in pulmonary function were apparent 24 hours following the therapist-assisted ACBT. In this group of subjects, a reduction in airways obstruction was observed as a carry-over effect following the therapist-assisted ACBT (77).

Thompson et al 2002 performed a randomised crossover study in 17 stable patients with non-cystic fibrosis bronchiectasis at home, in which 4 weeks of daily ACBT were compared with 4 weeks of daily physiotherapy with the Flutter device. No significant differences between the two techniques were found. Median weekly sputum weights were similar with a median treatment difference of 7.64 g ($p=0.77$) and there was no evidence of treatment order or order interaction effects ($p=0.70$). Health status (Chronic Respiratory Disease Questionnaire) and ventilatory function did not change significantly during either treatment period. There was no significant change in peak expiratory flow rate or in breathlessness (Borg score) after individual physiotherapy sessions with either technique. A questionnaire indicated subjectively that patients preferred the Flutter (11/17) to ACBT for routine use. Therefore, daily use of the Flutter device in the home is as effective as ACBT in patients with non-cystic fibrosis bronchiectasis and has a high level of patient acceptability (78) .

Phillips et al 2004 aimed to compare ACBT with the Hayek Oscillator Cuirass, performing HFCC on secretion clearance in children with CF during an exacerbation. Sputum weight increased significantly with ACBT compared with HFCC during treatment (5.2 g vs. 1.1 g, $P < 0.005$, morning; 4.1 g vs. 0.7 g, $P < 0.01$, afternoon). Pulmonary function improved significantly after morning ACBT

(FVC: 2.67 l to 2.76 l, $P < 0.03$; FEV_1: 1.59 l to 1.62 l, $P < 0.03$). Following afternoon ACBT, there was a significant increase in FVC, but no significant change in FEV_1. Pulmonary function did not change at any time following HFCC. Compared with ACBT, HFCC by Hayek Cuirass is not an effective airway clearance treatment modality for children with CF during an infective exacerbation (79).

Chatham et al 2004 was to determine whether repeated maximum inspiratory vital capacity manoeuvres against a fixed resistance increased effective short-term sputum clearance in adults with cystic fibrosis (CF). Twenty adults with CF were randomised to receive, on alternate days, either standardised physiotherapy (SP) for 30 min, comprising postural drainage and ACBT, or a series of resistive inspiratory manoeuvres (RIM) at 80% of their maximum sustained inspiratory pressure developed between residual volume and total lung capacity during the first 4 days of the treatment of an exacerbation of respiratory symptoms. Expectorated sputum was collected during and for 30 min after each treatment and weighed. Total protein, immunoreactive interleukin (IL)-8, human neutrophil elastase (HNE) concentrations, and the amount of each component expectorated were determined. Compared with SP, RIM increased sputum weight two-fold, independent of treatment order or day. The concentrations of protein, IL-8 and HNE in sputum were similar for both treatments, while the quantity expectorated was greater with RIM treatment. In conclusion, short-term resistive inspiratory manoeuvres treatment was more effective at clearing sputum and inflammatory mediators than standardised physiotherapy (69).

Patterson et al 2004 was to compare the efficacy of the test of incremental respiratory endurance (TIRE) with ACBT [incorporating postural drainage and vibration] as methods of airway clearance in adults with bronchiectasis. Sputum weight expectorated during and 30 min post-ACBT treatment was significantly greater than the sputum weight expectorated during and 30 min post-TIRE treatment [mean difference 2.44 g (95% CI 0.43-4.45). ACBT is a more effective method of airway clearance in bronchiectasis than TIRE during single treatment sessions (70) .

Patterson et al 2005 was to compare the efficacy of ACBT with Acapella as methods of airway clearance in adults with stable, productive bronchiectasis in the objective of the study. No significant differences were found at baseline indicating that patients were stable. No significant differences were found between weight of sputum expectorated with ACBT treatment and weight of sputum expectorated with Acapella treatment-mean difference 0.54 g (95% CI -0.39 to 1.46). A greater proportion of patients preferred Acapella (14/20). Acapella is as effective a method of airway clearance as ACBT and may offer a user-friendly alternative to ACBT for patients with bronchiectasis (71).

2.4.3 The Studies of Pursed Lips Breathing

Schmidt et al 1964 were studied the effects of different expiratory air-flow rates and positive expiratory oral pressure upon vital capacity in normal subjects and in patients with a definite clinical diagnosis of either bronchial asthma or diffuse obstructive pulmonary emphysema. Increased oral pressure during exhalation, to simulate the phenomenon of lip-pursing was shown to have no beneficial effect upon the vital capacity measurement in any group, provided that flow rate was unaltered. Reduction in expiratory air flow allowed marked increases in the vital capacities of the patients with emphysema, but no changes in the vital capacities in asthmatic or normal subjects. It is suggested that the beneficial effect attributed to lip-pursing in emphysematous subjects is due not to the increase in oral pressure, but to a reduction in initial expiratory flow rate. The reduction in the initial expiratory flow rate reduces the Bernouilli effect created by air flow and therefore reduces the tendency for poorly supported airways to collapse. The emphysematous subject with pursed lips is able to reduce his initial expiratory flow rate so that the patency of the airways with increased compliance is maintained for a longer period during exhalation. Retaining the patency of these airways would result in the reduction in airway resistance at a given lung volume. Furthermore, by preventing the collapse of these airways the patient is able to reduce the amount of air-trapping and reduce his residual volume (80).

Thoman et al 1966 conducted to elucidate the efficacy of pursed-lips breathing (PLB) and the mechanism of the presumed improvement in ventilation. Pursed-lips breathing has a significant effect in decreasing respiratory rate, increasing tidal volume, decreasing $PaCO_2$ and increasing the ventilatory rate of the most slowly ventilated component of the FRC. Therefore, it would appear that pursed-lips breathing is definite value in patients with chronic obstructive pulmonary disease and that this demonstrated value is due to the decrease in respiratory rate rather than an increase in intra-airway pressure (81).

Tiep et al 1986 found that successful pursed lips breathing was accompanied by markedly increased tidal volume and reduced respiratory rate with no consistent change in minute volume. These findings are consistent with previous studies. Pursed lips breathing training with the adjunct of ear oximetry is a useful technique for temporarily improving SaO_2 and lends physiologic support for its clinical use. One might speculate that when patients have the knowledge that they can increase the oxygenation of their blood by a simple breathing technique, they might not panic during times of respiratory distress. Thus, self confidence could be improved, as well as patient quality of life (82).

Roa et al 1991 studied work of breathing and ventilatory muscle recruitment during pursed lip breathing (PLB) in patients with chronic airway obstruction. This study conclude that PLB increased the overall work of breathing. The decrease in gastric pressure and more negative pleural pressure implies inspiratory recruitment of the rib cage muscles with less recruitment of the diaphragm/abdomen. The simultaneous decrease in respiratory rate, increase in tidal volume and changes in ventilatory muscles recruitment may be more important than the actual work of breathing in relieving dyspnea in some patients with chronic airway obstruction (83).

Breslin EH 1992 indicate a change in the pattern of chest wall muscle recruitment and improved ventilation with pursed-lip breathing in COPD. PLB led to increased rib cage and accessory muscle recruitment during inspiration and

expiration, increased abdominal muscle recruitment during expiration, decreased duty cycle of the inspiratory muscles and respiratory rate, and improved SaO_2. In addition, PLB resulted in no change in pressure across the diaphragm and a less fatiguing breathing pattern of the diaphragm. Changes in chest wall muscle recruitment and respiratory temporal parameters concomitant with the increased SaO_2 indicate a mechanism of improving ventilation with PLB while protecting the diaphragm from fatigue in COPD. Therefore, PLB leads to a marked increase in expiratory abdominal and rib cage muscle recruitment. Theoretically, contraction of abdominal muscles with PLB can facilitate expiration by increasing intra-abdominal pressure and by cephalad displacement of the diaphragm and the rib cage in the thorax. This may reduce functional residual capacity below the passively determined end-expiratory volume, thereby 1) making available elastic energy in the chest wall for use by the inspiratory muscles, 2) lengthening inspiratory muscle fibers and providing more tension generation for a given level of activation. Expiratory muscle recruitment with PLB may improve length-tension relationships of the inspiratory muscles, particularly the rib cage and accessory muscles, improving their mechanical efficiency and leading to greater force generation capacity in ventilation. However, it is possible that the integration of respiratory muscle changes with PLB, while enhancing respiratory muscle efficiency in force generation and improving ventilation, contributes also to the reduction in dyspnea reported by patients with COPD (84).

Bianchi et al 2004 hypothesized that the effect of PLB on breathlessness relies on its deflationary effect on the chest wall. Volumes of chest wall (Vcw) compartment were assessed using an optoelectronic plethysmograph. Compared to spontaneous breathing, patients with PLB exhibited a significant reduction in end-expiratory volume of the chest wall (Vcwee) and a significant increase in end-inspiratory volume of the chest wall (Vcwei). The decrease in Vcwee mostly due to the decrease in end-expiratory volume of the abdomen (VAbee) related to baseline FEV_1 and to the increase in expiratory time and total time of the respiratory cycle, but not to baseline functional residual capacity. Increase in tidal volume of the chest wall was shared between V_T of the abdomen and V_T of the rib cage. Borg score decreased with PLB. Their finding of a decreased Vcwee associated with less Borg

score appears to validate that hypothesis. It has been demonstrated that reduction in respiratory frequency and minute ventilation and increase in V_T in patients with COPD during PLB are likely factors contributing to the improvement of dyspnea in some patients. In addition, PLB leads to a decrease in inspiratory time/ total time of the respiratory cycle and independent correlate of dyspnea. Their analysis of timing components of breathing pattern has confirmed that the decrease in respiratory frequency by allowing more time for expiratory was the reason for the decrease in Vcwee and VAbee. One has also to consider that limiting the increase in end-inspiratory lung volume would prevent esophageal pressure from reaching a higher fraction of maximal inspiratory pressure, thus preventing dyspnea from increasing. In conclusion, changes in Vcwee related to baseline airway obstruction but not to hyperinflation(FRC). By decreasing respiratory frequency and lengthening expiratory time, PLB decrease Vcwee and modulates breathlessness (85).

Garrod et al 2005 was designed to test the effects of pursed lips breathing during exercise in patients with COPD who did not spontaneously perform PLB. There was no significant difference between walks PLB and non-PLB nor any difference in dyspnea. There was a significant reduction in end exercise respiratory rate (RR) and recovery time with PLB. Patients who showed a good response with the PLB walk has significantly higher baseline breathlessness. Natural PLB patients demonstrated lower exercise tolerance on the baseline walk and a trend toward greater resting breathlessness than those who did not. This study shows PLB during exercise and recovery results in lower post exercise RR and speeds return to pre-exercise breathlessness, compared with exercise and non-PLB. Reductions in RR appear to be greatest in those patients with resting breathlessness (22) .

2.5 Evaluation of Chest Physiotherapy in Airway Clearance Techniques

Chest physiotherapy can be defined as the external application of a combination of forces to increase mucus transport. More recently, new physiotherapeutic interventions have been introduced as alternatives or adjuncts to the conventional methods. It can be difficult to judge the relative efficacy of the different

components of chest physiotherapy in the treatment of mucus retention. These usually consist of a combination of different techniques. There are no simple measurements that reliably reflect changes in mucus transport. Chest physiotherapy has been evaluated using measurements of airflow, changes in gas exchange, measurements of pulmonary mucus clearance and measuring the volume of expectorated mucus. These evaluation techniques range from methods that are complex and difficult to perform but reproducible and quite accurate for short-term studies, to very simple methods that produce results that are next to meaningless (86). Chest physiotherapy interventions can be evaluated using different outcome variables as following

2.5.1 Mucus Transport Assessment

Transport rates of mucus in the human airways can be assessed by timing the transport rate of a tracer deposited on the bronchial mucus layer. There are three different types of tracers used (86, 87).

1) A bolus of a tracer, usually Teflon® discs or albumin microspheres, is deposited on the large airways through a bronchoscope or by inhalation. The transport of the tracer is visualized by bronchoscopy, radiography or scintigraphy if radiolabelled particles are used. With bronchoscopic particle deposition, airway cilia can be damaged, disturbing mucociliary transport. Measurement of mucus transport rates using this technique are limited to local measurements in the large airways.

2) A radiopaque dust, usually tantalum powder, is blown into the lungs through an endotracheal tube and deposition and clearance of the tracer in monitored radiographically. The amount of tantalum remaining in the lungs after a given time interval is scored visually and is expressed as a percentage of the initial amount. This technique is invasive, can damage the airways, and uses a relatively high radiation dose depending on the number of chest radiographs. Therefore, this technique is rarely used for measuring mucus transport.

3) A radioactive aerosol tracer (RAT) is inhaled and deposited on the airway surfaces. The amount of radioactive tracer is counted using a gamma camera or scintillation counters. Transport of the tracer is expressed as the percentage retention or the percentage decrease of the initial amount of radioactivity in defined regions of the lungs after a fixed time. This technique is one of the most reliable methods to measure mucus transport over a short period of time in the bronchial tree.

2.5.2 Measurement of Expectorated Mucus Volume

It may be expected that the straightforward measurement of expectorated sputum volume would be an accurate method to assess the effectiveness of therapeutic interventions directed toward improving mucus clearance. However, sputum volume measurements can be inaccurate because of patients reticence to expectorate, inadvertent swallowing of secretions and salivary contamination of the secretions expectorated. The actual volume of secretions expectorated is extremely variable from day to day and even at different times of the day, with greater volumes generally being produced in the early morning. Finally, increased volumes of collected secretions could represent increased production of mucus as well as increased clearance. Measurement of a volume of expectorated mucus can give a global impression of transport assuming that mucus production in the airways is stable during the time of the measurements. Contamination with saliva can be partially corrected by drying the mucus and taking the dry weights for analysis.

In most studies investigating the effect of a physiotherapeutic intervention, the results of mucus transport measured by the RAT technique are checked by weighing the quantity of expectorated mucus. Van der Schans et al 1999 suggested that the RAT technique is more sensitive than assessing the volume of expectorated mucus to quantify changes in bronchial mucus transport, especially when mucus production is low. A combination of measurement of mucus transport using the RAT technique and measurement of the volume of expectorated mucus is probably the most reliable method to quantify acute changes in mucus transport (86).

2.5.3 Assessment of Subjective Effects Associated with Mucus Retention

An important but often overlooked aspect of sputum expectoration is the subjective experience of the patient. One of the potential effects of chest physiotherapy is to make expectoration more efficient or less tiring or to concentrate expectoration over specific periods of the day. For the patient, these effects can be very important. The instruments that may be valuable are the "Questionnaire for ease of cough and sputum clearance" developed by Petty et al 1990 and the St George's Respiratory Disease questionnaire by Jones et al 1992. The first questionnaire quantifies the subjective difficulty, frequency and severity of cough and expectoration. The second is used to quantify the health-related quality of life including symptoms such as cough and sputum (86).

2.5.4 Pulmonary Function Assessment

It has often been assumed that mucus has a measurable effect on pulmonary function and that improvement of mucus transport will improve pulmonary function. Retention of mucus can theoretically reduce airway diameter and contribute to airflow obstruction. Therefore, in many studies, pulmonary function and particularly spirometry, have been used to evaluated the effect of airway clearance interventions meant to improve mucus transport. However, the measurement of airflow and simple lung volume do not appear to reflect changes in mucus transport and are relatively insensitive to airway clearance maneuvers. It is clear that improvement in mucus transport is not necessarily reflected by an improved pulmonary function. Therefore, spirometry alone should not be used to evaluate changes in bronchial mucus transport. It is important to assess the effect of physiotherapy on pulmonary function to evaluate side effects secondary to the intervention or to test the theorethical basis on which a certain intervention is based. Testing the rate of change in pulmonary function over time may also be worthwhile to investigate the long-term effects of chest physiotherapy on the course of the disease. Spirometry is neither sensitive nor specific in assessing immediate changes in mucus transport (8, 86).

2.5.5 Hospitalization

Improvement of bronchial mucus transport is thought to reduce the retention of infected secretions and thus the frequency of respiratory tract infections. In patients with CF, the application of chest physiotherapy is thought to contribute to increased longevity. There are difficult ethical problems in evaluating these effects as an intervention that has been shown to have short-term beneficial effects on mucus transport cannot be ethically withheld from patients .

2.5.6 Quality of Life

Hypersecretion, reduced mucus transport and airflow obstruction are impairements, while chronic coughing and expectoration of mucus or dyspnea can limit the patient in daily or recreational activities and can therefore be classified as disabilities. Chronic coughing, expectoration and dyspnea can also limit the patient in their social functioning and thus lead to a handicap. The effects of intervention can also be evaluated in these terms. Most studies have focused on effects on impairment level such as mucus transport and pulmonary function. Interventions should also evaluate changes in the disability level, e.g. subjective experience of coughing and activities of daily living and on handicap level using quality of life questionnaires. However, an intervention may be effective on impairment level by improving bronchial mucus transport, but may have negative effects on disability or handicap level due to the dependence on another person or a complicated device. There are limited data concerning the psychological and social aspects of chest physiotherapy.

For examples, the studies of airway clearance technique or therapeutic intervention, as assessed by parameters show in Table 2.5

Table 2.5 The studies of airway clearance techniques or therapeutic intervention, as assessed by parameters.

Pryor et al 1981 (88)	Title : A comparison of mechanical and manual percussion as adjuncts to postural drainage in the treatment of cystic fibrosis in adolescents and adults Parameters : PFT - FEV1, FVC, Weight of sputum - during, 45 min after Px and over 24 hr period,the time for Px. Note : PFT represent airways obstruction, Weight of sputum and the time for Px represent efficiency of Px.
Bateman et al 1981 (89)	Title : Is cough as effective as chest physiotherapy in the removal of excessive tracheobronchial secretions? Parameters : The labelling of tracheobronchial secretions by radioaerosol with ^{99m}Tc (half-life 6 h), external gamma camera Counts were collected from anterior chest over five-minute periods as half-hourly intervals from 30-150 min. Note: Using the radioaerosol tracer technique, they were able to establish the efficacy of the PT technique in aiding the removal of excessive secretions from central, intermediated and peripheral lung regions.
Petty TL 1990 (90)	Title : The national mucolytic study: results of a randomized, double blind, placebo-controlled study of Iodinated glycerol in chronic obstructive bronchitis. Parameters : 8 primary symptom efficacy parameters - cough frequency, cough severity, chest discomfort, dyspnea, ease in bringing up sputum, patient and physician global assessments and a derived patients's global assessment six secondary parameters- frequency of bronchodilator use, incidence and duration of acute exacerbation, frequency of concomitant medication use, incidences of adverse experiences and dropouts Note : This study supports the usefulness of objectively evaluating symptoms as a measurement of Px (drug) efficacy
VanHengstum et al 1991 (91)	Title : Effect of positive expiratory pressure mask physiotherapy (PEP) versus forced expiration technique (FET/PD) on regional lung clearance in chronic bronchitics Parameters : radioaerosol technique on regional lung clearance with ^{99m}Tc, gamma camera (the deposition pattern, penetration index, regional lung clearance) Note : The clearance in separate regions of the lung was assess by objective radio-aerosol technique

Table 2.5 The studies of airway clearance techniques or therapeutic intervention, as assessed by parameters (Continued)

Cecins et al 1999 (92)	Title : The active cycle of breathing techniques - to tip or not to tip ? Parameters : Sputum expectorated-during, after 30 min and 23 hr., the number of productive cough-during, after 30 min PFT-FVC, FEV1, SaO2, rate the intensity of breathlessness, patient preference. Note : the use of wet weight of sputum as an outcome measure and the power of the study to detect a difference between interventions, There was designed to evaluat a simple, independent airway clearance regimen and a treatment time of 30 min was considered realistic and reflects clinical practice.
Thompson et al 2002 (78)	Title : Randomised crossover study of the Flutter device and the active cycle of breathing technique in non-cystic fibrosis bronchiectasis Parameters : The daily weight of sputum produced, the duration of physiotherapy, PEFR, and breathlessness before and after each session, Postbronchodilator spirometric tests, PEFR, and health related quality of life (CRQ) at baseline and after each technique. Questionnaire was asked perferred for routine use Note : A recent review of ACTs in adults has suggested that, if the objective differences are small between the different techniques, then individual preferences are likely to play an important part in compliance with treatment
Phillips et al 2004 (79)	Title : Comparison of active cycle of breathing and high-frequency oscillation jacket in childrent with cystic fibrosis Parameters : weight of wet sputum produced -15 min following Px, sputum produced over a 24-hr period, PFT-FVC, FE V1 before, immediately following, 10 minafter Px , arterial oxygen saturation and HR -continuously recorded, BP -before, every 10 min during and immediately following Px.,five-item questionnaire to rate the Px mode: 1)ease of technique 2)comfort 3)secretion clearance 4) breathlessness and 5) recommendation to a friend. Note : The improvement in lung function, together with increased expectoration of sputum, both support the conclusion
Chatham et al 2004 (69)	Title : A short-term comparison of two methods of sputum expectoration in cystic fibrosis Parameters : Sputum weight, Total protein concentration & human neutrophil elastase of sputum, PFT-FVC,FEV_1, FEV_1/FVC Note : Clearance of total protein, indicator of increased microvascular exudation and celluar breakdown in the airway, and cause of increased sputum viscosity, clearance of HNE indicates potential for removal of injurious products

2.6 Radioaerosol Technique for the Assessment of Mucociliary Clearance

The radioaerosol technique or a radioactive tracer technique (RAT) is probably the most direct outcome parameter for assessment of MCC (87, 93, 94). Mucociliary transport and mucus clearance are measured by quantifying the removal of an inhaled radiolabelled aerosol deposited on the tracheobronchial mucosa. This technique is noninvasive and reliable in vivo method of monitoring the mucociliary clearance in healthy subjects and patients with various chronic lung diseases (86). RAT is more sensitive to quantify changes in bronchial mucus transport, especially when mucus production is low (74, 91, 95-98). It can provide the most physiological information about the deposition and clearance of particles in the lung regions of interest and can be expressed as the percentage of activity clearance at a designated time point. However, assessment of regional clearance in this technique is limited only two-dimensional picture.

A Radiopharmaceutical

On the basis of procedure, a radiopharmaceutical consists of a radionuclide and biochemical, two considerations apply in designing or developing a radiopharmaceutical, one relating to the radionuclide and the other relating to the biochemical. The choice of a radionuclide for imaging purposes is chiefly dictated by the necessity of minimizing the radiation dose to the patient and the detection characteristics of present-day nuclear medicine instrumentation. To minimize the radiation dose to the patient, a radionuclide should have a half-life as short as compatible with the biological phenomena under study. Moreover, a radionuclide should be available easily, economically and uncontaminated form. Technetium-99m, with its 6-hour half-life and 140-keV γ-ray emission, little emission of corpuscular radiation, and easy economical availability from a generator, comes very close to fulfilling the above requirements. This accounts for its wide use in nuclear medicine (99).

Technetium-99m labeled human serum albumin is primarily radiopharmaceutical used for blood pool imaging such as heart or placenta. It also used for radioactive tracer technique for assessment of MCC**.** After administration, it

is retained in the body for a long period of time. However, Technetium-99m labeled albumin is not as stable in vivo as albumin labeled with radioiodine or radiochromium. Therefore, it is not the preferred agent for plasma volume determination.

The Precautions of the Use of Technetium-99m Human Serum Albumin

Technetium-99m human serum albumin is a gamma-emitting radionuclide imaging agent used for the diagnosis of diseases in many tissues, particularly in cardiovascular and cerebral circulation. This radiopharmaceuticals is substrate nonspecific agents which do not participate in a specific chemical reaction (100). Then, it is suitable for administration to humans for diagnosis (100, 101)

With scintigraphic methods of MCC assessment, this radiopharmaceuticals (1-5μm of particle size) will be delivered to the tracheobronchial surfaces as aerosols and used noninvasive technique. Technetium-99m human serum albumin aerosol is an inert and nonpermeable substance to the pulmonary epithelium (102). Removal of radioactivity from the lung can be accomplished in two ways; 1) the airways by mucociliary transport, 2) the blood circulation. Previous studies have demonstrated that significant amounts of radioactivity do not appear in the bloodstream for several hours after it has disappeared from the lung. In primary ciliary dyskinesia, there is no mucociliary transport, the radioactivity in the lung remained virtrually unchanged over a 2.5 hour period after inhalation of a radiolabelled aerosol (103). Base of literature reviews, Technetium-99m Human serum albumin is presumably a constant condition throughout the study and safety of use in the subject (75, 96, 102-105).

Nevertheless, one of the precautions is radiopharmaceuticals preparation such as kit components, storage conditions, preparation considerations, stability, radiochemical purity and general applications of technetium radiopharmaceuticals prepared from kits. It is important to required aseptic preparation, quality control, storage and disposal of radiopharmaceuticals in the study.

The Adverse Effects of Radioaerosol Technique

From most of the previous studies, the technique was well tolerated by subjects and patients. No significance of adverse events were reported (97, 103, 105, 106). Most of studied suggest that RAT is one of the most reliable method to measure mucus transport over a short period of time in the bronchial tree. It is high monitoring precision (94, 97, 107), useful for visual and qualitative evaluation of the actual dynamic mucociliary clearance mechanisms in the lung (74, 91, 95, 96, 103, 105-110). The physiological function of MCC provided by RAT is unique and unattainable by using other procedures. Moreover, there were not any reported about the adverse effects to the persons undergoing RAT (111). Because nuclear medicine procedure utilize very small doses of short-timed isotopes (ones that only stay radioactive for a few hours or days), the amount of radiation received is generally less than or equal to that of an x-ray. The dose is almost entirely limited to the area being examined, the whole body radiation dose due to scattered radiation being low. Moreover the use of aerosols of RAT is the small amount of activity, approximately 2-10%, actually delivered to the patients. Usually about 30 mCi (1.11 GBq) is placed in the system nebulizer, with only 1 or 2 mCi (37-74 MBq) actually being delivered to the patients or normal adult administered activity 25 to 35 mCi (900 to 1300 MBq) in the nebulizer from which the patients receives about 0.5 to 1.0 mCi (20 to 40 MBq) (111, 113). Therefore, activities administered to patients for RAT_procedures are too low for the possible risk.

In addition, radiation safety refers to the activities and control measures used to limit the amount of radiation exposure received by radiation workers, members of the general public and patients undergoing radiologic procedure. The international commission on radiological protection (ICRP) recommends radiation dose limits. From Annual Radiation Dose Limits, total effective dose equivalent limits is 50 mSv for occupational radiation workers, 1 mSv for general public and 5 mSv for embryo-fetus (entire pregnancy) (99, 100, 112). In conclusion, RAT procedures are very low radiation dose and are based on the Annual Radiation Dose Limits. There is safety for patients undergoing diagnostic test and extremely rare adverse effects.

CHAPTER III
METHODS

This dissertation was composed two studies. The first study was compared the efficacy of pursed lips breathing with forced expiration techniques (PLB& FETs) and active cycle of breathing technique (ACBT) with respect to acute change on pulmonary mucus clearances in healthy subjects. The second study was compared the effectiveness of PLB&FETs and ACBT in patients with chronic obstructive pulmonary disease.

3.1 The First Study: Efficacy of Pursed Lips Breathing with Forced Expiration Techniques and Active Cycle of Breathing Technique on Pulmonary Mucus Clearances in Healthy Subjects

3.1.1 Subjects

A convenience sample of three healthy male subjects who were volunteered to this study, were eligible for the study. The participants's ages were nearly identical in ranged from 33-35 years. They were entered in the study by the following criteria :

Inclusion criteria

1. Age > 20 years.
2. Healthy with no problems of verbal, hearing that affect to verbal instruction and practice.
3. No any infection or hospital admission in a period of 4 weeks prior to the study
4. No problem of neurological system or psychological disorder that affect to verbal instruction and ability to practice technique

Exclusion criteria

1. The history of asthma, chronic respiratory diseases or history of chest trauma
2. Current smoker

3.1.2 Instrumentation

3.1.2.1 ADAC Single Head Genesys Nuclear Gamma Camera

(Philips medical systems, Milpitas, CA)

A single head SPECT with PegaSys Digital Acquistion System and full body gamma camera linked to the computer system for detect static scintigraphic image of nuclear medicine with optimum digital quality and high throughout total body and SPECT Imaging

Figure 3.1 ADAC Single Head Genesys Nuclear Gamma Camera (Philips medical systems, Milpitas, CA)

3.1.2.2 Venti-Scan III™ Radioaerosol Administration System

(Biodex Medical system,Inc. NY, USA) consists of radioaerosol delivery system and Venti-scan III disposable radioaerosol kit.

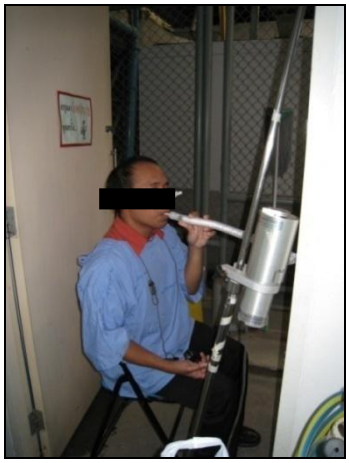

Figure 3.2 Venti-Scan III™ radioaerosol administration system (Biodex Medical system,Inc. NY, USA).

3.1.2.3 Technetium-99m Human Serum Albumin Aerosol

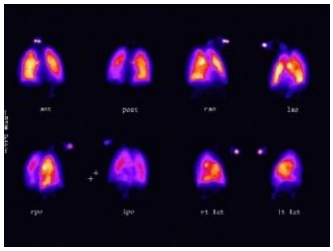

Figure 3.3 Technetium-99m human serum albumin aerosol.

Technetium-99m labeled human serum albumin is primarily radiopharmaceutical used for radioactive tracer technique for assessment of MCC**.** Technetium-99m is the 6-hour half-life with 140-keV γ-ray emission, little emission of corpuscular radiation and easy economical availability from a generator. This accounts is wide use in nuclear medicine. It is suitable for administration to humans for diagnosis and it is not stable in vivo .

3.1.2.4 Pony FX Desktop Spirometer and Cosmed® syringe (Cosmed USA, Inc. Chicago, USA)

Figure 3.4 Pony FX desktop spirometer and Cosmed® syringe 3 liters

Pony FX is desktop-size spirometer developed for lung function screening. It is available with a Turbine flowmeter. It is the perfect combination for all-inclusive spirometry, easy access to all functions with an immediate visual analysis and integrated fast thermal printer provides high quality reports in just a few seconds. Pony FX includes an internal memory with high storage capacity. It is furnished with a powerful PC software for downloading and storing data. Quality control messages according to the ATS guidelines are displayed for spirometry tests. Interpretation of pulmonary function test is based on reference spirometric values for healthy lifetime nonsmokers in Thailand or predicted normal values of Thai people in 2000 (114).

3.1.2.5 Nonin 9550 Onyx II Finger Pulse Oximeter (Nonin Medical ,Inc. Plymouth, MN, USA)

The Nonin 9550 is simple and easy to use. It automatically turns on for fast, easy spot-checks and provide superior accuracy. The new turn-off mechanism allows for 2500 spot-checks or 21 hours of continuous use, and the versatile unit accommodates a wide range of finger sizes from pediatric to adult. The enhanced design has resulted in a smaller unit with enclosed spring for safety. The Nonin 9550 has a wider LED viewing angle for easier use for monitoring percentage of oxygen pulse saturation and heart rate.

Figure 3.5 Nonin 9550 Onyx II Finger Pulse Oximeter (Nonin Medical,Inc. Plymouth,MN USA.

3.1.2.6 Mini-Wright™ Peak Flow Meter (C3103104, Clement Clarke International limited, Harlow, UK).

It is a built-in one-way valve to monitor peak expiratory flow rate (PEFR) with standard range 60-800 L/minute. There are available in Wright scale and ATS scale.

Figure 3.6 Mini-Wright ™ peak flow meter.

3.1.2.7 Modified Borg Scale

For subjective rating of dyspnea, Modified Borg scale measures the subjects'perception of how short of breath. The number represents how subjects' breathing feel. Number "0" means that they are breathing without thinking about it and feel normally. Number "10" is the most out of breath they can imagine.

The Borg category scale for rating breathlessness

0	Nothing at all
0.5	Very, very slight (just noticeable
1	Very slight
2	Slight
3	Moderate
4	Somewhat severe
5	Severe
6	
7	Very severe
8	
9	Very, very severe (almost maximal)
10	Maximal

Figure 3.7 Modified Borg Scale.

3.1.3 Procedure

Subjects who met the inclusion criteria were invited to participate in the study. Participants were asked to read and sign an informed consent. All subjects were in stable condition throughout the experimental period. Subjects were all fully trained in two airway clearance techniques: PLB&FETs and ACBT. They were proficient in self-treatment of both techniques.

A randomized crossover study was performed. Each subject attended three separate occasions at least three days apart and underwent an identical experimental procedure with the three treatment protocols. These protocols were a single-intervention of control (normal breathing), PLB&FETs and ACBT. There were three study days for each subject. Protocol I (control) was carried out on the first study day. Protocol II (PLB&FETs) and protocol III (ACBT) was used in a randomized order. All experiments on an individual subject were performed within 3 days at the same time of day within one week. The format of the 70 minute experimental period was illustrated in Figure 3.8. The study began with a baseline camera data collection

immediately after inhalation of the radioaerosol (time zero). For each protocol, 1 minute measurements of lung radioactivity were made at every 10 minutes throughout the 70 minutes.

Protocol I - control (normal breathing) : A quiet breathing experiment was conducted during the subject rest in upright position throughout the experimental period. Subjects were permitted to cough when they need to. No physical therapy was performed.

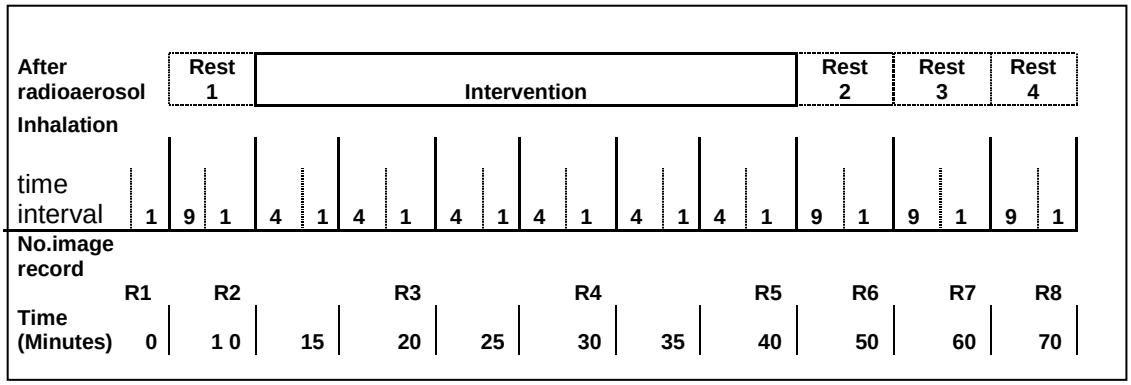

Figure 3.8 Experimental period. Scintigraphic imaging is indicated by R1-R8. The set of images is obtained at baseline, during intervention and after intervention.

Protocol II – PLB&FETs : The subject rest in upright position for the first 10 minute. From 10^{th}- 40^{th} minute, the subject performed PLB&FETs (approximately 4 minute/set) with 1 minute period between each set for rest and was monitoring of lung radioactivity. For PLB, verbal instruction of pursed lips breathing was as follow "Breathe in through your nose, not a deep breath, just a normal inhalation. Count to two in your mind. Your breath out should take two or three times as long as you breathe in. Keep your lips firmly together except for the very center. When exhaling, blow the air out in a firm, steady stream through the center of your lips. Remember to breathe out slowly; Do not blow too hard, but do keep the stream of air firm by blowing through the small opening left between your lips in the center of your mouth while counting to four or six " (22, 59, 82). For FET, it was a forced expiration or huff combined with periods of breathing control technique. One or two huffs from mid lung volume to low lung volume (this being the range at which more

peripheral secretions were mobilized) were followed by breathing control. To produce an effective huff, the patient take a short breath in and then breathes out forcefully through the mouth, contracting the abdominal muscles. Breathing out loudly with a partially closed larynx or just clearing the back of the throat does not produce an effective huff (15, 17, 59, 115). Subject was instructed to perform 5 PLB with 1 forced expiration per minute. Subject then rests again from 40^{th} – 70^{th} minute.

Protocol III - ACBT : The subject rest for the first 10 minute. From 10^{th}- 40^{th} minute, ACBT was performed a set of breathing technique for 4 minute periods with 1 minute rest between each set. This technique combines three breathing methods to move mucous out of the lungs: 1) Breathing control (gentle relaxed breathing), 2) Thoracic expansion exercises (deep breaths, often with a three-second-breath hold and quiet unforced breath out) and 3) Forced expiration technique (breathing out one or two huffs which uses "huffing" from various lung volumes to assist in removal of secretions). These three steps were done in sequence to loosen and expel the mucous, then repeated for a time period designated by Pryor et al in 2002 (17). The lung radioactivity was monitored. Subject then rest again from 40^{th} – 70^{th} min.

Outcome measurements for the first study consisted of the percentage retention of radioactivity in each zone as a function of time in radioaerosol technique, oxygen pulse saturation levels (SpO_2) , heart rate (HR), peak expiratory flow rate (PEFR) and Modified Borg scale for dyspnea.

Mucociliary transport and mucus clearance associated with airway clearance techniques were measured by quantifying the removal of inhaled radiolabeled aerosol deposited on the bronchial mucosa. 15-30 mCi (555-1,100 MBq) Technetium-99m human serum albumin aerosol was administered via the Venti-Scan III^{TM} radioaerosol administration system (Biodex Medical System, Inc. NY, USA) (111-113). This system was generated by the compressed air driven nebulizer with O_2 airflow rate 10 liters per minute at a pressure of 50 psi. The mean mass median aerodynamic diameter (mean MMAD) of the aerosol generated by this system was

0.50 ± 0.01 (S.D.) μm, range from 0.48 to 0.52 μm and mean geometric standard deviation (mean GSD) 1.8 (polydispersed) μm (116). With normal adult administered activity, 15 to 30 mCi (555-1,100 MBq) in the nebulizer from which the subjects received about 0.5 to 1.0 mCi (20 to 40 MBq). Each subject received a lung radiation dose of approximately 0.7 mrad/mCi and the average radiation exposure to the whole body is approximately 0.026 rads/mCi (0.007 mGy/MBq). For the controlled inhalation of radioaerosol, the subjects inhaled the aerosol via a mouthpiece while wearing a noseclip and sitting upright. They were asked to breath slowly in normal tidal breathing then deeply with three seconds breath-hold approximately every 10 breaths until material inhaled with the total activity over the posterior chest of 100,000 counts. This indicated that 0.5-1.0 mCi was retained. The inhalation period required to obtain this count rate was usually 4-6 min. Subjects were trained to use of the radioaerosol administration system so that similar deposition of aerosol could be assured on each study day. Immediately after inhalation of the radioaerosol, subjects gargled, expectorated and then swallowed water to clear the throat, mouth and esophagus of excess labeled radioaerosol. A single head gamma camera (Genesys, Philips medical systems, Milpitas, CA) linked to a computer was used to assess the initial topographical distribution and subsequent clearance of the radioaerosol particles from the lungs. Eight sets of static scintigraphic image were obtained with the format of the 70-min experimental period. Each set of scintigrams consisted of images in the posterior view, acquired for 1 minute and stored in a 128 x 128 matrix. Regions of interest (ROI) were drawn by a technologist to obtain counts in each lung region on each image. Division of the lung image into central, intermediate and peripheral zones of this study was according to the study of Bateman et al in 1981 related by area in the ratio 2:1:2 (Figure 3.9) (89). The data from the right lung was analyzed for each region. All counts were corrected for radionuclide decay and background.

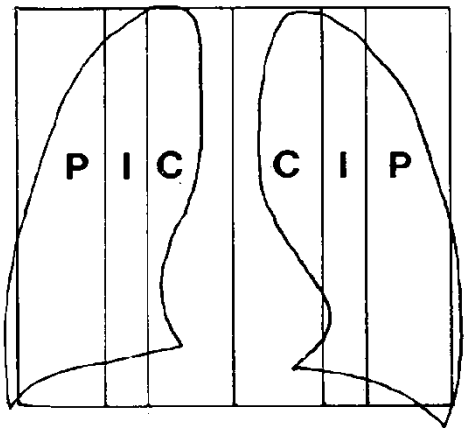

Figure 3.9 The selected lung regions: central (C), intermediate(I) and peripheral (P), related by area in the ratio 2: 1: 2. (89)

The initial whole lung deposition pattern or the baseline deposition pattern for each study day was quantified by the ratio of the percentage of radioactivity count in the central lung zone to the whole right lung zone. Transport of the tracer or clearance was expressed as the percentage retention of radioactivity in each zone as a function of time or the percentage decrease of the initial amount of radioactivity in defined regions of the lungs after a fixed time (86,103). Retention, calculate as a percentage of baseline deposited radioactivity, was plotted for the whole lung and for each of the 3 regions (86, 89, 97). Retention curves were drawn for each subject for each study day.

Peak expiratory flow rate (PEFR) was carried out using a Mini-Wright^{TM} peak flow meter in standard range 60-800 L/min (C3103104, Clement Clarke International limited, Harlow, UK). Before and after the experimental period, PEFR was determined to assess possible effects of the procedure on bronchial narrowing and to ensure comparable baseline pulmonary function on the days of measurement (74). The highest of three acceptable measurement was recorded.

Oxygen pulse saturation levels (SpO_2) and heart rate (HR) was recorded during each protocol using Nonin 9550 Onyx II Finger Pulse Oximeter (Nonin Medical ,Inc. Plymouth, MN, USA). The resting levels of SpO_2 and HR was also recorded before and after protocol.

Subjects were asked to rate the sensations of breathlessness that they perceived during the treatment by using a Modified Borg scale. This scale measured the subject's perception of how short of breath. The number represented the breath feeling. Number "0" means that they were breathing without thinking about it and felt normally for them and number "10" was the most out of breath they can imagine. The subject was then requested to rate the intensity of their breathlessness before each treatment session. There was repeated immediately following treatment and in the 30 minute after treatment without the subject viewing the initial record.

3.1.4 Data Analysis

The data was analyzed by descriptive statistics. All parameters of the study were described an individual's response to each condition (normal breathing, PLB&FETs, ACBT). An ungrouped (simple) frequency distribution with line graph of the picture technique were also represented the percentage retention of radioactivity in the central, intermediate, peripheral and whole zones of the right lung, heart rate and percentage of oxygen pulse saturation among the control (normal breathing), PLB&FETs and ACBT at the 10^{th}, 20^{th}, 30^{th}, 40^{th}, 50^{th}, 60^{th} and 70^{th} minute of experimental period.

3.2 The Second Study : Comparisons of Pursed Lips Breathing with Forced Expiration Techniques and Active Cycle of Breathing Technique in Patients with Chronic Obstructive Pulmonary Disease

3.2.1 Subjects

All patients were recruited from COPD clinic, Division of Respiratory Disease and Tuberculosis, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University and Outpatient Unit of Respiratory Disease, Chest Disease institute, Department of Medical Services, Ministry of Public Health. Twenty-two COPD patients with mild to severe severity included as volunteers in this study.

Inclusion Criteria

1. Stable COPD of stage I- III according to GOLD updated 2006criteria
2. Age $\geq$ 35 years.
3. Clinically condition without any infection or hospital admission in a period of 4 weeks prior to the study. There were medical therapy and no changes in medication during the study.
4. No problems of verbal, hearing that affect to verbal instruction and practice.
5. No problems of neurological system or psychological disorder that affect to verbal instruction and ability to practice technique

Exclusion Criteria

1. Acute exacerbation within 6 months prior to the study
2. Unable control hypertension or severe hypertension with Systolic BP $\geq$180 mmHg, diastolic BP $\geq$ 110 mmHg
3. Symptomatic cardiac disease such as uncontrolled cardiac arrhythmia or had history of acute myocardial infarction within 3 months prior the study
4. Chronic renal failure
5. History of asthma
6. Current smoker

7. History of recent hemoptysis, pneumothorax or chest trauma within 3 months of treatment prior the study

Ethics

All subjects were given an information sheet outlining the procedure, purpose and significance of the study. Written informed consent was obtained from all subjects prior to the study. Proposals of the study and the consent forms were approved by the Ethics Committee of Faculty of Medicine Siriraj Hospital, Mahidol University, Committee on Human Rights Related to Researches Involving Human Subjects, Faculty of Medicine, Ramathibodi Hospital Mahidol University and the Ethics Committee of Chest Disease institute, Department of Medical Services, Ministry of Public Health .

3.2.2 Instrumentation

3.2.2.1 Pony FX Desktop Spirometer and Cosmed® Syringe (Cosmed USA, Inc. Chicago, USA) shown in Figure 3.4

3.2.2.2 Nonin 9550 Onyx II Finger Pulse Oximeter (Nonin Medical ,Inc. Plymouth, MN, USA) shown in Figure 3.5

3.2.2.3 Mini-Wright™ Peak Flow Meter (C3103104, Clement Clarke International limited, Harlow, UK) shown in Figure 3.6

3.2.2.4 Sputum Collection Containers

The container are made of polypropylene. These disposable containers are size 70 milliliter and used for collecting samples of sputum. Graduated on the outer surface, each container has cap that works in a press and fit manner and make them leakproof.

Figure 3.10 Sputum collection container.

3.2.2.5 Modified Borg Scale

For subjective rating of dyspnea, Modified Borg scale measures the subjects'perception of how short of breath. The number represents how subjects' breathing feel. Number "0" means that they are breathing without thinking about it and feel normally. Number "10" is the most out of breath they can imagine. (Figure 3.7)

3.2.2.6 Daily log book

Daily log book was used to self evaluation by patient. There are composed of peak expiratory flow rate (PEFR), sputum volume and Modified Borg score of dyspnea. PEFR was measured by Mini-Wright^{TM} peak flow meter in the morning and evening. Daily sputum volume was recorded the volume of wet sputum in milliliter unit and subjective rating of dyspnea was determined by Modified Borg scale. This scale measured the subjects' perception from Number "0" to "10" to rate the intensity of their breathlessness in the evening on everyday.

3.2.2.7 Questionnaires: This study included 1) Modified patient evaluation questionnaire and Modified patient satisfaction questionnaire to evaluate objectively the symptom assessment in determining the effectiveness of ACTs in patient with COPD.

Modified patient evaluation questionnaire included assessment of the following: cough frequency, cough severity, chest discomfort, difficulty breathing and ease in bringing up sputum. The patient evaluation questionnaire was modified from Petty in 1990 (90) ; as follows.

Modified patient evaluation questionnaire

1. Cough episodes : Frequency – throughout the day

How frequency were your cough episodes on a typical day during the past week:

1) None – Unaware of coughing
2) Rare – Cough now-and-then
3) Occasional-Less than hourly
4) Frequent –One or more times an hour
5) Almost constant-Never free of cough or feeling free of the need to cough

2. Cough episodes : Severity – on arising and throughout the day

How severe were your coughing episodes on a typical day during the past week :

1) None – Unaware of coughing
2) Mild – Did not interfere with usual morning or daily activity
3) Moderate- Must stop activity during coughing episode
4) Marked – Must stop activity during and for a brief period after coughing episode
5) Severe- Stops all activity for sometime and is exhausting; may be accompanied by dizziness, headache, and/or pain in chest or abdomen

3. Chest discomfort: Tightness and/or congestion – on arising and throughout the day

How much chest discomfort did you have on a typical day during the past week:

1) None – Unaware of any discomfort
2) Mild – Noticeable now-and-then but is not bothersome and passes quickly; does not limit activity
3) Moderate-Noticeable less than hourly; limits and is aggravated or brought on by moderate activity
4) Marked-Noticeable one or more times an hour; may be accompanied by dyspnea; limits and is aggravated or brought on by normal activity, such as walking
5) Severe- Almost constant; accompanied by dyspnea; present even when resting; limits all activity

4. Difficulty breathing : Dypsnea (short of breath) - on arising and throughout the day

How much difficulty did you have breathing on a typical day during the past week:

1) None – Unaware of any difficulty
2) Mild – Noticeable during more strenuous activity; such as morning exercise; walking more than one block or up more than one flight of stairs without stopping
3) Moderate-Noticeable during light activity; such as making beds or taking out the garbage, walking one block or up one flight of stairs, or running or jogging
4) Marked-Noticeable when washing or dressing in the morning; after slowly walking less than one block or up one flight of stairs
5) Severe- Almost constant; present even when resting (sitting on bed or chair)

5. Ease in bringing up sputum – on arising and throughout the day.

Indicate any change in the ease with which you brought up sputum, on a typical day during the past week:

1) Marked improvement
2) Moderate improvement
3) Slight improvement
4) No change
5) Slightly worse
6) Moderately worse
7) Markedly worse

Modified patient satisfaction questionnaire is a five-point, four-item questionnaire. The patients would be asked to rate the treatment mode for 1) ease of technique; 2) comfort; 3) secretion clearance; and 4) recommendation to a friend (78). The scale is assigned a point value concerning the patients' level of satisfaction. The rating scales are from 5 to 1 (5 = excellent, 4 = good, 3 = fair, 2 = poor, 1 = very poor).

Modified patient satisfaction questionnaire

Please indicate the overall satisfaction of technique you have experienced during study.

Items	5 (Excellent)	4 (Good)	3 (Fair)	2 (Poor)	1 (Very poor)
1) Ease of technique					
2) Comfort					
3) Secretion clearance					
4) Recommendation to a friend					

3.2.3 Procedure

Twenty-two chronic obstructive pulmonary disease patients, diagnosed by respiratory physician were invited to participate in the study. Spirometric values were assessed before and after the administration of a bronchodilator with a period of 20 minutes for classify severity of COPD with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) updated 2006 criteria (1). All patients also complained of cough with difficult expectoration after waking in the morning, or episodes of repeated coughing and little or no effective expectoration. They were in a stable clinical condition without any infection. The patient's basic medication remained unchange during the course of the study (14 consecutive days). If any other change in therapy was required, the patient was excluded from the study. Participants who meet the inclusion criteria were asked to read and sign an informed consent.

In order to evaluate the effective of these two techniques, COPD patients were treated in comparison study with Two-way design with one repeated measure (2x3 mixed design). Each patient was randomly assigned to one of the two treatment groups. One group of patients received PLB&FETs therapy, while the other group underwent the ACBT therapy. They were asked to perform the airway clearance techniques twice a day at the same time of day with 30 minute of each session. On the first day of training session, subjects were all fully trained in PLB&FETs or ACBT under the supervision of a physical therapist (Saowanee Woravutrangkul) until they

were proficient in self-treatment of airway clearance technique to ensure reliable performance.

All subjects of both groups performed twice-daily ACTs with 14 consecutive days. The procedure of this study was illustrated in Figure 3.11. If subjects routinely used inhaled bronchodilators prior to airway clearance technique, these subjects were administered 30 min prior to the pre-treatment period. The study detected changes in pulmonary function test, Modified patient evaluation questionnaire on 1st, 7th, 14th day of the study and Modified patient satisfaction questionnaire on 14th day of the study. In daily log book, self evaluation of patient on everyday (peak expiratory flow rate, sputum volume and Modified Borg score were examined in the first and second week of the study as the result of therapy.

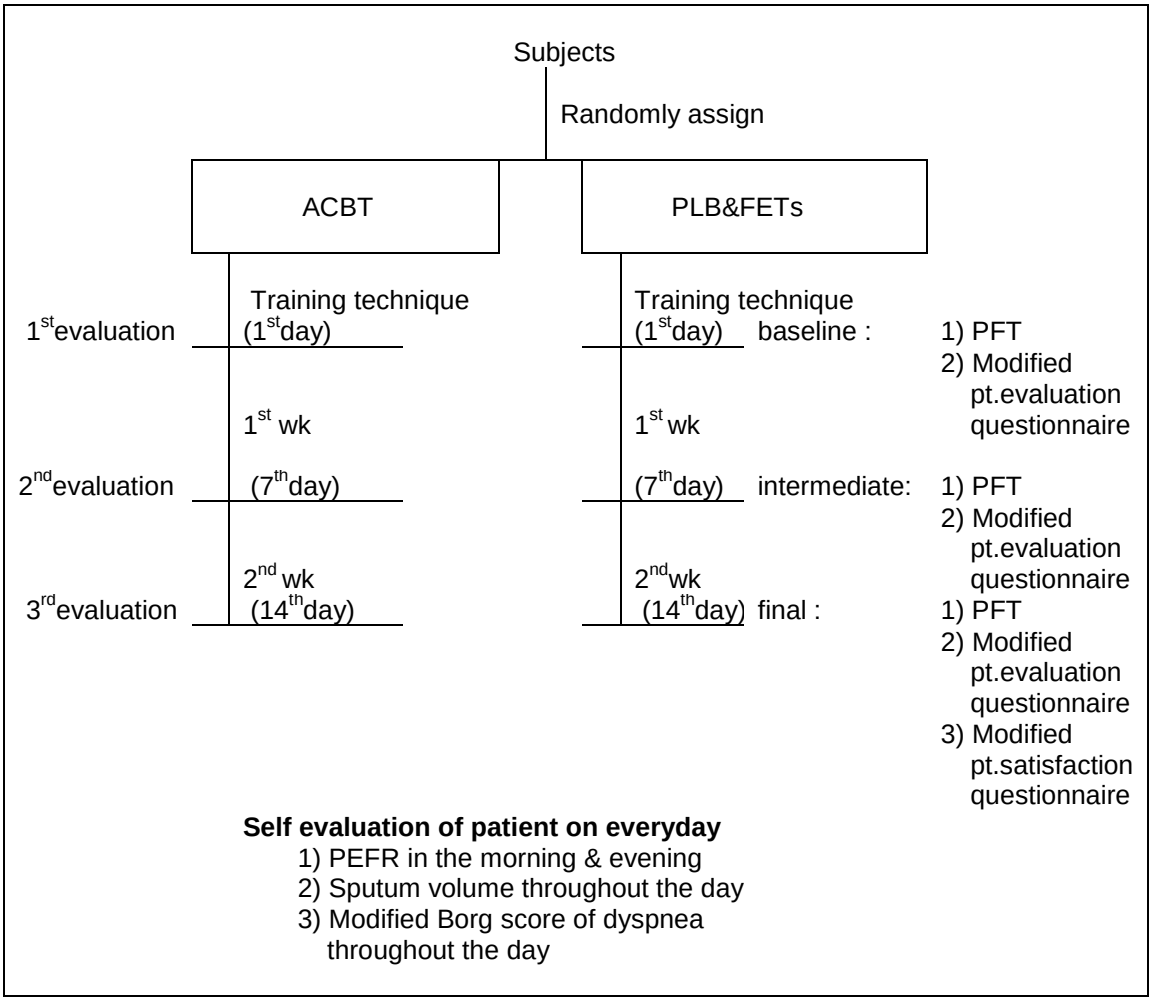

Figure 3.11 Flowchart of procedure of the second study.

Pursed lips breathing with forced expiration techniques group: Subject performed PLB&FETs (approximately 4 minute/ set) with 1-minute period between each set for rest. For PLB, verbal instruction of pursed lip breathing was as follow "Breathe in through your nose, not a deep breath, just a normal inhalation. Count to two in your mind. Your breath out should take two to three times as long as you breathe in. Keep your lips firmly together except for the very center. When exhaling, blow the air out in a firm, steady stream through the center of your lips. Remember to breathe out slowly; Do not blow too hard, but do keep the stream of air firm by blowing through the small opening left between your lips in the center of your mouth while counting to four or six" (22, 59, 82). For FET, it was a forced expiration or huff combined with periods of breathing control technique. One or two huffs from mid lung volume to low lung volume (this being the range at which more peripheral secretions are mobilized) were followed by breathing control. To produce an effective huff, the patient take a short breath in and then breathes out forcefully through the mouth, contracting the abdominal muscles. Breathing out loudly with a partially closed larynx or just clearing the back of the throat does not produce an effective huff (15, 17, 59, 115). The patients were instructed to perform 5 PLB with 1 FET per minute.

Active cycle of breathing technique group: ACBT was a cycle of technique of 1) breathing control (tidal breathing at the patient's own rate and depth, encouraging use of the lower chest with relaxation of the upper chest and shoulders), 2) thoracic expansion exercises (deep breathing exercises emphasizing inspiration with or without a breath hold; expiration is quiet and relaxed) and 3) the forced expiration technique (one or two huffs combined with periods of breathing control). ACBT was performed a cycle of breathing technique for 4-minute periods with 1-minute rest between each set. These three steps were done in sequence to loosen and expel the mucous, then repeated for a time period designated by Pryor et al in 2002 (17).

Outcome measurements of the second study consisted of pulmonary function tests, peak expiratory flow rate by peak flow meter, sputum volume,

Modified Borg score, Modified patient evaluation questionnaire and Modified patient satisfaction questionnaire.

Pulmonary function tests included forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV_1), FEV_1/FVC ratio, mid expiratory flow rate at 25% to 75% of vital capacity ($FEF_{25-75\%}$) and peak expiratory flow (PEF) were taken at the 1st day (baseline), 7th day and at 14th day of the study by Pony FX desktop spirometer (Cosmed USA,Inc. Chicago, USA). The spirometer was calibrated with a 3-liter syringe (Cosmed®) for calibration before each study and measurements were made in accordance with American Thoracic Society Standard (118). FVC, FEV_1, FEV_1/FVC ratio, $FEF_{25-75\%}$ and PEF data were utilized for analysis of the therapy effect. Interpretation of pulmonary function test is based on the data reference (predicted) values of Thai in 2000 (114).

Peak expiratory flow rate (PEFR) was performed by self evaluation of patient on everyday. Subjects were asked to assess and record PEFR in the morning and evening using Mini-Wright peak flow meter (C3103104, Clement Clarke International limited, Harlow, UK). The best of three measurements was recorded in daily logbook by the patient.

Daily sputum volume was gently expectorated into sputum collection containers. The patients were record the volume of wet sputum in daily logbook in milliliter unit by themselves.

Subjective rating of dyspnea was determined by Modifed Borg scale. This scale measured the subjects' perception of how short of breath. The number represents the breath feeling. Number "0" means that they are breathing without thinking about it and feel normally for them and number "10" is the most out of breath they can imagine. The subject was then requested to rate the intensity of their breathlessness in the evening on everyday.

The Modified patient evaluation questionnaire and Modified patient satisfaction questionnaire were used to evaluate objectively the symptom assessment in determining the effective of ACTs in patients with COPD. The patient evaluation questionnaire was modified from Petty in 1990 (90). Five efficacy parameters of modified patient evaluation questionnaire were assessed on the 1^{st}, 7^{th} and 14^{th} day of the study. The parameters included assessment of the following: cough frequency, cough severity, chest discomfort, difficulty breathing and ease in bringing up sputum.

After 14-day course of twice-daily airway clearance technique, subjects were also asked for their overall satisfaction of the technique using the Modified patient satisfaction questionnaire. The questionnaire was a five-point, four-item questionnaire. The patients were asked to rate the treatment mode for 1) ease of technique; 2) comfort; 3) secretion clearance; and 4) recommendation to a friend (79).

3.2.4 Data Analysis

The level of statistical significance was set at probability level less than 0.05 ($p<0.05$) for all analyses. Results were expressed as means and standard deviations. Kolmogorov-Smirnov Goodness of Fit-test was performed to determine the distribution of the data (118). The statistics were used as followed.

1. Unpaired t-test was used to assess the demographic data of subject's characteristic, total mean of peak expiratory flow rate, total mean of sputum volume between groups of the study in each time of assessment and used to assess total scores of Modified patient satisfaction questionnaire at the end of the study.
2. Paired t-test was used to assess total mean of peak expiratory flow rate, total mean of sputum volume within each groups throughout the study.
3. Two-way Repeated Measures Analysis of Variance (ANOVA) was used to assess difference in all pulmonary function parameters, total scores of Modified patient evaluation questionnaire within each group throughout the study and between groups of the study in each time of assessment.

4. Bonferroni post hoc test was used to multiple comparisons between two groups or between difference times of assessment within each group if the results were statistically significant.
5. Mann-Whitney U test was used to examine the differences of Modified Borg score between group at the 1st and 2nd week of the study.
6. Wilcoxon signed ranks test was used to examine Modified Borg score within groups at the difference of time.

CHAPTER IV
RESULTS

This dissertation was composed of two studies. The first study involved comparison between the efficacy of pursed lips breathing with forced expiration techniques (PLB&FETs) and active cycle of breathing technique (ACBT) with respect to acute change on pulmonary mucus clearances in healthy subjects. The second study involved comparison of PLB&FETs and ACBT in patients with chronic obstructive pulmonary disease.

4.1 The First Study : Efficacy of Pursed Lips Breathing with Forced Expiration Techniques and Active Cycle of Breathing Technique on Pulmonary Mucus Clearances in Healthy Subjects

Three healthy male subjects volunteered to join this study. The participants's physical characteristics and pulmonary function were showed in Table 4.1. All subjects had been non-cigarette smokers and stable health condition throughout the experimental period. The data of this study were analyzed by descriptive statistics with comparisons of bronchial mucus clearance during control (normal breathing), PLB&FETs and ACBT. All parameters were described as an individual's response in each intervention. An ungrouped frequency distribution with line graph of the picture technique was expressed as the percentage retention of radioactivity in the central, intermediate, peripheral and whole zone of the right lung, heart rate and percentage of oxygen pulse saturation at the 10^{th}, 20^{th}, 30^{th}, 40^{th}, 50^{th}, 60^{th} and 70^{th} minute of the experimental period.

Table 4.1 Physical characteristics and pulmonary function of subjects in the first study

Characteristics	Individual subject number		
	N1	N2	N3
Age (yr.)	34	33	35
Weight (kg.)	80	82	64
Height (cm.)	170	174	160
BMI (kg/m^2)	27.68	27.08	25.00
Spirometer parameters (% predicted value)			
FVC	88	99	103
FEV_1	89	99	106
ratio FEV_1/FVC	81	82	86
$FEF_{25-75\%}$	71	79	99
PEF	67	90	89

The relative value of control (normal breathing), PLB&FETs and ACBT for removal of pulmonary mucus clearance has been assessed in three healthy subjects. After inhaled radioaerosol, the initial distribution of the deposited radioaerosol across the three selected zones of the right lung expressed as a ratio of the radioactivity count in the central lung zone to the whole right lung zone showed little intersubject and intrasubject variation (Table 4.2)

Table 4.2 The baseline deposition of radioaerosol pattern for each study day determined by ratio of the radioactivity count in the central right lung to the whole right lung zone.

Subject No.	**Ratio of central lung zone / whole right lung zone**		
	Control	**PLB&FETs**	**ACBT**
1	0.35	0.35	0.37
2	0.38	0.36	0.37
3	0.40	0.39	0.39

4.1.1 Comparison of the percentage retention of radioactivity in the central, intermediate, peripheral and whole zone of the right lung among the control (normal breathing), PLB&FETs and ACBT during the experimental period

For individual data, transport of the tracer or clearance of the central right lung zone of the subject number 1 showed in Figure 4.1. There was a gradual decline of radioactivity after 10 minutes in PLB&FETs curve. During 10^{th} to 40^{th} minute, all curves were slowly up the incline approximately 1% - 2%. However, there was a marked fall in deposited radioactivity in PLB&FETs curve and control curve from 40^{th} to 70^{th} minute, whereas ACBT curve were standstill to the initial baseline.

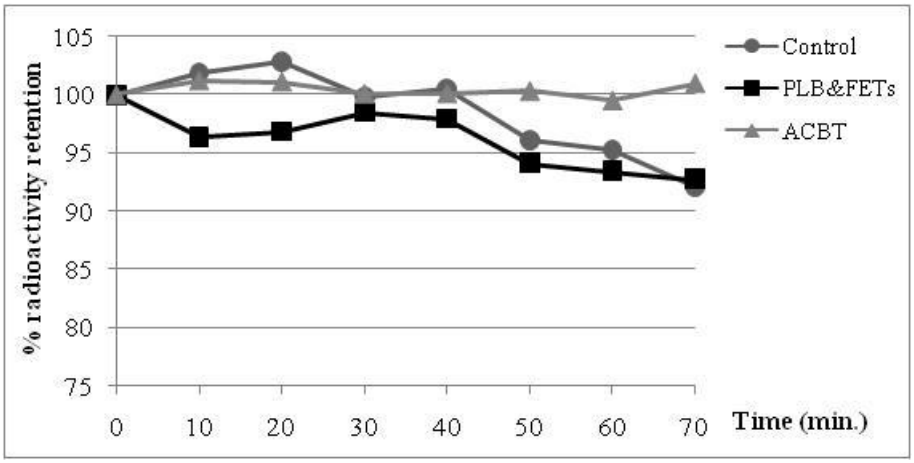

Figure 4.1 Clearance of the radioactivity from the central right lung zone expressed as percentages of the starting values on three interventions of measurement of subject number 1. (Decay-corrected data)

In the intermediate right lung zone, the radioactivity for all interventions of subject number 1 (Figure 4.2) were decreased in the same way from 10^{th} to 40^{th} minute. Nevertheless, the clearance of the radioactivity in PLB&FETs curve and ACBT curve were greater than control curve from 40^{th} to 70^{th} minute after intervention period.

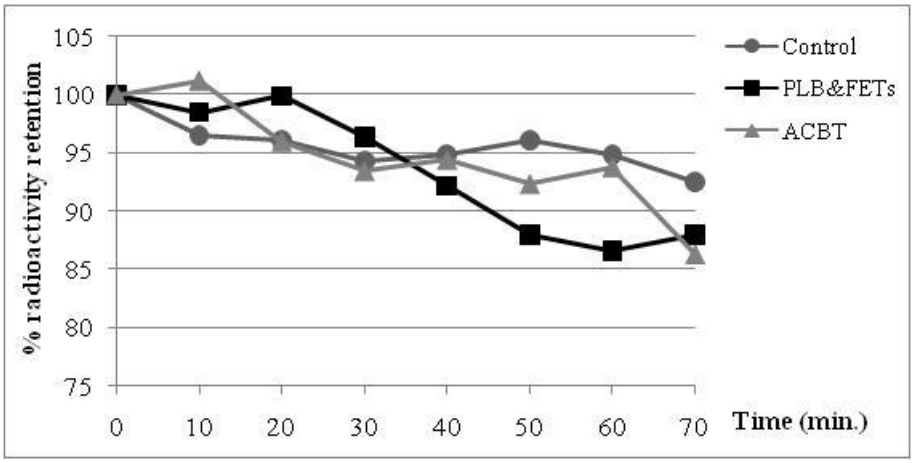

Figure 4.2 Clearance of the radioactivity from the intermediate right lung zone expressed as percentages of the starting values on three interventions of measurement of subject number 1. (Decay-corrected data)

The peripheral right lung clearance curve of all interventions were similar pattern from 10th to 30th minute (Figure 4.3). Interestingly, PLB&FETs and ACBT curves showed enhanced clearance during and after intervention from 10th to 70th minute. Moreover, the radioactivity clearance of both curves were higher than control curve at the end of experimental period.

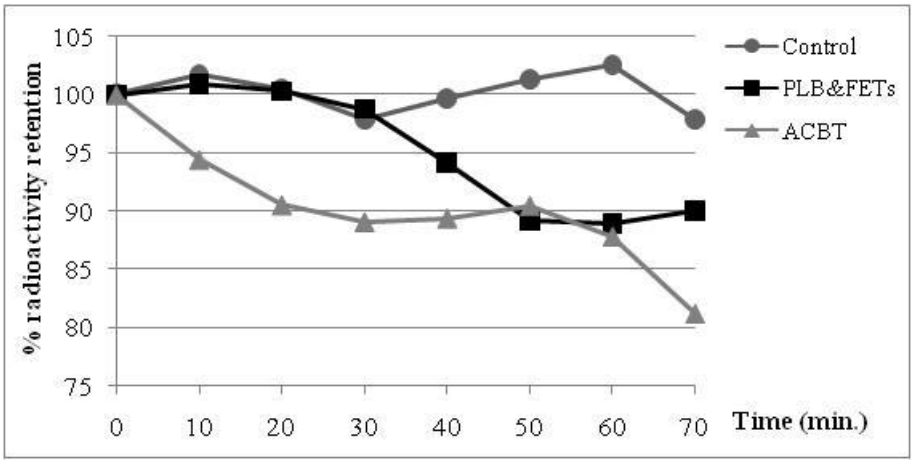

Figure 4.3 Clearance of the radioactivity from the peripheral right lung zone expressed as percentages of the starting values on three interventions of measurement of subject number 1. (Decay-corrected data)

Furthermore, the results of the whole right lung clearance in subject number 1 (Figure 4.4) were also facilitated by PLB&FETs and ACBT. These findings confirm that both techniques could enhance lung clearance, especially in the intermediate and peripheral zone.

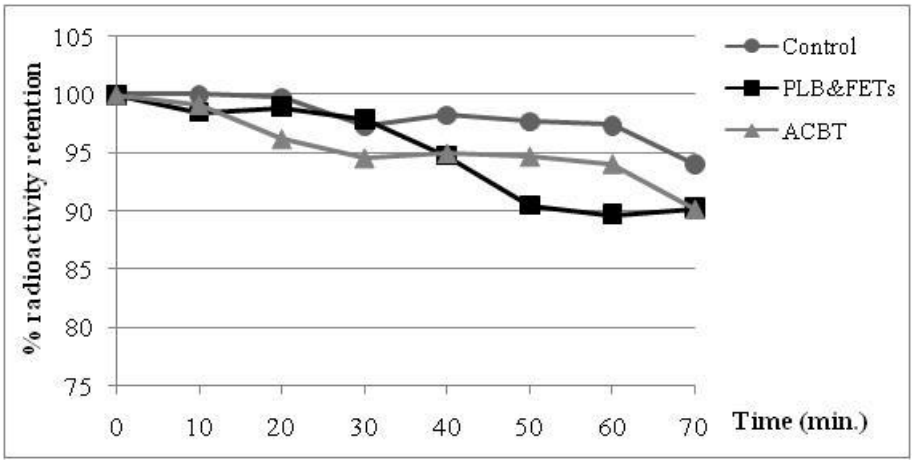

Figure 4.4 Clearance of the radioactivity from the whole right lung zone expressed as percentages of the starting values on three interventions of measurement of subject number 1. (Decay-corrected data)

With individual data of subject number 2, the clearance of central right lung zone in ACBT curve (Figure 4.5) was greater than in the control and PLB&FETs curves. ACBT curve was the most enhancement of radioactivity clearance from the central lung zone during and after intervention period from 20^{th} to 70^{th} minutes.

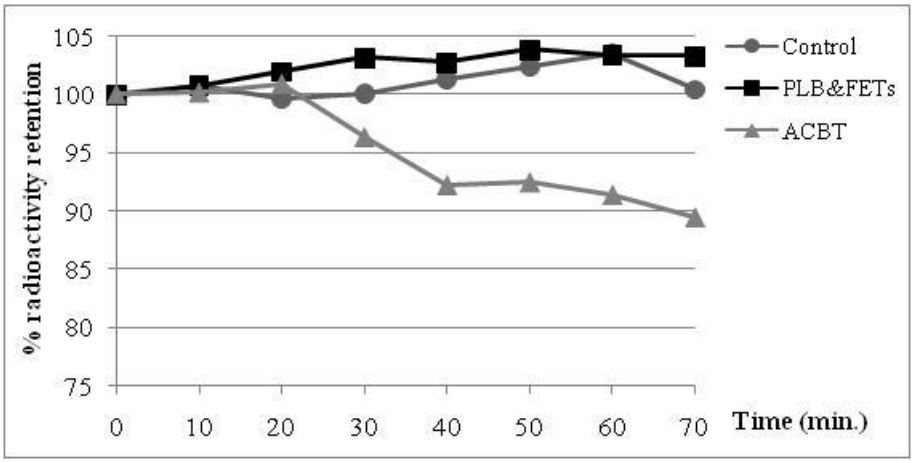

Figure 4.5 Clearance of the radioactivity from the central right lung zone expressed as percentages of the starting values on three interventions of measurement of subject number 2. (Decay-corrected data)

For intermediate right lung zone of subject number 2 (Figure 4.6), PLB&FETs and ACBT curves were clearly occurred declination of radioactivity during and after intervention, whereas the control curve was lightly decline from 10^{th} to 40^{th} minute and up to the initial baseline from 50^{th} to 70^{th} minute.

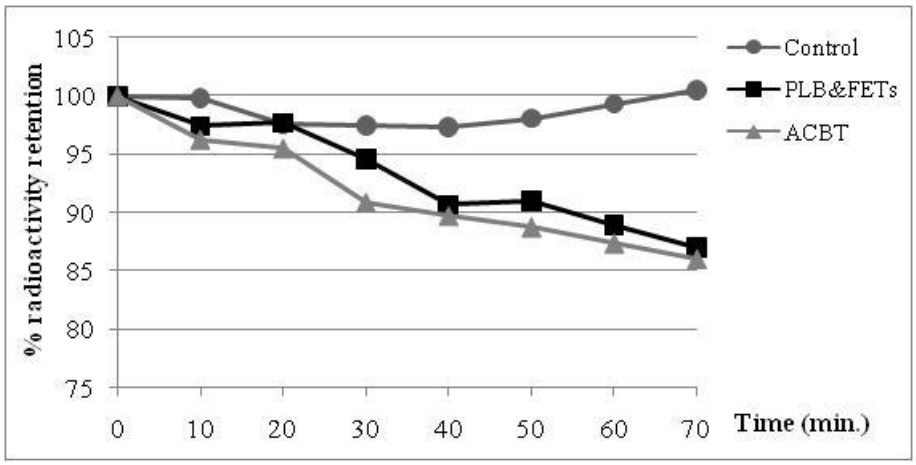

Figure 4.6 Clearance of the radioactivity from the intermediate right lung zone expressed as percentages of the starting values on three interventions of measurement of subject number 2. (Decay-corrected data)

For peripheral zone of subject number 2, the lung clearance curve of all interventions (Figure 4.7) were appeared similarity of slope pattern. However, the PLB&FETs curve was high radioactivity clearance in this lung zone.

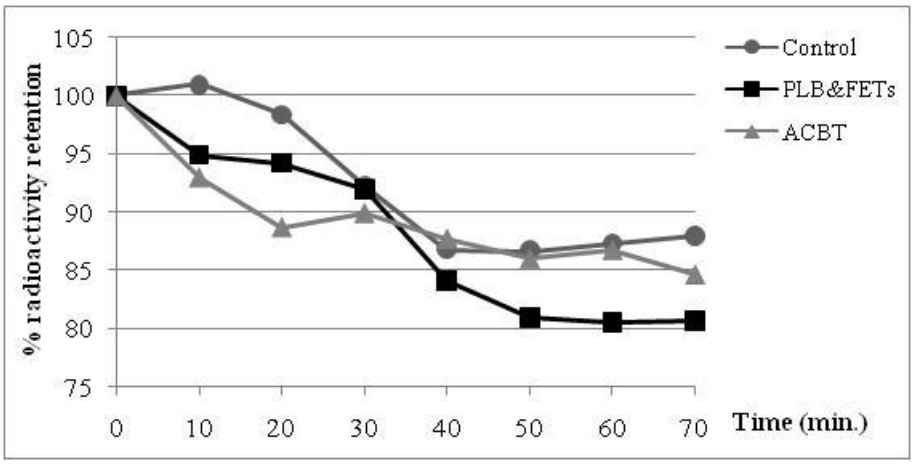

Figure 4.7 Clearance of the radioactivity from the peripheral right lung zone expressed as percentages of the starting values on three interventions of measurement of subject number 2. (Decay-corrected data)

With the whole right lung field, all clearance curves of subject number 2 (Figure 4.8) were showed diminish of radioaerosol retention. Furthermore, PLB&FETs and ACBT were obviously enhanced clearance of radioaerosol tracer of lung zone when comparison with control study.

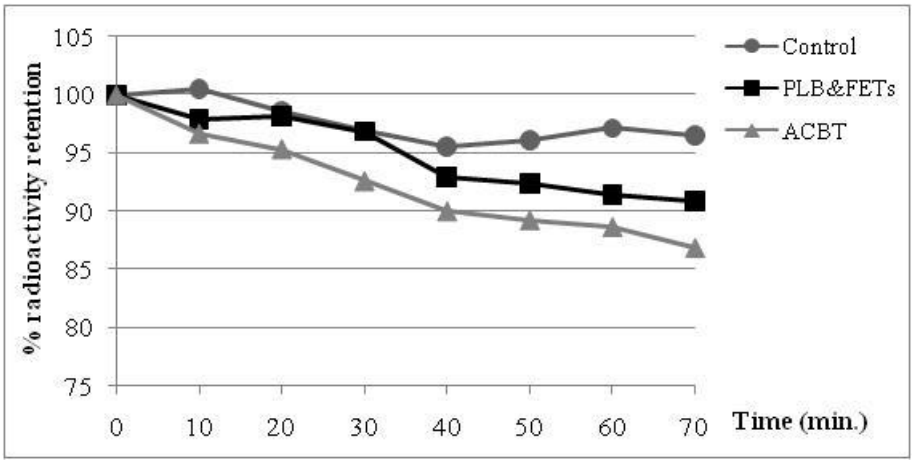

Figure 4.8 Clearance of the radioactivity from the whole right lung zone expressed as percentages of the starting values on three interventions of measurement of subject number 2. (Decay-corrected data)

The result of radioactivity clearance in the central right lung zone of subject number 3 was slightly sloped down in ACBT and control curves (Figure 4.9). Interestingly, PLB&FETs was greatly facilitated this lung zone clearance during and after intervention period from 10^{th} to 70^{th} minute.

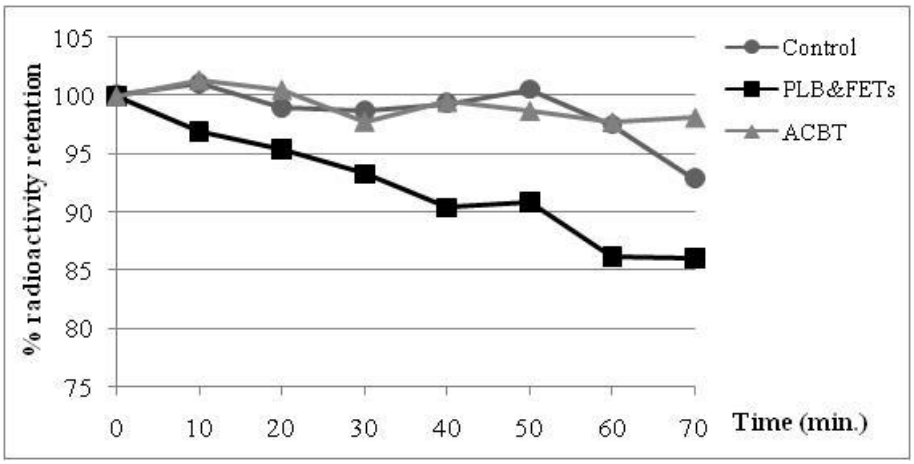

Figure 4.9 Clearance of the radioactivity from the central right lung zone expressed as percentages of the starting values on three interventions of measurement of subject number 3. (Decay-corrected data)

From radioactivity clearance in intermediate right lung zone, subject number 3 was remarkable reduced radioactivity retention by PLB&FETs and ACBT (Figure 4.10). Both techniques were approximately 14% difference clearance from the control study at the end of experimental period.

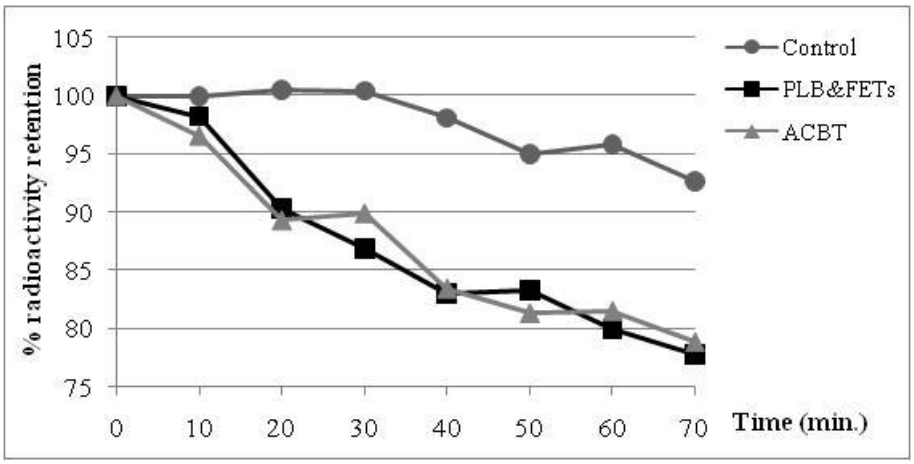

Figure 4.10 Clearance of the radioactivity from the intermediate right lung zone expressed as percentages of the starting values on three interventions of measurement of subject number 3. (Decay-corrected data)

From radioactivity clearance in peripheral right lung zone, subject number 3 was also obviously revealed high clearance of radioactivity by PLB&FETs and ACBT (Figure 4.11). Both technique curves were appeared likeness pattern of declination. There were differ clearance from the control study during and after intervention.

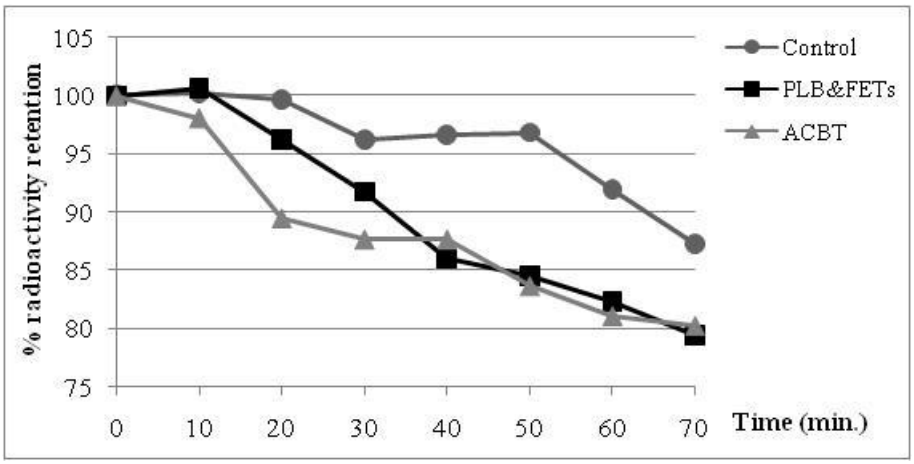

Figure 4.11 Clearance of the radioactivity from the peripheral right lung zone expressed as percentages of the starting values on three interventions of measurement of subject number 3. (Decay-corrected data)

From the whole right lung clearance in subject number 3 (Figure 4.12), all intervention curves were showed declination of radioactivity from 10th to 70th minute. PLB&FETs and ACBT curves were also obviously increase radioactivity clearance from the whole right lung zone in this subject.

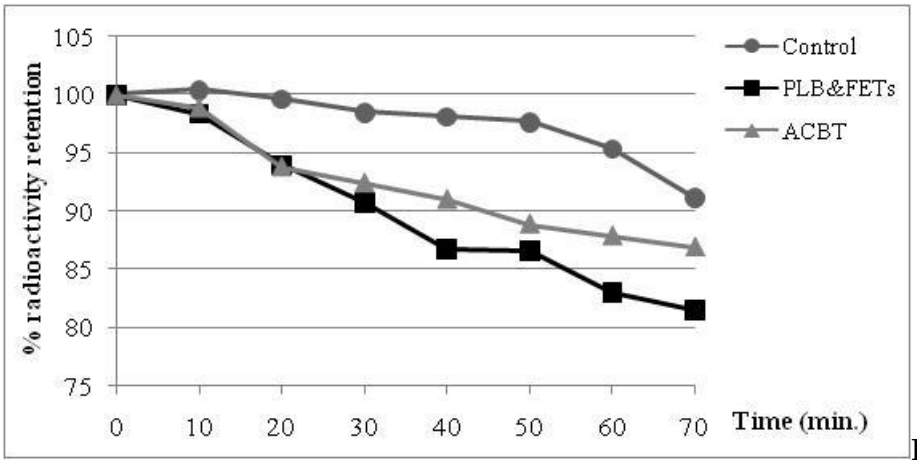

Figure 4.12 Clearance of the radioactivity from the whole right lung zone expressed as percentages of the starting values on three interventions of measurement of subject number 3. (Decay-corrected data)

In summary, the central right lung clearance curves had high enhance radioactivity clearance by PLB&FETs from 30th to 70th minute in Subject N1 and N3. Nevertheless, clearance of subject N2 was more enhanced radioactivity clearance by ACBT. In intermediate zone, lung clearance curve were remarkable reduced radioactivity retention by PLB&FETs and ACBT in all subjects from 30th to 70th minute. Both techniques were nearly facilitated radioactivity clearance and clearly high enhanced radioactivity when comparison with control study in subject N2, N3. Moreover, the peripheral lung clearance curve of PLB&FETs and ACBT were also appeared slop pattern during and after intervention period from 30th to 70th minute in all subjects. Both techniques were approximately 7% - 9% difference clearance from the control study after intervention period from 50th to 70th minute. The result of the whole right lung clearance were remarkable reduced radioactivity retention by PLB&FETs and ACBT. Interestingly, both techniques were nearly cleared radioactivity during and after intervention period. Overall, this results confirmed that PLB&FETs and ACBT could be achieved of lung clearance in healthy subject, especially in the intermediate and peripheral lung zone.

4.1.2 Comparison heart rate, oxygen pulse saturation among the control (normal breathing), PLB&FETs and ACBT during the experimental period

The value of heart rate (HR) in each healthy subject were minor fluctuation. There was showed in Figure 4.13, Figure 4.14, Figure 4.15. During the experimental period, heart rate parameter were appeared swing up and down of the values. However, there were no any critical difference. Interestingly, HR values of both subjects were declined in the period when PLB&FETs or ACBT was applied. Therefore, heart rate parameter of this study was showed minor fluctuation and no critical change during experimental period.

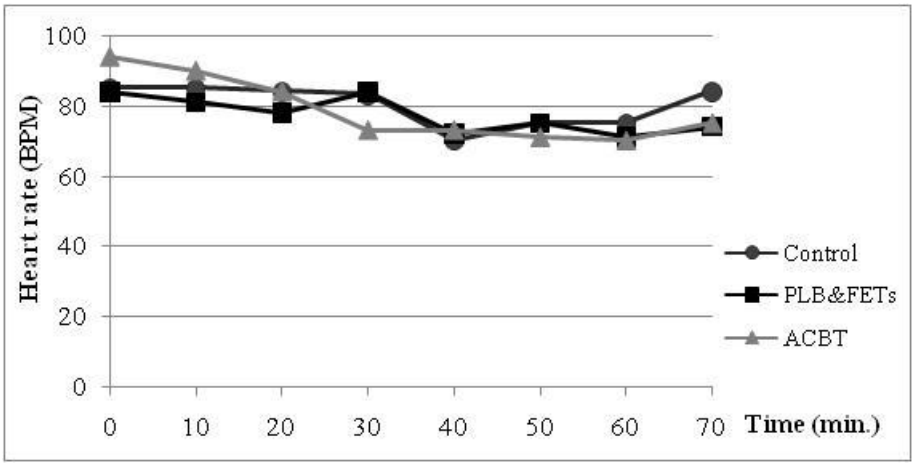

Figure 4.13 The values of heart rate among the control, PLB&FETs and ACBT during the experimental period for individual data of subject number 1.

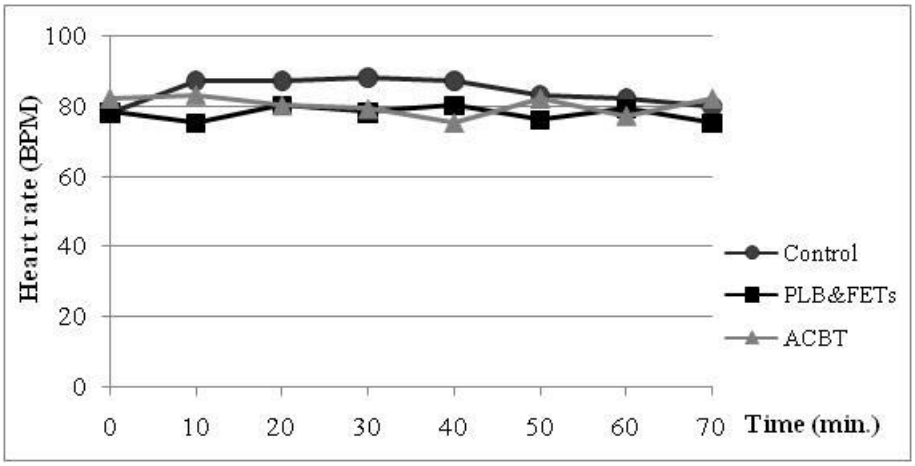

Figure 4.14 The values of heart rate among the control, PLB&FETs and ACBT during the experimental period for individual data of subject number 2.

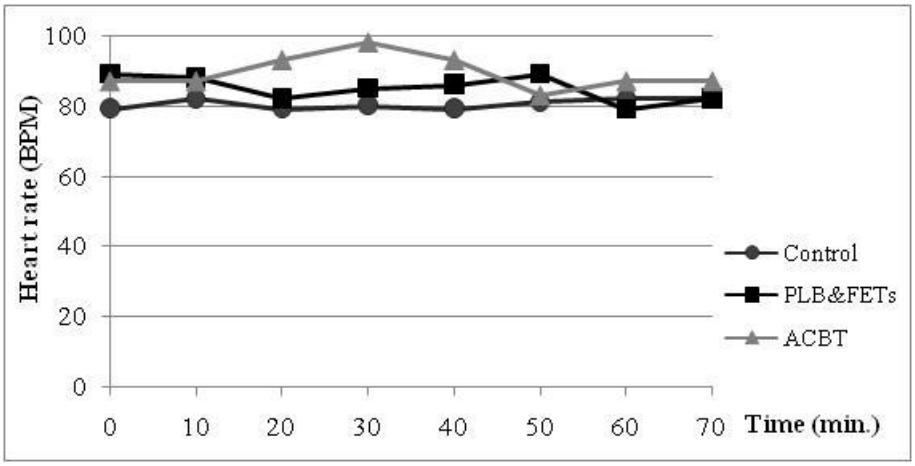

Figure 4.15 The values of heart rate among the control, PLB&FETs and ACBT during the experimental period for individual data of subject number 3.

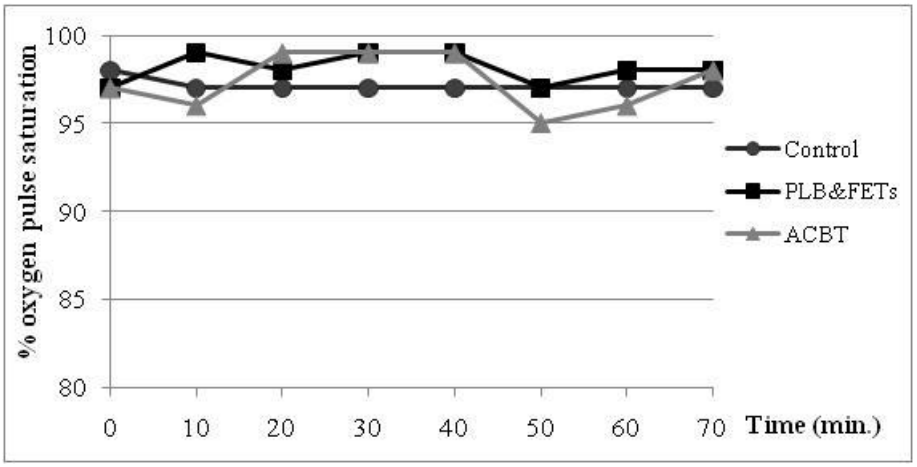

Figure 4.16 The values of oxygen pulse saturation among the control, PLB&FETs and ACBT during the experimental period for individual data of subject number 1.

The percentage of oxygen pulse saturation of each healthy subject (Figure 4.16, Figure 4.17, Figure 4.18) was similar baseline values for all three study days. In control study, this parameter of all subjects were showed minor swing down about 1% of values along the experimental period of time. Therefore, there was quiet stable of this parameter during control study. For PLB&FETs study of all subjects, the oxygen pulse saturation values were occurred swing up 1% during intervention period (from 20^{th} to 40^{th} minute) and comeback to the baseline values after intervention period. With ACBT study of all subjects, there were obvious that oxygen pulse

saturation values were greater in the period when ACBT was applied (20^{th}- 40^{th} minute) than when the subjects was breathing quietly (0 -10^{th}, and 50^{th} - 70^{th} minute). The results of this study showed that airway clearance techniques could slightly increase oxygen pulse saturation values in healthy subject especially in ACBT.

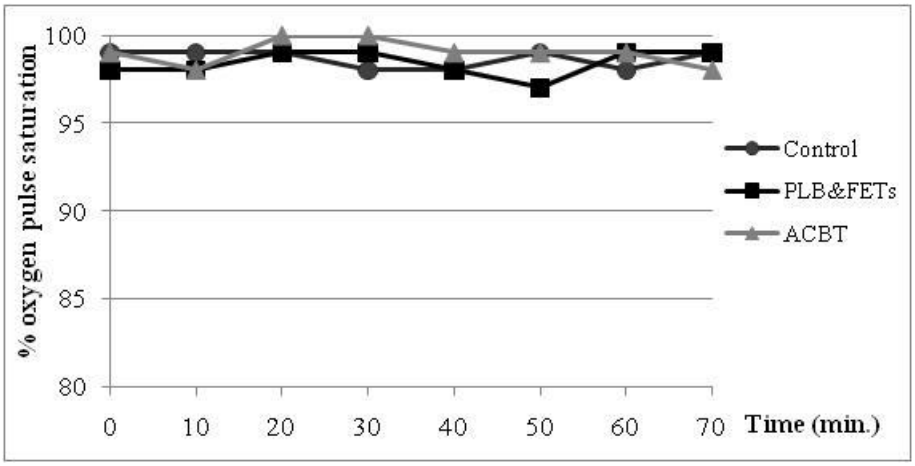

Figure 4.17 The values of oxygen pulse saturation among the control, PLB&FETs and ACBT during the experimental period for individual data of subject number 2.

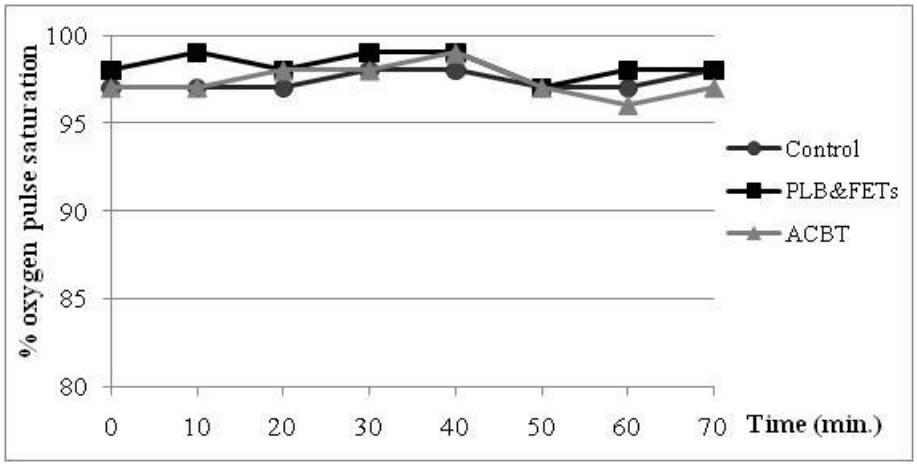

Figure 4.18 The values of oxygen pulse saturation among the control, PLB&FETs and ACBT during the experimental period for individual data of subject number 3.

4.1.3 Comparison the percent change of peak expiratory flow rate and Modified Borg scores of dyspnea among the control (normal breathing), PLB&FETs and ACBT at before and immediate after the experimental period.

This study was lightly difference in baseline value of peak expiratory flow rate (PEFR) on any of the study days. There was also no significant change in the PEFR when repeated immediately after each intervention period. In individual data, the percent change of PEFR in each subject were in ranges of 0% - 9% of subject No.1 (Figure 4.19), 3% - 14% of subject No.2 (Figure 4.20) and no percent change in subject No.3. (Figure 4.21). Overall, this study was no obvious different in percent change of PEFR in each individual data when compared among interventions.

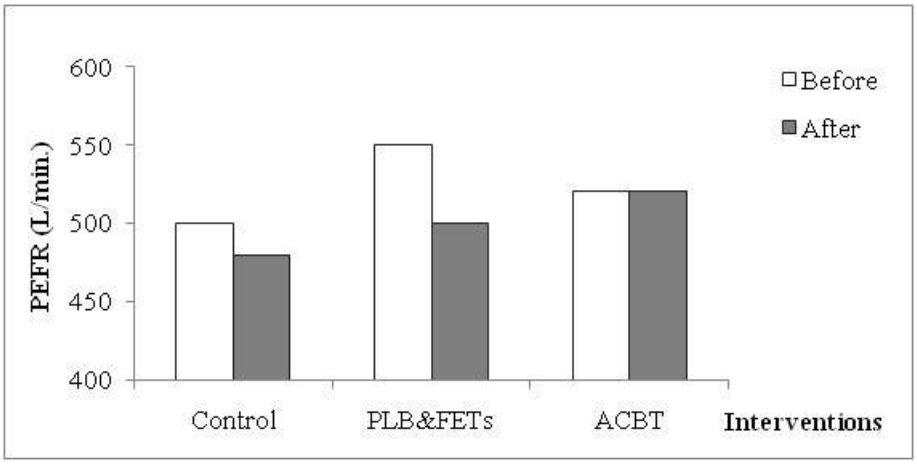

Figure 4.19 The values of peak expiratory flow rate among the control, PLB&FETs and ACBT at before and immediate after the experimental period for individual data of subject number 1.

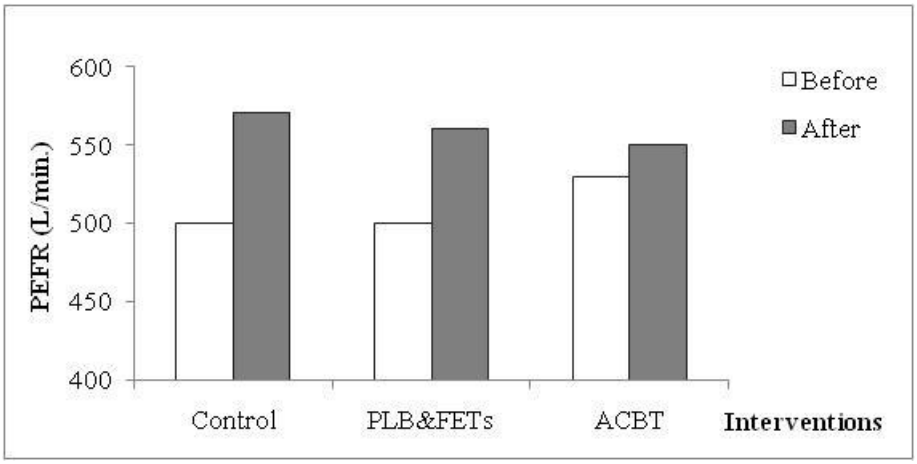

Figure 4.20 The values of peak expiratory flow rate among the control, PLB&FETs and ACBT at before and immediate after the experimental period for individual data of subject number 2.

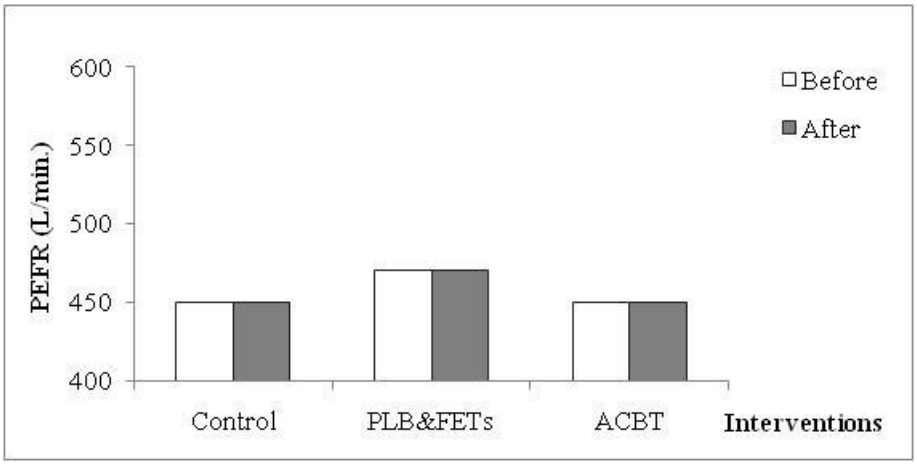

Figure 4.21 The values of peak expiratory flow rate among the control, PLB&FETs and ACBT at before and immediate after the experimental period for individual data of subject number 3

The Modified Borg scores of dyspnea in each study day were similarity values. For all subjects, the results of this parameter were shown consistency in before and immediate after the experimental period in each intervention study. Therefore, there were no percent change of Modified Borg scores of dyspnea among the control, PLB&FETs and ACBT at before and immediate after the experimental period.

Table 4.3 The values of Modified Borg scores of dyspnea among the control, PLB&FETs and ACBT at before and immediate after the experimental period for individual data

Intervention	Borg score (0-10)					
	N1		N2		N3	
	Before	After	Before	After	Before	After
Control	0	0	0	0	0	0
PLB&FETs	0	0.5	0	0	0	0
ACBT	0	0	0	0	0	0

4.2 The Second Study : Comparisons of Pursed Lips Breathing with Forced Expiration Techniques and Active Cycle of Breathing Technique in Patients with Chronic Obstructive Pulmonary Disease

In this study, a total of 541 COPD patients were contacted to primary screen from COPD clinic, Division of Respiratory Disease and Tuberculosis, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University and Outpatient Unit of Respiratory Disease, Chest Disease institute, Department of Medical Services, Ministry of Public Health during March,2008 to January, 2009. From history of medical chart and individuals interview, 96 patients were had to meet the inclusion criteria of the study. Only twenty-two stable COPD patients ranging in age from 55 to 84 (mean ± SD = 70.18 ± 7.74) year with mild to severe severity were included as volunteers in the study**.** The detail of subject recruitment of the second study were shown in Figure 4.22.

Twenty-two COPD patients were allocated to pursed lips breathing with forced expiration techniques group (PLB&FETs group) and active cycle of breathing technique group (ACBT group) until the number of subject in each group was eleven. Comparison between two groups, there were no statistically significant difference in age, weight, height, history of smoking, time of ex-smoking and stage of COPD. The characteristics of subjects were presented in Table 4.4.

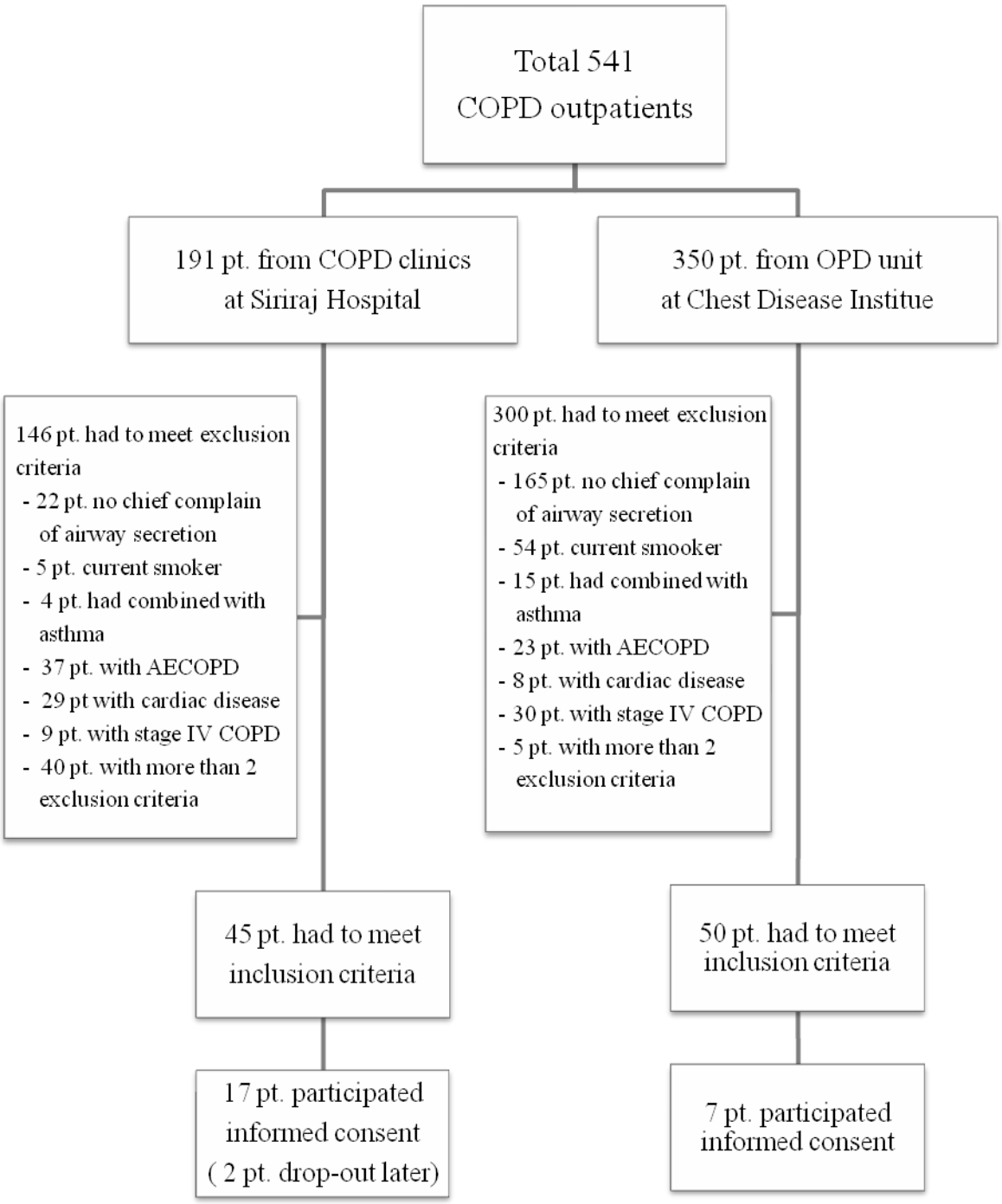

Figure 4.22 Flowchart of procedure of subject recruitment in the second study.

Table 4.4 Characteristics of subjects in the second study

Characteristics	**PLB & FETs gr. (n = 11)**	**ACBT gr. (n = 11)**	**p-value**
Age (yr)	70.64 ± 7.89	69.73 ± 7.95	0.791 [a]
Weight (kg)	58.26 ± 9.84	58.43 ± 9.44	0.969 [a]
Height (cm)	166.27 ± 4.67	163.64 ± 6.39	0.282 [a]
Smoke history (pack year)	43.68 ± 19.79	49.79 ± 45.06	0.687 [a]
Ex-smoke (year)	12.41 ± 11.06	10.23 ± 10.46	0.640 [a]
Severity of COPD (stage)			
I	3	1	0.561 [b]
II	4	5	
III	4	5	

a = p-value from unpaired t-test, b = p-value from Mann-Whitney u-test

4.2.1 Comparisons of mean percent predicted values of forced vital capacity, forced expiratory volume in one second, ratio of FEV_1/FVC, forced expiratory flow between 25% and 75% of the FVC and peak expiratory flow between PLB&FETs and ACBT group and within group at the difference of time

Two-way Repeated Measures Analysis of Variance (ANOVA) was used to assess difference in all pulmonary function test parameters within each group throughout the study (effect of time) and between groups of the study in each time of assessment (effect of treatment). Each of the repeated measure analyses revealed a slight departure from sphericity. Because of this violation, obtained F values were evaluated based on adjusted degree of freedom. Using the Geisser-Greenhouse correction, each F test was evaluated against a much more stringent criterion.

In this study, the values of forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), ratio of FEV_1/FVC, forced expiratory flow between 25% and 75% of the FVC ($FEF_{25-75\%}$) and peak expiratory flow (PEF) were

not statistically significant difference on the 1st, 7th, 14th day of the study between PLB&FETs and ACBT group. There was only a significant difference in PEF within ACBT group at the difference of time between the 1st and 14th day of the study.

4.2.1.1 Comparison of mean percent predicted values of FVC between PLB&FETs and ACBT group and within group at the difference of time

From the study, the data of FVC before receiving interventions or baseline data were similar between PLB&FETs and ACBT groups (80.94 ± 24.77 and 80.11 ± 9.09, respectively). After the first week of airway clearance technique, the subjects in both groups showed nearly identical predicted values of FVC on the baseline measurement. They were no statistical significant differences ($p > 0.05$). When compared with baseline data, FVC was showed lightly stable from the 7th day measurement to the 14th day measurement in both groups with no statistical significant differences ($p > 0.05$). Moreover, the comparison between two groups at any time of measurement had no difference (Table 4.5).

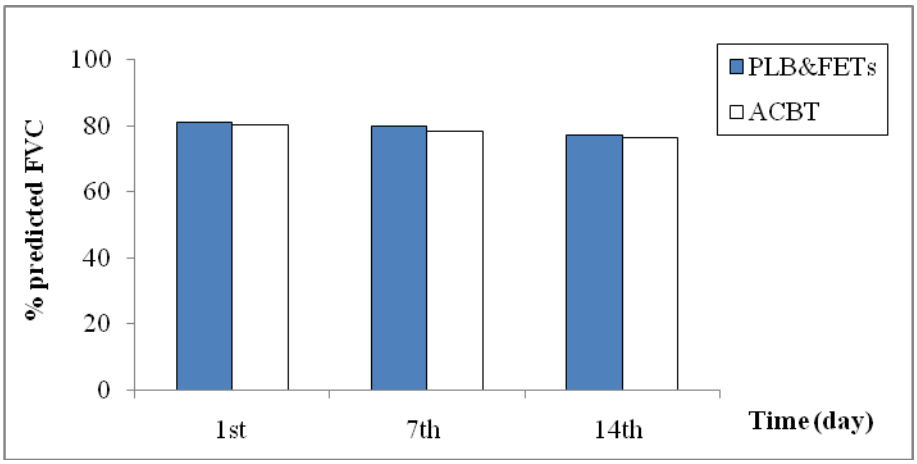

Figure 4.23 Means percent predicted values of FVC for PLB&FETs and ACBT groups.

Table 4.5 Comparison of mean percent predicted values of FVC between PLB&FETs and ACBT groups

Time (day)	% predicted FVC (mean ± SD)	
	PLB&FETs group	**ACBT group**
1st	80.94 ± 24.77	80.11 ± 9.09
7th	79.95 ± 20.06	78.14 ± 11.39
14th	77.01 ± 17.09	76.51 ± 4.19
p-value Within group	0.311	
p-value Between group	0.881	
p-value Interaction time x group	0.906	

p-value from Two-way Repeated Measures Analysis of Variance (ANOVA)
This analyze data was excluded one case of outlier in ACBT group

4.2.1.2 Comparison of mean percent predicted values of FEV_1 between PLB&FETs and ACBT group and within group at the difference of time

The study reported that the baseline data of FEV_1 were nearly identical values between PLB&FETs and ACBT groups (62.15 ± 23.98 and 57.12 ± 13.05, respectively). Compared with the baseline data, the subjects of both groups were likely to show stable results in FEV_1 at 7th and 14th day of the study (Figure 4.24). The statistical difference was not found ($p > 0.05$). In addition, the comparison between two groups at any time of measurement showed no difference (Table 4.6).

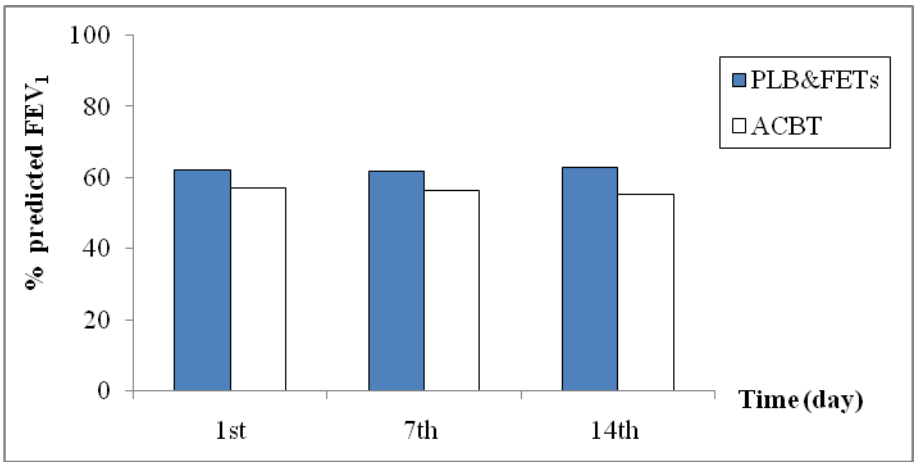

Figure 4.24 Means percent predicted values of FEV_1 for PLB&FETs and ACBT groups.

Table 4.6 Comparison of mean percent predicted values of FEV_1 between PLB&FETs and ACBT groups

Time (day)	**% predicted FEV_1 (mean ± SD)**	
	PLB&FETs group	**ACBT group**
1^{st}	62.15 ± 23.98	57.12 ± 13.05
7^{th}	61.89 ± 21.86	56.43 ± 11.01
14^{th}	62.71 ± 24.94	55.30 ± 14.18
p-value Within group	0.861	
p-value Between group	0.475	
p-value Interaction time x group	0.674	

p-value from Two-way Repeated Measures Analysis of Variance (ANOVA)
This analyze data was excluded one case of outlier in ACBT group

4.2.1.3 Comparison of mean percentage values of ratio of FEV_1/ FVC between PLB&FETs and ACBT group and within group at the difference of time

From the study, ratio of FEV_1/FVC of the baseline data in PLB&FETs and ACBT groups were 57.53 ± 11.11 and 53.78 ± 10.95, respectively. The comparison between two groups at baseline measurement had no difference. When the subjects had received airway clearance technique, the mean percentage values of ratio of FEV_1/FVC in the 7^{th} and 14^{th} day of study showed nearly identical the values on the baseline measurement. Both groups were no statistical significant differences when compared with baseline data ($p > 0.05$), as shown in Table 4.7. Also, the comparison between two groups at any time of measurement had no difference.

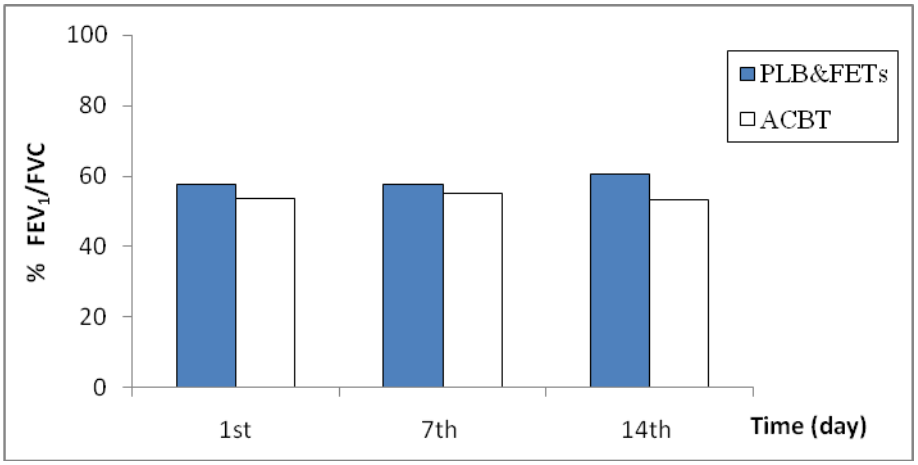

Figure 4.25 Means percentage values of ratio of FEV_1/FVC for PLB&FETs and ACBT groups.

Table 4.7 Comparison of mean percentage values of ratio of FEV_1/FVC between PLB&FETs and ACBT groups

Time (day)	**% $FEV_{1/}$/FVC (mean ± SD)**	
	PLB&FETs group	**ACBT group**
1^{st}	57.53 ± 11.11	53.78 ± 10.95
7^{th}	57.60 ± 11.50	55.27 ± 11.59
14^{th}	60.54 ± 17.42	53.29 ± 22.82
p-value Within group	0.752	
p-value Between group	0.455	
p-value Interaction time x group	0.499	

p-value from Two-way Repeated Measures Analysis of Variance (ANOVA)
Data was excluded one case of outlier in ACBT group.

4.2.1.3 Comparison of mean percent predicted values of $FEF_{25-75\%}$ between PLB&FETs and ACBT group and within group at the difference of time

The baseline data of $FEF_{25-75\%}$ in PLB&FETs and ACBT groups were 28.56 ± 16.23 and 24.11 ± 10.15, respectively. After the first week, the mean predicted values of $FEF_{25-75\%}$ showed nearly identical predicted values on the baseline measurement. However, this values was showed lightly improve from the 7^{th} day-measurement to the 14^{th} day- measurement when compared with baseline data. Also, there were no statistical significant differences ($p > 0.05$). In addition, the comparison between two groups at any time of measurement had no difference, as shown in Table 4.8.

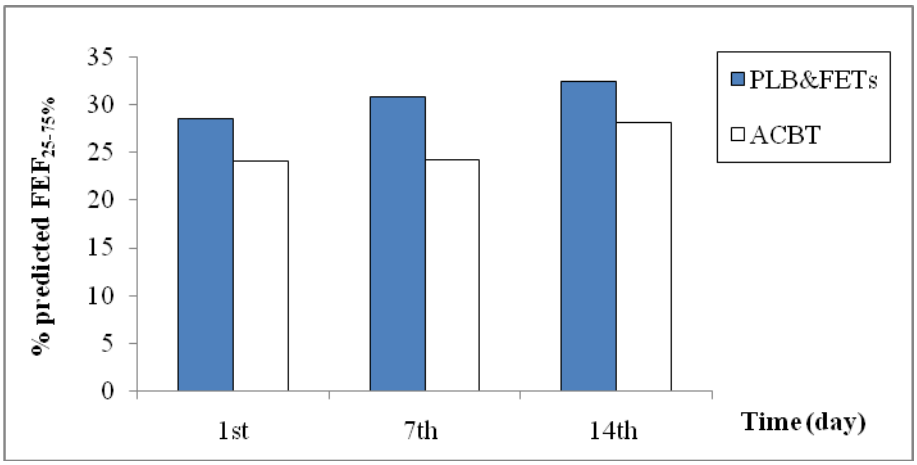

Figure 4.26 Means percent predicted values of $FEF_{25-75\%}$ for PLB&FETs and ACBT groups.

Table 4.8 Comparison of mean percent predicted values of $FEF_{25-75\%}$ between PLB&FETs and ACBT groups

Time (day)	**% $FEF_{25-75\%}$ (mean ± SD)**	
	PLB&FETs group	**ACBT group**
1^{st}	28.56 ± 16.23	24.11 ± 10.15
7^{th}	30.78 ± 16.93	24.25 ± 9.67
14^{th}	32.47 ± 20.46	28.15 ± 15.24
p-value Within group	0.050	
p-value Between group	0.441	
p-value Interaction time x group	0.737	

p-value from Two-way Repeated Measures Analysis of Variance (ANOVA)
This analyze data was excluded one case of outlier in ACBT group

4.2.1.5 Comparison of mean percent predicted values of PEF between PLB&FETs and ACBT group and within group at the difference of time

From the study, the baseline data of PEF in PLB&FETs and ACBT groups were 54.93 ± 25.91 and 46.90 ± 19.12, respectively. Compared with the baseline data, the subjects of both groups were likely to show better results in PEF at the 7th and 14th day-measurement (Figure 4.27). However, the statistical difference was not found in multiple comparison of time for both groups except between baseline and the 14th day of study in ACBT group (Table 4.11). In addition, the comparison between two groups at any time of measurement had no difference, as shown in Table 4.9.

The values of both groups and statistical analysis between two groups are shown in Table 4.9, and multiple comparisons among various times of measurement for each group are reported in Table 4.10 and Table 4.11.

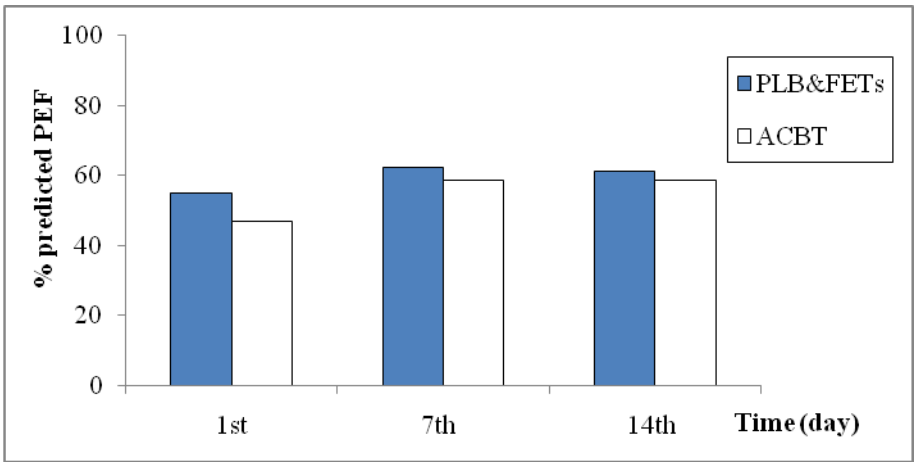

Figure 4.27 Means percent predicted values of PEF for PLB&FETs and ACBT groups.

Table 4.9 Comparison of mean percent predicted values of PEF between PLB&FETs and ACBT groups

Time (day)	**% PEF (mean ± SD)**	
	PLB&FETs group	**ACBT group**
1st	54.93 ± 25.91	46.90 ± 19.12
7th	62.43 ± 27.03	58.47 ± 14.68
14th	61.10 ± 30.86	58.6 ± 16.45
p-value Within group	0.005*	
p-value Between group	0.626	
p-value Interaction time x group	0.535	

p-value from Two-way Repeated Measures Analysis of Variance (ANOVA)
This analyze data was excluded one case of outlier in ACBT group

Table 4.10 P-values of the multiple comparison of PEF value in PLB&FETs group among various times of assessment

Time	1st day	7th day	14th day
1st day	-	0.216	0.838
7th day	-	-	1.000
14th day	-	-	-

Table 4.11 P-value of the multiple comparison of PEF value in ACBT group among various times of assessment

Time	1st day	7th day	14th day
1st day	-	0.098	0.038*****
7th day	-	-	1.000
14th day	-	-	-

4.2.2 Comparisons of total mean values of peak expiratory flow rate, sputum volume and Modified Borg scores of dyspnea between PLB&FETs and ACBT group and within group at the difference of time

4.2.2.1 Comparison of total mean values of PEFR between PLB&FETs and ACBT group and within group at the 1st and 2nd week of the study

In the first week, total mean values of PEFR measured by Mini-Wright peak flow meter in PLB&FETs and ACBT groups were 258.50 ± 89.91 L/min and 257.23 ± 102.05 L/min respectively. The comparison between two groups showed no significant difference at the first week. Moreover, this values was also not significant difference between groups at the second week, as shown in Table 4.12.

When the subjects received airway clearance technique, total mean of PEFR were positive changes gradually increased throughout the study for both groups. Especially, for PLB&FETs group, the values were significantly higher from the first week at the second week with statistical significances of p = 0.044, see also in Table 4.12.

Table 4.12 Means comparison of total mean values of PEFR between groups at the difference of time

Time (week)	PEFR (mean ± SD, L/min.)		p-value Between group [a]
	PLB & FETs gr. (n = 11)	ACBT gr. (n = 11)	
1	258.50 ± 89.91	257.23 ± 102.05	0.976
2	279.51 ± 70.70	260.39 ± 93.50	0.594
p-value Within group [b]	0.044*	0.496	

a = p-value from unpaired t-test, b = p-value from paired t-test

4.2.2.2 Comparison of total mean values of sputum volume between PLB&FETs and ACBT group and within group at the 1st and 2nd week of the study

In the first week, total mean values of sputum volume in PLB&FETs and ACBT groups were 18.95 ± 9.12 ml. and 17.82 ± 7.81 ml. respectively. The comparison between two groups showed no significant difference at the first week. Moreover, this values were also not significant difference between groups at the second week, as shown in Table 4.13.

When the subjects received airway clearance technique, total mean of sputum volume were positive changes gradually decreased throughout the study for both groups. Especially, for PLB&FETs group, the values were significantly lower from the first week at the second week with statistical significances of p = 0.007, see also in Table 4.13.

Table 4.13 Means comparison of total mean values of sputum volume between groups at the difference of time

Time (week)	Sputum volume (mean ± SD, ml.)		p-value Between group [a]
	PLB & FETs gr. (n = 11)	ACBT gr. (n = 11)	
1	18.95 ± 9.12	17.82 ± 7.81	0.759
2	11.79 ± 7.65	14.74 ± 10.43	0.458
p-value Within group [b]	0.007*	0.155	

a = p-value from unpaired t-test, b = p-value from paired t-test

4.2.2.3 Comparison of the total mean values of Modified Borg score of dyspnea between PLB&FETs and ACBT group and within group at the 1st and 2nd week of the study

With rating of perceived dyspnea, total mean values of Borg score in the first week were similar between PLB&FETs and ACBT groups. The comparison between two groups showed no significant difference at the first week. Moreover, this values were also not significant difference between groups at the second week, as shown in Table 4.14.

When the subjects received airway clearance technique, total mean values of Borg score were positive changes gradually decreased throughout the study for both groups. However, the difference was not found between various times of measurement for each group, as shown in Table 4.14.

Table 4.14 Means comparison of total mean values of Modified Borg scores between groups at the difference of time

Time (week)	Borg scores (mean ± SD)		p-value Between group [a]
	PLB & FETs gr. (n = 11)	ACBT gr. (n = 11)	
1	1.86 ± 1.10	1.64 ± 1.34	0.706
2	1.59 ± 1.16	1.54 ± 1.01	0.957
p-value Within group [b]	0.500	1.000	

a = p-value from Mann-Whitney U test, b = p-value from Wilcoxon Signed Ranks Test

4.2.3 Comparison of total scores of Modified patient evaluation questionnaire between PLB&FETs and ACBT group and within group at the difference of time

The Modified patient evaluation questionnaire was used in this study to indicate the symptom parameters that presented in the subjects. There are five items questionnaire with scores ranged from 5 to 27. The higher scores represent the worse symptom and the falling scores suggest the improve symptom.

The baseline data of total scores of Modified patient evaluation questionnaire in PLB&FETs and ACBT groups were 12.27 ± 3.23 and 13.18 ± 1.94 respectively without between group difference. The positive changes gradually increased throughout the study for both groups. The decrease of the scores still occurred at the 7th day and 14th day-measurement for both groups. Especially, the total scores of PLB&FETs group were significantly lower from baseline data at the 14th day of the study with statistical significances of p = 0.021. Also, this values for ACBT group were found significantly difference among various times of measurement (except between the 7th and 14th day of the study), see also in Table 4.16, Table 4.17. Nevertheless, the comparison between two groups at any time of measurement showed no difference (Table 4.15).

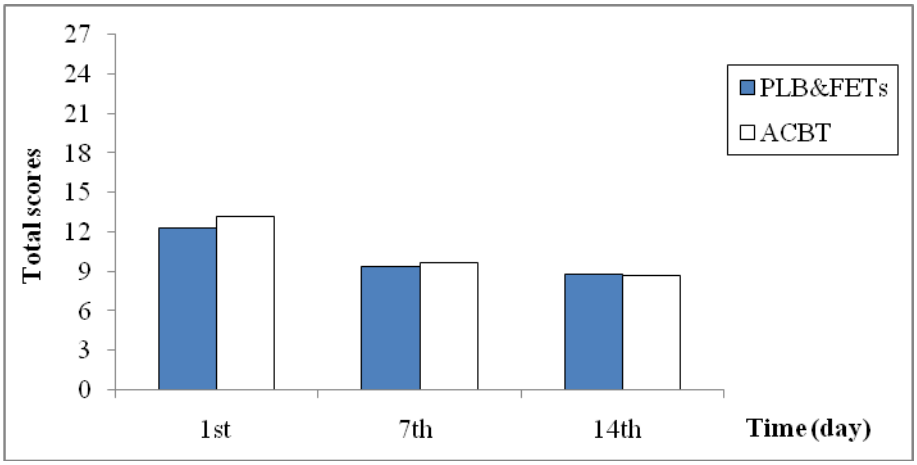

Figure 4.28 Means total scores of Modified patient evaluation questionnaire for PLB&FETs and ACBT groups.

Table 4.15 Comparison of mean total scores of Modified patient evaluation questionnaire between PLB&FETs and ACBT groups

Time (day)	**Total scores of Modified patient evaluation questionnaire (mean ± SD)**	
	PLB&FETs group	**ACBT group**
1st	12.27 ± 3.23	13.18 ± 1.94
7th	9.36 ± 1.50	9.64 ± 1.96
14th	8.73 ± 2.10	8.64 ± 1.63
p-value Within group	0.001*	
p-value Between group	0.608	
p-value Interaction time x group	0.540	

p-value from Two-way Repeated Measures Analysis of Variance (ANOVA)

Table 4.16 P-values of the multiple comparison of total scores of Modified patients evaluation questionnaire in PLB&FETs group among various times of assessment

Time	1st day	7th day	14th day
1st day	-	0.078	0.021*
7th day	-	-	0.570
14th day	-	-	-

Table 4.17 P-values of the multiple comparison of total scores of Modified patients evaluation questionnaire in ACBT group among various times of assessment

Time	1st day	7th day	14th day
1st day	-	< 0.001*	< 0.001*
7th day	-	-	0.056
14th day	-	-	-

4.2.4 Comparison of total scores of Modified patient satisfaction questionnaire between PLB&FETs and ACBT group at the 14th day of the study

The Modified patient satisfaction questionnaire was used in this study to indicate the overall satisfaction of both airway clearance techniques that presented in the subjects. There are four items questionnaire with scores ranged from 4 to 20 with the higher scores represent high satisfaction and the lower scores suggest on unsatisfaction.

The baseline data of total scores of Modified patient satisfaction questionnaire in PLB&FETs and ACBT groups were 17.09 ± 2.62 and 16.54 ± 2.50 respectively. The comparison between two groups at the 14th day of the study (the end of the study) showed no difference (Table 4.18).

Table 4.18 Means comparison of total scores of Modified patient satisfaction questionnaire between groups at the 14th day of the study

Time (day)	Total scores of Modified patient satisfaction questionnaire (mean ± SD)		p-value Between group [a]
	PLB & FETs gr. (n = 11)	ACBT gr. (n = 11)	
14th	17.09 ± 2.62	16.54 ± 2.50	0.623

a = p-value from unpaired t-test

CHAPTER V
DISCUSSION

5.1 The First Study : Efficacy of Pursed Lips Breathing with Forced Expiration Techniques and Active Cycle of Breathing Technique on Pulmonary Mucus Clearances in Healthy Subjects

The efficacy of PLB&FETs and ACBT on pulmonary mucus clearance were compared in three healthy subjects. The participant's age had very little different among three subjects and the parameters of pulmonary function also interpreted in normal lung function. Thus, the data of subject characteristics might reflect that all subjects had similar physical aspects.

In radioaerosol tracer technique, the retention of any radioaerosol was determined both by deposition and by clearance. It is well known that the deposition of aerosol particles in the lung depend on particle size and shape, density, airway dimensions, inspiratory flow rate, patterns of breathing (32, 105, 119). Therefore, these factors were maintained relatively constant throughout this study. From the results of this current study, the deposited radioaerosol in the lung for each subject for the three experiment days showed little intersubject variation and little intrasubject variation. Anyhow, there were very little difference in the initial distribution of radioactivity on the three study days. So, the difference in clearance during the period of intervention could not be explained by a difference in radioaerosol deposition. In addition, clearance of radioaerosol within the lung influenced the amount of tracer available for imaging. Clearance mechanisms included sobubilisation and absorption, direct clearance by coughing, mucociliary transport and alveolar mechanisms that included absorption and phagocytosis by pulmonary macrophages were influenced the site at which radioaerosol particle deposit. According to the previous mentions, this

study was excluded the difference mechanisms of the subject by a randomized cross-over study design. Each subject acted as his own control to compared the changes in retention observed under the various condition. In addition, healthy subjects who had no history or other evidence of chest disease were stable in tracheobronchial airway and ventilation. Therefore, mucociliary transport was presumably a constant condition throughout this study. Any changes in radioaerosol tracer retention might be due to the specific interventions occurring on each study day.

5.1.1 Comparison of the percentage retention of radioactivity in central, intermediate, peripheral and whole zones of the right lung among the control (normal breathing), PLB&FETs and ACBT during the experimental period

The results of this present study demonstrated the effects of PLB&FETs and ACBT in terms of radioactivity clearance from the central, intermediate, peripheral and whole right lung zones. Clearance of the central lung zone for individual data were different pattern for all interventions. The clearance of PLB&FETs curve were greater than the control and ACBT curves. Therefore, PLB&FETs had lightly high enhanced clearance.

For intermediate lung zone of individual data, the clearance of PLB&FETs and ACBT curve were clearly greater than control curve during and after intervention period from 20^{th} to 70^{th} minute. PLB&FETs and ACBT curve of all subjects were represented nearly percentage of radioactivity clearance. Therefore, both techniques were remarkable the near effects of declination of radioactivity deposition from intermediate lung zone.

The peripheral lung zone clearance curve of all interventions were similarity of slope pattern in all subjects. Interestingly, there were obviously revealed high clearance of radioactivity by PLB&FETs and ACBT during and after intervention period from 30^{th} to 70^{th} minute. Both technique curves were appeared likeness pattern of declination. Both techniques were approximately 7%- 9% difference clearance from the control study after intervention period (from 50^{th} to 70^{th} minute).

The result of the whole right lung clearance, all clearance curves of subjects were showed declination of radioactivity deposition from 10^{th} to 70^{th} minute. PLB&FETs and ACBT were obviously enhanced clearance of radioactivity of this lung zone during and after intervention period from 40^{th} to 70^{th} minute when comparison with control study. These finding confirmed that PLB&FETs and ACBT could be achieved of lung clearance in healthy subject especially in intermediate and peripheral zone.

To date, the gamma camera has been little exploited for studying airway clearance technique from different lung regions. In our knowledge, the immediate effect of the two techniques on mucus clearance in healthy subjects or in patients has never been study before. With control condition, the assessment of regional mucus transport of this study found that the percentage clearance of radioactivity during experimental period was closely similar to the result of earlier study of Wolff et al in 1977 (120), Agnew et al in 1984 (108) and Mortensen et al in 1991 (121). Although, we should keep in mind that there were some different measurement of mucociliary clearance in the radioaerosol tracer technique, the image collection and analysis of the study.

From previous study in the patient, Isawa and associated in 1984 (122) found that the data of lung clearance mechanisms in patients with obstructive airway disease was not different of the overall lung retention ratio during the initial 120 minute when comparison of normal subject. However, the airway deposition ratio was significantly above normal, airway clearance efficiency was below and the alveolar deposition ratio was also significantly smaller than the normal subjects. All patients showed nonhomogeneous aerosol deposition patterns in the lung and the migration of radioactivity over the trachea and the major bronchi was extremely protean in its direction and transportation pattern. From the sense of lung clearance mechanism, there were the difference pattern in each respiratory disease. Moreover, mucociliary clearance was a very complex process in which many variables were involved, all of which may modify the final outcome (33, 34). Therefore, we should be

careful consider to comparison of airway clearance techniques on mucus clearance in other studies. These also made difficulties to interpretation in this study.

In the result of current study, the speeding clearance in subjects were appeared toward the end of and after intervention period. There appeared to be a delay in onset and persistence of the effect after the initiating stimulus has ceased. This observed delay in speeding of clearance was in agreement with the finding of Wolff and associates in 1977 (120). They described that it could result from a delay between initial stimulation of mucus production and its appearance on the epithelial surface. It could also be due to regional difference in clearance. Clearance from the more peripheral lung zones seemed to increase earlier than clearance from the central zone. These results might be interpreted as showing that speeding in clearance first affect the deeper, more peripheral airways, probably due to mechanical factor of lung movement but then later a speeding in the central airways becomes evident as an increased amount of mucus must be transported. Therefore, our study might be expect of this observed delay of clearance.

Overall, the results of this study showed that PLB&FETs or ACBT could be achieved in healthy subject. There also demonstrated improvement in regional mucus transport using inhaled Technetium-99m aerosol particles in both techniques. Although the results were surprisingly inconsistent in central lung zone. In some cases, PLB&FETs produced a greater improvement in central lung zone than ACBT and the other the reverse occurred. Anyhow, the group mean clearance of central lung zone could represented the great enhancement of clearance by PLB&FETs. Despite this, clearance rates were lightly faster with PLB&FETs than with ACBT for central lung region, but there was not critical difference. Moreover, the number of subjects were very small and impossible to analyse statistically. Therefore, there was insufficient evidence to support PLB&FETs was more effective than ACBT in central lung zone. In summary, PLB&FETs and ACBT were clearly accelerated the whole right lung clearance in healthy subject especially in intermediate and peripheral zone. Therefore, it is possible to indicated that both airway clearance techniques might

respond to pulmonary mucus clearances indifferently and the consequences after radioaerosol tracer technique of airway were similar as well.

Our finding confirmed that PLB&FETs could be achieved of lung clearance in healthy subject. In particular, most of previous studies found that successful PLB was marked reduce respiratory rate and dyspnea, improve tidal volume, increase in the vital capacity and oxygen saturation of patients with emphysema (19, 20, 82, 123). Furthermore, healthy individuals performing volitional PLB have also previously been found to exhibit significant increases in tidal volume during resting breathing and exercise by the study of Spahija et al in 1996 (124). They suggested that the ability of PLB to promote changes in breathing patterns does not depend on the presence of expiratory flow obstruction. Nevertheless, this current study was an original research designed to evaluate the effects of pursed lips breathing combined with forced expiration techniques for mucociliary clearance. Of course, we were unable to clearly identify the reasons of PLB&FETs for enhancing airway clearance. There was as generally assumed, but fews documented previously support. The increased clearance achieved by PLB&FETs resulted in a speeding of mucociliary transport in the present study could be the result of a) mechanical effect of pursed lips breathing (PLB), b) stimulation of mucociliary clearance resulting from forced expiration techniques (FETs) and c) mechanism of Two-phase gas-liquid flow (TPGLF) facilitated by PLB&FETs.

With the mechanical effect of PLB, the active expiration through the half-opened lips inducing expiratory mouth pressure of about 5 cmH_2O (19, 20, 24). The positive back pressure may splints the airway open, preventing compression or premature closure. There was theorized that positive pressure is built up distal to an obstruction, promoting the movement of secretions toward the large airways. In addition, airway stability is maintained with positive expiratory pressure breathing which results in improved ventilation and gas exchanges as well as in airway clearance (8, 11, 12, 17, 24, 59, 63). Moreover, the previous mention of David A (53) stated that the equal pressure point is moved towards the mouth with avoiding compression of a

collapsible segment by performing expiratory through pursed lips. Therefore, we are believed that the positive expiratory mouth pressure of PLB might be some additional effect in enhancing the removal of pulmonary mucus from the lung. In considering respiratory mechanics, expiratory muscle recruitment with PLB may improve length-tension relationships of the inspiratory muscles, particularly the rib cage and accessory muscles, improving their mechanical efficiency and leading to greater force generation capacity in ventilation (22, 23). It is possible that the integration of respiratory muscle changes with PLB might be some enhancing mucociliary clearance in the total lung.

From forced expiration techniques, it consist of one or two huffs followed by controlled breathing. According to the previous literatures, the active forms of forced expiratory manoeuvres of a “huff” are the most effective part of physiotherapy intervention. The physiological concepts of the equal pressure point (EPP) and the shear forces explain the mechanism of the effectiveness of huff (7, 8, 10, 14, 15). FET may change the position of the equal pressure point in the airways allowing for greater clearance of mucus form further down the airway (9, 11, 15). Few studies of FETs were available which examine the effectiveness of mucus clearance by radioaerosol study.

Based on patients with copious sputum, Sutton and coworkers in 1983 (106) suggested that both FET and particular FET and postural drainage have been shown to be more effective than directed coughing or control. After 30 minute of FET period, the percentage of radioactivity in the whole lung was approximately 70%. In the present study, we found PLB&FETs to be relatively effective as Sutton’s study in terms of the percentage of radioactive clearance.

van der Schans et al 1990 (74) showed that peripheral mucus clearance during control was significantly lower than during the periods when FET was performed or the patient was coughing but central mucus clearance did not differ significantly in patients with chronic bronchitis. Whereas, patients with emphysema was no significant difference in either the control or the peripheral lung mucus clearance at any time period. They mentioned that forced expirations increased

peripheral mucus transport in the patients with normal or high elastic recoil pressure but had little effect in patients with low elastic recoil pressure probably because of dynamic bronchial collapse during forced expiration in these patients. The study has shown that both forced expiration and coughing were also effective in patients who expectorate less. Additionally, the results of Hasani and coworkers in 1994 (125) showed that clearance was significantly enhance following cough and FET compared with control. They confirmed that cough and FET were equally effective in clearing lung secretions in COPD patients, although the latter could be achieved with less effort on the part of the patient. Furthermore, the enhancement of whole lung radioaerosol clearance following FET by Hasani et al was in keeping with the observations of Sutton and coworkers. Our current study also reported that PLB&FETs in healthy subject was effective in clearing mucus of all regions of right lung. Although the subject of study were unlikely to account for van der Schans et al and Hasani et al. It could be support that healthy subjects who had normal elastic recoil pressure, FET might be effective to enhance mucus clearance.

From literature reviews, it seems possible that PLB&FETs might facilitate the mechanism of Two-phase gas-liquid flow (TPGLF) to contribute to mucus clearance. To date, a secondary clearance mechanism known as TPGLF plays an essential role in removing mucus from the lung. In nonciliary dependent phasic flow, energy is transmitted from the moving air to the static liquid, shearing and moving the liquid in the direction of flow. At low gas flow rate, air may flow through the mucus plug as small bubbles (bubble flow). As the airflow rate increases, the bubbles grow in size, combine together (plug flow) and eventually from a continuous channel through the mucus plug (annular flow). At an extreme airflow rate the mucous layer may be peeled off from the surface of the airways and blown away as in the case of a cough or a huff. The major factors influencing flow include surface velocity, liquid layer thickness and the rheological properties of the liquid. The cephalad mucus transport could be achieved by keeping the expiratory flow. In addition, the ratio of the expiratory to the inspiratory flow rate of 1.5 with a tidal volume of 500 ml was sufficient to transport the mucus in a vertical tube model (55-57, 66). Therefore, this

study postulated that the increased mucus clearance achieved by PLB&FETs could be the result of the mechanical effect of pursed lips breathing, forced expiration techniques and the second clearance mechanic of Two-phase gas-liquid flow.

The results of ACBT in this study could be achieved of lung clearance in healthy subject. Until recently, there was only one previous research has focused on ACBT in terms of mucus clearance of radiolabelled aerosol. Miller et al in 1995 (75) reported that autogenic drainage and ACBT were equally effective in secretion clearance in cystic fibrosis. With radioaerosol, the average clearance rates of ACBT were high in peripheral lung region, whole lung and central lung, respectively. Although Miller's study was difference from our study in regions of interest which drawn over the right and left lungs and designation of the central and peripheral lung region. These result also might be support the results of ACBT in our study that evidence support the area of lung clearance. Moreover, it is postulated that ACBT was developed and renamed from FET. This technique was performed in conjunction with breathing exercise and FET in a set of cycle. From previous reviews found that no controlled data are available to assess the relative contribution of the components of ACBT. Only FET has been systematically evaluated (7, 10). Based on previous studies in radioaerosol measurement, FET was also effective in the enhancement of peripheral lung clearance (74). Therefore, one explanation for the effective of mucus clearance in ACBT is the potentially effects of FETs. We could be believed that the mucus clearance of ACBT were likely to be better for the lung periphery than the central lung

Fews of airway physiology reviews, the period of breathing control in ACBT is essential so as to prevent bronchospasm or airflow obstruction and the period of thoracic expansion, which increases lung volume and promotes collateral ventilation, allow air to get behind secretions and assist in their mobilization. This portion of the cycle aids with problems of asynchronous ventilation and blocked airways (11, 16, 17, 58). From review by Lapin CD in 2002 mentioned that even in normal lungs, time constants vary among lung regions, and asynchronous ventilation occurs secondary to regional and stratified inhomogeneity. So, airway clearance technique include a breath-hold to compensate for asynchronous ventilation.

Additionally, lower respiratory frequency and large tidal volume should increase the degree of collateral ventilation. Therefore, collateral ventilation channels between adjacent contiguous lobules and adjacent alveoli are probably not important in normal ventilation, but may be important when there is airway obstruction (16). With ACBT, it is possible that the component of breathing technique may have been responsible in part for augmenting mucus clearance or influence the localization of airway clearance by the principle of collateral ventilation system.

Comparison of ACBT, PLB&FETs of this study showed the trend toward greater clearance in the whole right lung zone in healthy subjects. It possibly relates to the differences in the total number of FETs performed during the active treatment sessions. PLB&FETs was performed 5 PLB followed by 1 FETs per minute. This sequence was repeated 4 times in each 5 minute period (with 1 minute of rest). So, FETs was performed 24 times along 30 minute of PLB&FETs intervention period whereas ACBT was performed 2 set of breathing technique combine breathing control, thoracic expansion exercise and FETs for 5 minute period. FETs was performed only 12 times along 30 minute of ACBT intervention period. It is feasible that the effect of mucus clearance by PLB&FETs showed slightly greater enhance than ACBT might be due to the major benefit of FETs.

5.1.2 Comparison heart rate, oxygen pulse saturation among the control (normal breathing), PLB&FETs and ACBT during the experimental period

During experimental period, the value of heart rate (HR) were minor fluctuation and no critical changes. All three study day, this variable resulted in little differences between baseline and intervention period. This study also showed that HR values were declined during and after PLB&FETs or ACBT was applied when compared to the control study. No differences between the effects of both techniques were observed. Also, our finding that oxygen pulse saturation was quite stable values during control study but this parameter was increased in the period when PLB&FETs or ACBT was applied. Therefore, airway clearance techniques of this study could slightly increase oxygen pulse saturation values in healthy subject especially in ACBT. This might be suggest that our subjects were healthy subject with no history or other

evidence of systemic disease. So, any change of HR, SpO_2 may probably reflects from the effect of airway clearance techniques. This study could be indicated that both techniques seem to be reduced heart rate and improve oxygen pulse saturation. This might be due to the components of breathing technique includes breathing control and thoracic expansion exercise in ACBT and PLB in PLB&FETs or it might be suggested that our subjects expended less energy during performed both techniques.

Previous observation using radioaerosol measurement in ACBT, there were not clinically significant in the change of heart rate from the value measure just before treatment to the average value during and immediately after treatment. Also, no differences were found in mean SaO_2 over the series. However, four patients with moderate to severe disease desaturated during the ACBT session. They explained that the falls in SaO_2 may due to postural drainage and percussion that combined during ACBT cycle in patients with cystic fibrosis (120). Conversely, of the various components of the ACBT, our study did not adapted of postural drainage and percussion to the technique. So, both parameters were not effect of either postural drainage and percussion in evaluation. Nevertheless, the effects of ACBT on HR and SpO_2 may vary according to the underlying pathophysiological disease of subject in the study. Also, the subjects in our study did not had any pathophysiological disease influencing to the results of study.

Based on our knowledge, it might be possible reasons of ACBT influencing oxygen pulse saturation. Firstly, the period of breathing control in ACBT was prevent bronchospasm and minimize fatigue by encourage use of the lower chest with relaxation of the upper chest and shoulders. Secondly, thoracic expansion exercises consist of deep inspiration with breath hold also recruit the collateral ventilator system (8, 10). Thirdly, sputum contributed relatively little to total airway resistance in healthy subjects. So, The unless airways were occluded by sputum in our subject. All of previous mentions, this should enable air to flow into ventilated parts of the lung and improve oxygen pulse saturation or may not reflect any adverse effect to overall ventilation. Furthermore, most of previous studies of ACBT has been shown

to ability to maintain (8, 75) and improve oxygen saturation (76, 77) whereas the change in heart rate was small decrease and not clinical significant (75, 77).

In PLB&FETs, it could slightly increase oxygen pulse saturation and decrease heart rate during and after intervention was performed. Recently, PLB aims to improve expiration both by its active and prolonged expiration and by preventing airway collapse, especially in chronic respiratory disease patient. By reviews the possible effects of PLB on oxygen pulse saturation, Thoman and colleagues in 1966 (81) found that tidal volume increased while respiratory rate decreased and carbon dioxide elimination improved using PLB. The effect of increasing the tidal volume would be an alteration of dead space volume/tidal volume and thereby improves alveolar ventilation. Tiep et al in 1986 (82) observed that PLB significantly improved SaO_2 over relaxation and baseline values in COPD patients. Relaxation did not significantly improve SaO_2 over baseline. PLB was accompanied by both a significant increase in mean tidal volume and a significant decrease in mean respiratory rate. Breslin EH in 1992 (84) also reported that PLB led to improved SaO_2, decreased respiratory rate in COPD. Changes in chest wall muscle recruitemetn and concomitant with the increased SaO_2 indicate a mechanism of improving ventilation with PLB while protecting the diaphragm from fatigue in COPD. In addition, Gosselink R in 2004 (19, 20) reviewed breathing techniques in patients with chronic obstructive pulmonary disease. Evidence existed to support the effectiveness of PLB to improve gas exchange and reduce dyspnea. In the other way, the effect of FET by a radioaerosol study was no direct measurement on oxygen saturation. Conversely, it seems likely that oxygen saturation levels and heart rate were recorded before, during and after each treatment session for detect any adverse effect by the radioactivity after inhalation to the subject. The results of our study was no critical changes in heart rate and oxygen pulse saturation levels for three study day. It could be mentioned that mucus clearance measurement with radioaerosol in this study was safety and no any adverse effect, probably due to particle deposition, airway obstruction or bronchoconstriction. Moreover, the improvement in oxygenation and decreased heart rate with PLB&FETs and ACBT were likely related to most previous studies of PLB

and FET. Therefore, we could be expected that PLB&FETs and ACBT could slightly increased oxygen pulse saturation and reduced heart rate in healthy subject.

5.1.3 Comparison the percent change of peak expiratory flow rate and Modified Borg scores of dyspnea among the control (normal breathing), PLB&FETs and ACBT at before and immediate after the experimental period.

The value of peak expiratory flow rate (PEFR) were nearly similarity between the initial on all consecutive study days. Additionally, no critical improvement or deterioration in PEFR was demonstrated when repeated immediately after each intervention period. Also, there were no obvious different in percent change of PEFR in this study.

From the radioaerosol study, two previous researches of mucociliary clearance were no significant change in pulmonary function (103, 106). Conversely, Miller and coworkers in 1995 (75) measured pulmonary function parameters at the beginning of the day and before and after each session of chest clearance in cystic fibrosis patients. No overall difference were found in the pulmonary function parameters results between autogenic drainage and ACBT. Nevertheless, more patients had improved $FEF_{25-75\%}$ with autogenic drainage, while more showed an improved forced vital capacity with ACBT. This study was noted that pulmonary function were decreased after inhalation of the aerosol. This showed an adverse effect probably due to bronchoconstriction. Although this effect rapidly disappeared. The authors noted that further research using inhaled radiolabelled aerosols might be an adverse effect on deposition. In our study, we performed PEFR value by peak expiratory flow monitoring, which a rapid, safe and reproducible technique to objective measurement of airflow obstruction. It could be used to investigate abnormal deposition, airway obstruction and the effective of therapy. However, this parameter was limited to providing information from mostly in the trachea and the major bronchi and thus may not accurately reflect obstruction throughout tracheobronchial tree. Although PEFR monitoring was not an adequate substitute for office spirometry, currently available inexpensive devices were acceptable for serial monitoring of

airflow obstruction. This monitoring allowed early detection of worsening airflow obstruction (126).

PEFR values were nearly similarity between the initial on all three study days. There were no critical improvement or deterioration in PEFR when repeated immediately after each intervention period. Our subjects seem to be the stable condition on three study day and might not have any adverse effect due to bronchoconstriction in all subjects after experimental period. Indeed, subject of this study were healthy subject with no history or other evidence of systemic disease. They might be normal mucociliary clearance and normal bronchopulmonary feature of the lung. So, the adverse effect seem to be rarely occurred.

The Modified Borg scores of dyspnea in each subject were showed consistency in before and immediate after the experimental period. There were no difference in percent change of scores among the control, PLB&FETs and ACBT groups. Normally, the Modified Borg scale used magnitude estimation to estimate the intensity of dyspnea and allow comparison between subjects. The scale has a range between 0 and 10. In this present study, subjects were asked to rate the sensation of "breathlessness" that they perceived before and after experimental period. None of our subjects claimed to have dyspnea. Nevertheless, there was only one subject showed 10 percent change of the scores after performed PLB&FETs. (Borg score from 0 to 0.5). This changes might be represent very, very slight (just noticeable) some of breathlessness during subject performed technique.

In the radioaerosol study, there was no objective assessment in dyspnea to look at the effect of airway clearance techniques. It might be had other parameters, especially SaO_2 and pulmonary function were best described any abnormal signs of ventilation. However, the general view of this study, dyspnea measurement using Modified Borg scale was a tool for self-reported shortness of breathing severity by subject. The scores might be indirect reflect any adverse symptom of physical and mental property during experimental period. In our study, Modified Borg scores of dyspnea were shown consistency in before and immediate

after the experimental period among the control, pursed lip breathing with forced expiration technique and active cycle of breathing technique groups. We could be suggested that PLB&FETs and ACBT were not reflect any breathlessness in healthy subjects of this study.

5.2 The Second Study: Comparisons of Pursed Lips Breathing with Forced Expiration Techniques and Active Cycle of Breathing Technique in Patients with Chronic Obstructive Pulmonary Disease

Twenty-two stable chronic obstructive pulmonary disease patients (COPD) ranging in age from 55 to 84 (Mean ± SD =70.18 ± 7.74) year with mild to severe COPD were included as volunteers in this study**.** Mean ± SD of forced expiratory volume in one second (FEV_1) of all patients was 59.75 ± 1.93 % of predicted. According to the classification of severity of COPD criteria, most patients of this study were moderate severity in stage II. The patients were allocated to pursed lips breathing with forced expiration techniques group (PLB&FETs) and active cycle of breathing technique group (ACBT). Eleven COPD patients obtained airway clearance techniques by PLB&FETs, while ACBT group (n = 11) received active cycle of breathing technique. Although this study recruited both male and female COPD patients for both PLB&FETs and ACBT group in order to study the efficacy of both techniques. From the results, there were not any the number of female patients were participated in this study. Therefore, this study were no considering of the gender.

From the characteristics of COPD patients, it is showed that the patients between both groups were no statistically significant difference in age, weight, height, history of smoking (pack year), ex-smoke time and severity of COPD. This similarity of characteristic represented the homogeneity of the subjects between two groups in this study. Therefore, there was minimize some confounding factors influencing the subjects performances or parameters' measurement.

5.2.1 Comparisons of mean percent predicted values of forced vital capacity, forced expiratory volume in one second, ratio of FEV_1/FVC, forced expiratory flow between 25% and 75% of the FVC and peak expiratory flow between PLB&FETs and ACBT group and within group at the difference of time

In this study, the values of forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), ratio of FEV_1/FVC, forced expiratory flow between 25% and 75% of the FVC ($FEF_{25-75\%}$) and peak expiratory flow were not statistically significant difference on the 1^{st}, 7^{th}, 14^{th} day of the study between PLB&FETs and ACBT group. There was only a significant difference in peak expiratory flow within ACBT group at the difference of time between 1^{st} and 14^{th} day of the study.

This results found that mean predicted values of FVC, FEV_1, ratio of FEV_1/FVC were nearly identical values on the 1^{st},7^{th} and 14^{th} day of the study in both groups. It is not surprising that the very small change in these parameters had no significant effect on lung function. So, our study had not demonstrated an improvement in FVC, FEV_1, ratio of FEV_1/FVC after performed airway clearance techniques in COPD patients on all consecutive study weeks in both PLB&FETs and ACBT groups. Commonly, the effects of chest physiotherapy have been evaluated using measurements of airflow, changes in gas exchange, measurements of pulmonary mucus clearance and measuring the volume of expectorated mucus . It has often been assumed that mucus has a measurable effect on pulmonary function and that improvement of mucus transport will improve pulmonary function. Retention of mucus can theoretically reduce airway diameter and contribute to airflow obstruction (86).

From interpretation of change in lung function, evaluation of an individual's change in lung function following an intervention or over time in often more clinically valuable than a single comparison with external reference (predicted) values. It is not easy to determine whether a measured change reflects a true change in pulmonary status or is only a result of test variability. All lung function measurements tend to be more variable when made weeks to months apart than when repeated at the

same test session or even daily. It is more likely that a real change has occurred when more than two measurement are performed over time. When there are only two tests available to evaluate change, the large variability necessitates relatively large changes to be confident that a significant change has in fact occurred (127).

Some of previous studies were able to detect an improvement in pulmonary function test or gas exchange after physiotherapy in patients with COPD by Cochrane et al in 1977, Newton et al in 1978, Feldman et al in 1979 and in patients with cystic fibrosis by Tecklin et al in 1975, Weller et al in 1980 (86). Savci et al in 2000 (76) compared autogenic drainage (AD) and ACBT in prospective randomized trial over 20 days in 30 patients with COPD. They reported similar improvement in pulmonary function with two techniques. However, the change in FEV_1 , $FEF_{25-75\%}$ of ACBT group was not statistically significant and they did not find a statistically significant improvement in $FEF_{75-85\%}$ in any of the treatment groups. From this observation, they concluded that ACBT and AD were effective in secretion clearance from the larger and the middle airways other than the smaller airways. However, a variety of factors including location of secretions, obstruction level and different disease conditions affect the functions of both AD and ACBT in the smaller airways. They believed that AD and ACBT used in their study improved lung function by ensuring collateral ventilation in segments of lung not previously involved in ventilation. They suggested that further studies are needed to evaluate the effects of these two different techniques on small airways (76). Our study could be argued this previous report that the number of packs per year in smoking history in our patients had more than Savci and coworkers. The smoking history (packs per year) of Savci ’s patient were 38.9 ± 17.3 in AD group and 35.9 ± 24.7 in ACBT group, whereas this present study were 41.80 ± 45.06 in PLB&FETs and 43.68 ± 19.80 in ACBT group. Considering the age of the subjects, this study recruited the patients with the age of 35 or older and the average values were 70.69 ± 7.89 years for PLB&FETs groups and 69.73 ± 7.95 for ACBT group. The age of patient in this study was older that the study conducted by Savci, et al. with the patients aged was 58.3 ±8.0 years for AD group and 61.3 ± 7.9 years for ACBT group. Therefore, It is reasonable to suggest that the effectiveness of ACBT in our patients might differ from previously report with the

difference of clinical characteristics in patients. In addition, difference in application duration and difference in the disease pathophysiology were probably partly responsible for these different outcomes.

Although, differences were statistically nonsignificant in our study. $FEF_{25-75\%}$ value was slightly improved following airway clearance technique compared with baseline assessment in both groups. Mean ± SD percent predicted $FEF_{25-75\%}$ of PLB&FETs were 4.72 ± 2.06, 5.11 ± 2.11, and 5.56 ± 2.91; $FEF_{25-75\%}$ in ACBT were 4.03 ± 1.54, 4.13 ± 1.64 and 4.71± 2.44, respectively. From pulmonary function test, the earliest change associated with airflow obstruction in small airways is thought to be a slowing in the terminal portion of the spirogram, even when the initial part of the spirogram is barely affected. This slowing of expiratory flow is most obviously reflected in a concave shape on the flow-volume curve. Quantitatively, it is reflected in a proportionally greater reduction in the instantaneous flow measured after 75% of the FVC has been exhaled ($FEF_{75\%}$) or in mean expiratory flow between 25% and 75%. Also, as excessive mucus in the airways may result in some limitation of airflow, a reduction in the mucus load may also improve airway function especially in the small airways (128). Therefore, our results may be expected that both techniques might benefit patients by reducing the mucus load acutely or it might have a prolonged effect on mucociliary clearance. We suggested that the change of $FEF_{25-75\%}$ was a reflection of improved mucus clearance in COPD patients.

In a Cochrane systematic review in 2000, Jones and coworkers (129) assessed the effects of conventional chest physical therapy (CPT) in subjects with COPD or bronchiectasis. CPT produced no significant effects on pulmonary function, apart from clearing sputum in COPD and bronchiectasis. The authors concluded that there is insufficient evidence to support or refute the effectiveness of CPT in subjects with COPD or bronchiectasis.

From previous studies of ACBT in COPD or bronchiectasis, the study of Cecin et al in 1999 (92) compared ACBT in position with and without a head-down tilt in nineteen subjects with bronchiectasis. There was no significant difference

in the wet weight of sputum expectorated. Also, there were no significant changes in oxygen saturation during or after either regimen and no change in FEV_1 after either treatment. ACBT in the head-down position might be possibly due to an increased work of breathing resulting from a resistive loading on the diaphragm from the weight of the viscera. Overall, subjects were less breathless and preferred ACBT in the horizontal position.

Thompson and coworkers in 2002 (78) performed a study in patients with bronchiectasis at home, comparing the efficacy of the Flutter® device with ACBT. No significant differences between the two techniques were found. Ventilatory function did not change significantly during either treatment period. There was no significant change in peak expiratory flow rate or in breathlessness. They suggested that if the objective differences are small between the difference techniques, then individual preferences are likely to play an important part in compliance with treatment.

Patterson et al in 2004 (70) compared the efficacy of the test of incremental respiratory endurance (TIRE) with ACBT incorporating postural drainage in bronchiectasis patients. There were no significant differences between pre-and post treatment lung function or oxygen saturation for either technique indicating neither ACBT nor TIRE causes airway obstruction. Equal numbers of patients preferred TIRE as preferred ACBT as home treatment modalities, although more than half of the patients perceived that ACBT was a more effective method of airway clearance that TIRE. The TIRE equipment and laptop required to run the software were expensive. There were also cost issues relating to care of equipment, cross infection and cleaning. Moreover, there were limitations associated with single intervention airway clearance studies. Despite these limitations, this single intervention study indicate that TIRE is not as effective a method of airway clearance as ACBT .

Our study was not found objective improvement in FEV_1, FVC, FEV_1/FVC parameters of lung function in COPD patients using PLB&FETs or ACBT. There was in agreement with the finding of other workers. It might be postulated that

the effect of airway clearance technique could be cumulative and that we failed to detect the objective benefit on FEV_1, FVC, FEV_1/FVC because of the short period of study when comparison with Savci and coworkers in 2000. Unfortunately, the lack of a placebo group (control) did not allow us to confirm any meaningful discussion about the period of time.

The small increase in $FEF_{25-75\%}$ during both techniques of the study suggested that PLB&FETs and ACBT might have probably reflects to move distal secretions in the small airways. Both techniques in this study consisted of the FET combined with breathing techniques. From previous literatures, the forced expiration technique is 1 or 2 forced expiratory maneuvers of huffs combined with breathing control. The concept of the equal pressure point (EPP) explains the mechanism of the effectiveness of the huff in airway clearance (7, 10, 16). In theory the maneuver starts with the equal pressure point at a middle lung volume, this dynamic compression point moves peripherally, with a concomitant migration at the high point of airflow linear velocity, promoting cephalad movement of secretion (130). Then, a huff down to a low lung volume will help to loosen and mobilize secretions from the smaller more peripheral airway and a huff at a high lung volume will clear secretions mobilized to the large more central airways (10, 16). Therefore, it is probably that the forced expiratory maneuver is the most effective part of our airway clearance regimen. Nevertheless, to assist in enhancing secretion removal, more recent efforts have been directed at using various breathing strategies which are directed at ventilating the area behind the obstruction and then utilizing increased expiratory flow rates to mobilize secretions up the airways. In our study, breathing control and thoracic expansion exercise included in ACBT and PLB in PLB&FETs was based on this concept. In a cycle of ACBT, breathing control or relaxed tidal breathing aims of decreasing the work of breathing and airflow obstruction. In addition, thoracic expansion exercise aim increasing the lung volume above tidal volume breathing reduced collateral ventilator resistance, allowing air to flow behind secretions aiding their mobilization, while at the same time forces exerted between adjacent alveoli aid lung re-expansion (16, 58). In PLB&FETs, the increased clearance may achieved by the mechanical effect of PLB. During PLB, the active expiration through the half-opened lips inducing

expiratory mouth pressure of about 5 cmH_2O (19, 20, 24). The positive back pressure may splints the airway open, preventing compression or premature closure. There was theorized that positive pressure is built up distal to an obstruction, promoting the movement of secretions toward the large airways. In addition, airway stability is maintained with positive expiratory pressure breathing which results in improved ventilation and gas exchanges as well as in airway clearance (8, 11, 12, 17, 24, 59, 63). Therefore, we are believed that the positive expiratory mouth pressure of PLB may be some additional effect in enhancing the removal of pulmonary mucus from the lung. In considering respiratory mechanics, expiratory muscle recruitment with PLB may improve length-tension relationships of the inspiratory muscles, particularly the rib cage and accessory muscles, improving their mechanical efficiency and leading to greater force generation capacity in ventilation. It is possible that the integration of respiratory muscle changes with PLB might be some enhancing mucociliary clearance in the total lung. Moreover, David A (53) mentioned that the equal pressure point is moved towards the mouth with avoiding compression of a collapsible segment by performing expiratory through pursed lips. Nevertheless, this current study was the first research designed to evaluate the effects of pursed lips breathing combined with forced expiration techniques for mucociliary clearance. Of course, we were unable to clearly identify the reasons of PLB&FETs for enhancing airway clearance. There was as generally assumed, but fews documented previously support.

This study carried out during the two week of airway clearance techniques. It is demonstrated that mean predicted values of peak expiratory flow (PEF) was slightly increased on the 7^{th} and 14^{th} day of the study in both groups when comparison of the baseline values. The change was significant different of the main effect of time within group ($p < 0.05$). Within group, PEF improved significantly after ACBT treatment. There was significant difference between the 1^{st} and 14^{th} day of the study. Although this parameter in PLB&FETs was also improved following treatment compared with baseline assessment (1^{st} day), but the differences were statistically nonsignificant. This could be postulated that the initial (baseline) of PEF was high in PLB&FETs, it may have been more difficult to detect significant changes.

Commonly, PEF is the highest flow achieved from a maximum forced expiratory manoeuvre started without hesitation from a position of maximal lung inflation. This parameter is dependent on effort and lung volume (117). In our study, the improvement of PEF of both techniques might be due to the essential components of breathing technique. ACBT utilized breathing control, which is gentle, relaxed breathing at the patient's own tidal volume and resting respiratory rate to allow recovery and prevent any increase in airflow obstruction and the theory of slow and deep breathing with inspiratory hold to enhance collateral ventilation by thoracic expansion exercise. This portion of the cycle aids with problems of asynchronous ventilation and blocked airway (16). From recent review of breathing techniques in patients with COPD (19), slow and deep breathing was commonly applied in physiotherapy practice attempting to correct abnormal chest wall motion, decrease work of breathing, accessory muscle activity and dyspnea, increase efficiency of breathing and improve distribution of ventilation. It is postulated that efficacy of breathing techniques in ACBT could be improvement of thoracoabdominal movements in COPD patients. This also might be positively associated with the increase effort and lung volume in COPD patients to improvement of PEF.

In PLB, it appears to be effective in improving gas exchange and reducing dyspnea in COPD patients by its active and prolonged expiration and by preventing airway collapse. It have been suggested that relaxed expiration produced less air trapping which results in a reduction of hyperinflation. Moreover, the decrease of airway compression and the slowing of expiration improved tidal volume and increase in vital capacity. In considering respiratory mechanics, expiratory muscle recruitment with PLB may improve length-tension relationships of the inspiratory muscles, particularly the rib cage and accessory muscles, improving their mechanical efficiency and leading to greater force generation capacity in ventilation. It is possible that the alteration of ventilation and respiratory muscle changes with PLB might be increase effort and lung volume in COPD and improve PEF in our study.

5.2.2 Comparisons of total mean values of peak expiratory flow rate, sputum volume and Modified Borg score of dyspnea between PLB&FETs and ACBT group and within group at the difference of time

Peak expiratory flow rate (PEFR), daily sputum volume and subjective rating of dyspnea by Modified Borg scales were measured by self evaluation of patient on everyday in daily logbook record. From the result of this study, total mean values of PEFR in patients who received PLB&FETs was no significantly different from those who obtain ACBT at 1^{st}, 2^{nd} week of the study. Within group, total mean values of PEFR in the first week of both groups were lower than in the second week. PEFR of the second week was significantly greater than the first week in the patient group of PLB&FETs.

In this parameter, PEFR was recorded using a patient-administered portable PEFR meter, it was expressed in L/min. This value must be achieved as rapidly as possible and at as high a lung volume as possible, in order to obtain the maximum value. Recently, standardisation of spirometry in 2005 viewed that when PEFR is a self-administered that recording, it is important that the subject has been adequately taught how to perform the test, when to perform it and what action to take depending on the resulting value obtained (117). Our study was regular checks of the patients's PEFR technique and meter in the follow-up period. Therefore, the variability of the results could be diminished and the measurement accuracy could be improved. Actually, PEFR was dependent on effort and lung volume. Thus, the improvement of PEF of both techniques in this study might be due to the essential components of breathing technique in either airway clearance technique. From our earlier mentioned that improvement of thoracoabdominal movement by ACBT and the alteration of ventilation and respiratory muscle changes by PLB might be increase effort and lung volume in COPD and due to improve PEFR in this study.

Very few studies were available which examine the effectiveness of airway clearance technique in PEFR parameter. Hasani and coworkers in 1994 (131) investigated that regional mucus transport in a group of subjects with airways obstruction who failed to expectorate following instructed cough and FET. An

objective radioaerosol technique was used to monitor regional mucus movement within the lungs of the patients and peak expiratory flow rate during cough and forced expiration was measured at the mouth using a pneumotachograph. There was no correlation between the radioaerosol clearance from all regions and mean peak flow during cough and forced expiration. They demonstrated that patients in mild hypersecretion apparently unproductive cough/ FET results in movement of secretions proximally from all regions of the lungs. It is reasonable to suggest that both cough and FET were probably at least effective down to airways equivalent to generations 10 or 12 of the Weibel model. However, the mean peripheral region clearance was considerably higher with both cough and FET for at least some of patients with airway obstruction. It is possible that cough and FET may have been effective down to the most distal ciliated airways. The lack of association between peak flow rate and efficacy of the cough and FET maneuvers may be clinically important. It implies that patients can achieve valuable enhancement of clearance without having to try excessively hard to achieve their highest possible flow rate. In the other hand, Henke et al in 2005 (132) mentioned that the high expiratory (peak) flow may decrease the viscosity of mucus. This phenomenon of frequency dependent shear stress reduction of viscosity in pseudoplastic materials is known as thixotropy. High PEF can facilitate detachment of adherent airway secretions from the epithelial surface. The mucociliary and mucus-epithelial interaction is most pronounced at the interface between the two surfaces. Detachment can be affected either by airflow forces or by application of physical therapy techniques. Once a critical airflow is reached (detachment velocity), there will be marked augmentation in mucus clearance from the airway as well as improvement in ciliary efficacy. Therefore, improvement of PEFR in this study might be indirect effects on mucociliary clearance. It could be postulated that both techniques might be increase absolute peak expiratory flow to move secretions towards the oropharynx and improving the expiratory bias of airflow to increase the annular flow of mucus towards the oropharynx by use two-phase gas-liquid flow. Therefore, the sputum retention was decreased. This condition may lead to an increase in this parameter. However, we should keep in mind that peak flow monitoring are not sensitive enough to accurately and predictably reflect lung function in all patients. Between-manoeuvre evaluation, the acceptability are within 0.67 L/s or 40 L/min

(117). Therefore, the range of variability among test of PEFR might be due to the statistical significance change in this study but it might not be really reflect in the clinical change in the patients.

In sputum volume, the patient were provided with container and instructed to collect all sputum produced over 24 hour period. The mean values of daily sputum production measured for each week was calculated for each patients. Total mean values of sputum volume in patients who receive PLB&FETs was no significantly different from those who obtain ACBT at 1^{st}, 2^{nd} week of the study. Within group, total mean of sputum volume in the second week of both groups were lower than in the first week. Sputum volume of the second week was significantly lower than sputum volume of the first week in the patient group of PLB& FETs. However, there was not significant between the first and second weeks in ACBT group

This study might expected that sputum from the airways of patients with PLB&FETs is cleared more than ACBT. Although no statistical difference between the effects of PLB&FETs and ACBT regimens were observed. In fact, discrepancy between results of sputum measurements has been the common finding in chest physiotherapy studies (86). Rossman and co-workers (103) suggests that the measurement of expectorated sputum volume may be less reliable method. Sputum is inevitably contaminated by an unknown saliva and furthermore, some patients swallow some of their sputum or are unable to expectorate at all. However, Drying of sputum to measure the dry macromolecular weight does not seem to improve the information obtained by assessing the wet weight of sputum which might be influenced by the mixing of saliva (97). In a study of airway clearance technique by Sutton, et al in 1983 (106), the ratios of dry to wet weight of sputum were similar. However, the results appear to be based on observation of the data and no statistical analysis was reported. From Cecins and coworkers study in 1999 (92), they conducted a pilot study to confirm whether wet weight of sputum was a good predictor for dry weight of sputum. For each subject, there was a strong relationship between the wet and dry weight of sputum. These finding indicate that wet weight of sputum is a good

predictor of dry weight of sputum and thus it is unlikely that the salivary content of the wet weight influences the reliability of the measure. Our finding possible to indicated that both techniques could be achieved of sputum expectorated in COPD patients. However, COPD patients of this study might be some vary in amounts of daily sputum production and no baseline record in the history of daily sputum production in each patient. Therefore, the difference in sputum volume during the period of study could not be exactly explained by a difference in techniques.

Published studies have shown that chest physical therapy is effective primarily in patients with copious secretion (89, 106). Moreover, several authors have suggested that physiotherapy is effective only when the mucus expectoration is more than 30 ml a day (75). Our study has shown that both ACTs are also effective in patients who expectorate less. Expectoration of mucus may not lead to an improvement of lung function but it may contribute to the prevention of pulmonary infections.

Measurement of sputum volume showed that total sputum expectorated was decreased when both techniques had performed. This would suggested that the mucus load along 2 week after ACTs was decreased. This finding might also supported by the patients comment with Modified patient evaluation questionnaire. However, this was difficult to explained this parameter without knowing the state of mucus, in terms of load and properties at baseline.

The sputum volume may have a role in reducing the volume during both airway clearance techniques on the second week, possibly by facilitating secretion clearance and improving the distribution of ventilation. The volume reduction between the first and second week suggested that the overall secretion retention of the subjects had improved.

The increased clearance achieved by PLB&FETs in this present study could be the result of the mechanical effect of pursed lips breathing, forced expiration techniques and the second clearance mechanic of two-phase gas-liquid

flow. In ACBT, it is possible that the component of breathing technique might have been responsible in part for augmenting mucus clearance or influence the localization of airway clearance in COPD patients by the principle of collateral ventilation system and the component of FET was also effective in mucus clearance by the physiological concepts of the equal pressure point (EPP) and the shear forces in the mechanism of the effectiveness of huff.

It is critical that the quantity of expectorated sputum of our patients on the second week was clearly lower than on the first week. PLB&FETs was showed significantly in the decrease of sputum volume on the second week. Moreover, the sputum volume of PLB&FETs group was lower than ACBT group in the second week. We could be expected that both techniques might be increased sputum expectoration in the first week and improved sputum retention in the second week. In addition, it is feasible that the effect of mucus clearance by PLB&FETs showed slightly greater enhance than ACBT in COPD patient. This might be due to the major benefit of FETs. From the twice-daily of airway clearance technique, PLB&FETs group was performed the repetition of FETs more than ACBT. So, the difference of sputum expectorated might be possibly related to the differences in the total number of FETs performed during the active treatment sessions. Overall, the values of PLB&FETs and ACBT of chest physiotherapy in the short-term period of this study had directly demonstrated improvement of sputum clearance. PLB&FETs and ACBT could be had short-term benefits in sputum expectorated in stable COPD patients. We did not see any harmful effects in our patients of study.

With rating of perceived dyspnea, total mean values of Borg score in the patient group of PLB&FETs was nearly value to the patient group of ACBT. There were failed to show significant difference of Borg score of dyspnea between groups in the first and the second week of the study. Also, this score did not significantly change from the first week to the second week of study in PLB&FETs group and in ACBT group.

Normally, the Modified Borg scale is a tool for self-reported shortness of breathing severity by subject. This scale used magnitude estimation to estimate the intensity of dyspnea and allow comparison between subjects. The scale has a range between 0 and 10. This clinical parameter was in part of subjective assessment for shortness of breathing severity in COPD patients. With twice-daily airway clearance technique of this study, patients were detected change in the sensation of “breathlessness” in everyday. Our results reported that Borg scores of dyspnea in each subject were showed slightly decreased along two week period. Both groups showed the dyspnea scores ranged between 0 - 4 in the first week and 0 - 3 in the second week. This scores were represented nothing at all of breathlessness to moderate or somewhat severe of breathlessness. Therefore, all patients who received their regular treatment in 14-day course of twice daily airway clearance technique showed trend decrease breathlessness. In addition, our subjects did not reported any increase in perceived breathing effort. This results could be explained by the fact that both techniques were reduced dyspnea and not occurred fatigue due to perform techniques. Additionally, this study might be indirect reflected that no any adverse symptom of physical and mental property in our subjects.

It is usually stated that breathlessness or dyspnea is the most clinically important feature of COPD. The resulting breathlessness reflects decreased pulmonary function and is associated with poor prognosis. As breathlessness progresses, patients rely increasingly upon accessory muscle group to support ventilation (84). Therefore, our study could be expected that the overall dyspnea symptoms of all COPD patient were also minor improvement. The possible reasons for decrease dyspnea in patients with COPD included the component of breathing technique in PLB&FETs and ACBT. From previous reviews of COPD, several pathophysiological factor known to contribute to dyspnea include: 1) increased intrinsic mechanical loading of the inspiratory muscles; 2) increased mechanical restriction of the chest wall; 3) functional inspiratory muscle weakness; 4) increased ventilatory demand related to capacity; 5) gas exchange abnormalities; 6) dynamic airway compression; or 7) cardiovascular effects (19, 20).

Recently, breathing pattern retraining is frequently used for exertional dyspnea relief in adults with moderate to severe COPD (133). Some previous research has focused on the effective of PLB in COPD patient. Bianchi and coinvestigators in 2004 (85) showed that PLB reduced dyspnea by both lengthening expiratory time and lengthening the full ventilator cycle. Dechman and Wilson in 2004 (21) examined the separate effects of PLB and diaphragmatic breathing and to identified the mechanisms responsible for improvements in people with COPD. This work suggested that PLB did relieve dyspnea in patient. It seem to optimize the mechanical function of the lungs, limiting increases in end expiratory lung volume, the deleterious effects of hyperinflation. Neild and coworkers in 2007 (133) compared 2 programs of PLB and expiratory muscle training on dyspnea and functional performance in COPD patients. The results showed that the PLB group had significant improvement at 12 weeks for exertional dyspnea and functional performance. In conclusion from their study, PLB provided sustained improvement in exertional dyspnea and physical function.

With a cycle of ACBT, breathing control was achieved to decrease the work of breathing and airflow obstruction. Likewise, thoracic expansion exercise was increased lung volume above tidal volume breathing reduced collateral ventilator resistance and aid lung re-expansion (16, 17, 58). Consequently, slow and deep breathing improved alveolar ventilation and breathing efficiency. Therefore, ACBT might be relieved dyspnea symptom by optimizing the pattern of thoracoabdominal motion (19, 20). This current study found that both airway clearance techniques were safe and effective to relieve dyspnea symptom in the care of patients with COPD.

5.2.3 Comparison of total scores of Modified patient evaluation questionnaire between PLB&FETs and ACBT group and within group at the difference of time

Total scores of Modified patient evaluation questionnaire in patients who receive PLB&FETs showed no significantly different from those who obtain ACBT at the 1st, 7th, 14th day of the study. Anyway, there were a significant difference of the main effect of time within group. Total scores of PLB&FETs group was

significant difference between the 1st and 14th day of the study. Moreover, ACBT group were also statistically significant difference of total scores between the 1st and 7th day and between 1th and 14th day of the study

The Modified patient evaluation questionnaire was developed by Petty and coinvestigators in 1990 (90). It was five items questionnaire with scores ranged from 5 to 27. The symptom efficacy parameters included assessment of the following: cough frequency, cough severity, chest discomfort, difficulty breathing and ease in bringing up sputum. In this scoring system, higher scores represent worse disease and falling scores suggest improvement. Petty and colleagues in 1990 supported the usefulness of objectively evaluating symptoms as a measurement of drug efficacy. This study demonstrated that the symptomatic parameters of efficacy were meaningful indices for evaluating therapy in COPD and that a therapeutic goal of treating patients with COPD should include not only an improvement in pulmonary function indices, but also an improvement in the symptom associated with COPD.

Indeed, cough is an essential mechanism for mucus clearance in chronic bronchitis, but severe chronic non-productive cough can result in fatigue or exhaustion and can worsen the patient's condition. Therefore, a reduction in cough frequency and severity is clinically important because the progression of disability in COPD patients tend to slow down when coughing either disappears or is controlled (90). Thus, our study was evaluated objectively the use of symptom assessment in determining the efficacy of airway clearance technique in patients with COPD. This approach might be the best available method. If airway clearance technique improve sputum clearance, changes in pulmonary function might be demonstrated coincident with the patient's sense of improved well being. Although it might be argued that the symptom efficacy questionnaire was limited on a few studies (86, 90, 134) and poorly standardized. However, the questionnaire developed by Petty was included symptomatic parameters of efficacy to objectively evaluate on the basis of the cardinal symptom of excess mucus.

Both airway clearance techniques in our study showed a trend toward reduction in total scores of Modified patient evaluation questionnaire. Mean ± SD in PLB&FETs group were 12.27 ± 3.23, 9.36 ± 1.50 and 8.73 ± 2.10; total scores in ACBT groups were 13.18 ± 1.94, 9.64 ± 1.96 and 8.64 ± 1.63, respectively. Therefore, cough frequency, cough severity, chest discomfort, difficulty breathing and patients' ease in bringing up sputum were significantly improved by PLB&FETs and ACBT as compared with the baseline within two weeks of treatment. Anyhow, ACBT showed early improvement within one week of treatment. Our study might be concluded that both techniques were effective in COPD patients who expectorate sputum daily to improvement in the symptom associated with disease.

ACBT or PLB&FETs should be the treatment of choice of physiotherapists for patients with chronic obstructive pulmonary disease in a stable phase of their disease. Overall, our results suggest that PLB&FETs and ACBT have similar short-term benefits in patients. There were not any harmful effects on clinical symptom.

5.2.4 Comparison of total scores of Modified patient satisfaction questionnaire between PLB&FETs and ACBT group at the 14th day of the study

Total scores of Modified patient satisfaction questionnaire for efficacy in patients who receive PLB&FETs showed no significant different from those who obtain ACBT at the end of the study (14th day). Total scores in the patients group of PLB with FETs (mean ± SD = 17.09 ± 2.62) was greater than the patients group of ACBT techniques (mean ± SD = 16.54 ± 2.50)

Nowaday, conventional chest physical therapy (CPT) is a widely used intervention in patients with airway disease. It is not clear which groups of patients benefit from which airway clearance modalities, so an n of 1 study with the various airway clearance modalities is probably the best way to determine which will benefit a given patient. At present, the patient's subjective preference is the best measure of which modality to use (135). Also, Homnick DN in 2007 (136) mentioned that several ACTs studies use questionnaires to gauge patient acceptance of a

particular ACTs device or technique, especially as compared to another. Validation of these tools is small, short-term studies is difficult or impossible, but can be used as a rough guide to the potential acceptance of any intervention. Adherence over time will be the ultimate measure of acceptance of an airway clearance technique. Recent review of ACTs, many studies were examine the patient's subjective preference to investigate the potential effects of ACTs especially ACBT.

Olseni, et al in 1994 (98) assessed the patient's preference to FET combined with either postural drainage or positive expiratory pressure breathing (PEP). The patients found both treatments equally efficient but most of the patients preferred PEP as a treatment. Although the difference in efficiency found in objective measurements was thus not perceived by the patients. They concluded that the difference in efficacy of the treatments must be considered in relation to patient preference.

Cecins and coworkers in 1999 (92) compared ACBT in positions with and without a head-down tilt. Subjects were asked which treatment they preferred, their reasons for this choice and which treatment they thought was more effective at the end of the second treatment day. The results of this study showed that ACBT is as effective in terms of the weight of sputum expectorated in the horizontal position as in the head-down position. Nevertheless, subjects were less breathless and preferred ACBT in the horizontal position. The results of this study indicated that it is preferable to perform ACBT in position without a head-down tilt, as it is effective and better tolerated by subjects than in the head-down tilt. In practice this means a simpler, more comfortable regimen which may improve adherence in individuals who are advised to carry out dialy airway clearance treatments.

Thompson and coinvestigaters in 2002 (78) performed a study in patient with non-cystic fibrosis bronchiectasis at home, in which 4 weeks of daily ACBT were compared with 4 weeks of daily physiotherapy with the Flutter device. This study showed that daily use of the Flutter device in the home is as effective as ACBT in patients and has a high level of patient acceptability. They suggested that if

the objective differences are small between the different techniques, then individual preferences are likely to play an important part in compliance with treatment.

Phillips et al in 2004 (79) compared ACBT with the Hayek Oscillator Cuirass, performing high-frequency external chest compression (HFCC) on secretion clearance in children with cystic fibrosis during an exacerbation. All subjects found treatment by ACBT comfortable to perform. Sixty percent found the Hayek Cuirass HFCC uncomfortable. Eighty percent of subjects felt in difficult trying to clear secretions by HFCC; however, ACBT made it easier to clear secretions. They commented short-term patient preference does not encourage the belief that long-term adherence to HFCC is likely. They can not exclude the possibility of HFCC benefit being demonstrated in other age groups or those with different severity of disease.

Patterson et al in 2004 (70) compared the efficacy of the test of incremental respiratory endurance (TIRE) with ACBT is methods of airway clearance in adults with bronchiectasis. Patient preference for each method and perceived effectiveness were recorded post-treatment day 2. Equal numbers of patients preferred TIRE as preferred ACBT as home treatment. However, more than half of the patients perceived that ACBT was a more effective method of airway clearance than TIRE. This study demonstrated that ACBT is a more effective ACTs than TIRE in patients with bronchiectasis during single treatment session. Nevertheless, the authors suggested patient preference may not have been based on patient perceived effectiveness but rather on the experience of using a new treatment technique involving technical equipment.

Our study was also interested in the overall satisfaction of both airway clearance techniques using the Modified patient satisfaction questionnaire. By revising the questionnaire developed by Phillips and coworker in 2004 (79), we evaluated the patient's perceived ease of technique, comfort, secretion and recommendation to a friend. The scores ranged from 4 to 20 with the higher scores represent high satisfaction and the lower scores suggest on unsatisfaction. Overall, our study found both techniques to be equally effective. The difference of satisfaction

found in objective measurement was thus not perceived by the patients. From total scores of Modified patients satisfaction questionnaire, patients acceptance thus seem to be equal for PLB&FETs and for ACBT. In this study, we has the impression that the effectiveness of the treatment techniques must be considered in relation to patient preference. The main advantage of both techniques in this study was that it is easily performed alone by the patient and thus avoids dependence on other individuals for treatment. PLB&FETs or ACBT was ease to perform, comfortable, effective clearance. Moreover, both techniques were safe and no identify possible adverse effects and represented the efficacy in the care of COPD patient.

5.3 Clinical Implication, Limitation and Further Study

This study was composed two studies. The first study was compared the efficacy of PLB&FETs and ACBT with respect to acute change on pulmonary mucus clearances in experimental settings. The second study was compared the effectiveness of PLB&FETs and ACBT in patients with chronic obstructive pulmonary disease in clinical settings.

In the first study, the values of PLB&FETs and ACBT of chest physiotherapy have been directly demonstrated using an inhaled radioaerosol method; both PLB&FETs and ACBT have been shown to be effective in the clearance of radioaerosol when compared to control study (normal breathing) in all lung zones, especially the intermediate and peripheral lung zone. However, compared to ACBT, PLB&FETs showed the trend toward greater clearance in the whole right lung zone in normal subjects.

The first study was conducted in laboratory setting based on radioactivity approach. The lung zone of radionuclide imaging were divided into the central, intermediate, peripheral and whole right lung based on area of ratio 2:1:2 of two-dimension images for interpretation. So, it did not the actual anatomy of lobes and segments of the lung. Moreover, clearance of radioaerosol occurred in three dimensions with dynamic movement but the analysis was based on a two-dimensional

representation of the lungs. Therefore, interpretation of images in our study was indirectly represent the reality of lung zone clearance. The results of each lung zone may possible risks in extrapolating data from in laboratory situation to what actually happens in clinical setting. So, the results must be interpreted with caution if the readers would consider about physiological matters. Nevertheless, analysis of the data in this study was only used from the right lung to avoid interference from activity in the esophagus and stomach. All data were corrected for background and radioactive decay. We assume that our sequential lung image showing acute pulmonary mucus clearance and the results was shown ideally obtained as near as possible in the actual situation. Overall, the first study only get an idea regarding what is happening in mucus clearance of the airways when ACTs was applied. We believe we can obtain a better idea of lung clearance by PLB&FETs and ACBT on quantitative basis.

From the result, PLB&FETs and ACBT were clearly facilitated the whole total right lung clearance in healthy subject especially in intermediate and peripheral zone. This study is possible to indicated that both airway clearance techniques might respond to pulmonary mucus clearances indifferently. These finding can necessarily be extended to patients with smaller sputum volumes. Nevertheless, in our knowledge, the immediate effect of PLB&FETs on mucus clearance in normal subjects or in patients has never been study before. Also, there was only one previous research has focused on ACBT in terms of mucus clearance of radioactivity. Moreover, methodology limitation of this study was small sample size. Therefore, this finding was insufficient evidence to strong support the benefit from the use of both techniques to improve secretion clearance in patient with chronic respiratory disease or patient with copious sputum. In addition, noninvasive radioaerosol techniques have been used to evaluate in patients with chronic airflow obstruction (74, 89, 91, 122, 125, 131). For effective clearance of inhaled radioaerosol particles, they have been found that spontaneous mucus clearance from the peripheral lung region was higher in the patients with emphysema than in those with chronic bronchitis (74), pulmonary clearance mechanism of patients with obstructive airways disease showed nonhomogenous aerosol deposition patterns in the lungs and the migration of radioactivity over the trachea and the major bronchi was extremely protean in its

direction and transportation patterns. Therefore, the transportation patterns were highly variable and the clearances also differed greatly from normal subject (122). In this sense airway clearance techniques of the first study are undoubtedly clearance mechanisms in COPD patients. We were unable to demonstrate mucus clearance of the airways in patient when PLB&FETs or ACBT was applied. Therefore, an idea of lung clearance of both techniques in the first study was limited to provide information on regional lung clearance in COPD patient in the second study. Until recently, few studies are available which examine the effectiveness of mucus clearance in both techniques. This should be noted for further research.

In the second study, there was conducted in clinical settings to compared the effectiveness of PLB&FETs and ACBT in COPD patients. From the results, it was found that the subjects in both groups were beneficial from ACTs as reported in increased mean predicted values of PEF, improved total mean values of PEFR, daily sputum volume and Borg scales of dyspnea by self evaluation of patient on everyday, decreased total scores of Modified patient evaluation questionnaire. Total scores of Modified patient preference questionnaire for efficacy in patients who receive PLB&FETs showed no significant different from those who obtain ACBT at the end of the study. Mainly, there was no significant difference between PLB&FETs and ACBT groups in any parameters but significant differences were indicated for the over-time changes in each group.

The limitations of our study mentioned that the patients number were limited, although they were recruited from the general hospital. In addition, the follow-up period of two weeks was relatively short for precisely determining the ACTs effect. Nevertheless, we have found that both techniques of this study are safe and effective procedures in the care of patients with COPD, but that they are no associated with an improvement in spirometric indices during short-term evaluation. Further studies are required to determine the long-term effects of chest physical therapy on these parameters. The effect of both techniques on long-term trials using outcomes measure such as health-related quality of life, rates of exacerbations, hospitalization and mortality is not known at this time. This may provide more clinically meaningful data

on the effective of airway clearance technique in the future. Our study could be conclusive that the effective of ACTs in COPD patients may probably results from PLB&FETs and ACBT. Both techniques may be useful and should be the treatment choice of physiotherapists for patients with COPD in a stable phase of their disease. However, ACTs have scantly been studied in patients with COPD. At present there are no data to support PLB&FETs as the ACTs of choice. Therefore, the effectiveness of PLB combined FETs for airway clearance needs further research.

CHAPTER VI
CONCLUSION

The purposes of this study were to compare the efficacy of pursed lips breathing with forced expiration techniques (PLB&FETs) and active cycle of breathing technique (ACBT) with respect to acute change on pulmonary mucus clearances in healthy subjects in the first study and to compare the effectiveness of both techniques in patients with chronic obstructive pulmonary disease in the second study.

In the first study, the results was directly demonstrated the efficacy of PLB&FETs and ACBT in terms of radioactivity clearance from the central, intermediate, peripheral and whole right lung zones. Clearance of the central lung zone for individual data were different pattern for all interventions. The clearance of PLB&FETs were greater than in the control study which no intervention was applied. Therefore, PLB&FETs had lightly high enhanced clearance.

For intermediate lung zone of individual data, the clearance of PLB&FETs and ACBT were clearly greater than control study. Both techniques were remarkable the near effects of declination of radioactivity deposition from intermediate lung zone.

The peripheral lung zone were obviously revealed high clearance of radioactivity by PLB&FETs and ACBT during and after intervention period from 30^{th} to 70^{th} minute. Both techniques were approximately 7% - 9% difference clearance from the control study after intervention period. Also, the result of the whole right lung clearance were remarkable reduced radioactivity retention by PLB&FETs and ACBT. Interestingly, both techniques were nearly cleared radioactivity during and after intervention period.

Overall, the efficacy of both airway clearance techniques were assessed in the ideal situation of pulmonary mucus clearance. This results confirmed that PLB&FETs and ACBT could be achieved of lung clearance in healthy subject, especially in the intermediate and peripheral lung zone. However, PLB&FETs showed the trend toward great clearance in the whole right lung zone in healthy subjects. In addition, PLB&FETs and ACBT were slightly increased oxygen pulse saturation and decreased heart rate. Also, there was no critical improvement or deterioration in PEFR when repeated immediately after each intervention period. This could be suggested that PLB&FETs and ACBT were not reflect any breathlessness in healthy subjects of this study.

The second study were to compare the effectiveness of PLB&FETs and ACBT in patients with COPD reporting in the parameters of pulmonary function, PEFR by peak flow meter, sputum volume, Modified Borg scores of dyspnea, total scores of Modified patient evaluation questionnaire and Modified patient satisfaction questionnaire. The study duration lasted up to 2 weeks by a follow-up on the 7^{th} and 14^{th} day after the 1^{st} day assessment (baseline).

In the result of the second study, the values of FVC, FEV_1, ratio of FEV_1/FVC, $FEF_{25-75\%}$ and PEF were not statistically significant difference between PLB&FETs and ACBT groups on the 1^{st}, 7^{th}, 14^{th} day of the study. There was only a significant difference in PEF within ACBT group between 1^{st} and 14^{th} day of the study.

As well as PEFR, daily sputum volume and Modified Borg scores of dyspnea by self evaluation of patient on everyday in daily logbook record, there were no difference between two groups at any time of measurement. However, the significant increases of total mean values of PEFR and the significant decreases sputum volume in patients who received PLB&FETs in the second week when compared to the first week.

Total scores of Modified patient evaluation questionnaire in patients who receive PLB&FETs showed no significantly different from those who obtain ACBT at the 1st, 7th, 14th day of the study. Anyway, total scores of PLB&FETs group was significant difference between the 1st and 14th day of the study. Also, ACBT group were statistically significant difference of total scores between the 1st and 7th day and between 7th and 14th day of the study

Total scores of Modified patient satisfaction questionnaire for effectiveness in patients who receive PLB&FETs showed no significant different from those who obtain ACBT at the end of the study. This finding supported both techniques to be equally efficacy. Both techniques were ease to perform, comfort, effective clearance. and no adverse effects. PLB&FETs and ACBT were represented the efficiency in the care of COPD patient.

Our finding supported the use of PLB&FETs and ACBT in terms of airway clearance techniques in clinical assessment and research. Both techniques may be useful and should be the treatment choice of physiotherapists for patients with COPD in a stable phase of their disease.

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APPENDIX

CONSENT FORM OF THE FIRST STUDY

หนังสือแสดงเจตนายินยอมเข้าร่วมโครงการวิจัย

สำหรับการศึกษาที่ 1

วันที่.....เดือน.....พ.ศ .....

ข้าพเจ้า..... อายุ ..... ปี อาศัยอยู่บ้านเลขที่ .....

ถนน.....ตำบล.....อำเภอ.....

จังหวัด.....รหัสไปรษณีย์.....โทรศัพท์.....

ขอแสดงเจตนายินยอมเข้าร่วมโครงการวิจัยเรื่อง ผลของเทคนิคการหายใจแบบห่อริมฝีปากร่วมกับการหายใจออกอย่างแรงและเทคนิคการหายใจแบบวงจรด้วยตนเองต่อการขจัดเสมหะของทางเดินหายใจในผู้ป่วยโรคปอดอุดกั้นเรื้อรังและในผู้ป่วยโรคหลอดลมโป่งพอง ในการศึกษาที่ 1 คือ การศึกษาผลของเทคนิคการหายใจแบบห่อริมฝีปากร่วมกับการหายใจออกอย่างแรง และเทคนิคการหายใจแบบวงจรด้วยตนเองต่อการขจัดเสมหะของทางเดินหายใจในคนปกติด้วยเทคนิคการตรวจวัดละอองสารเภสัชรังสีร่วมกับการถ่ายภาพปอด

ชื่อผู้วิจัย นางสาวเสาวณีย์ วรวุฒางกูร

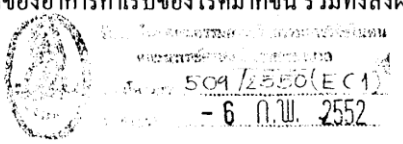
สถานที่ทำวิจัย 1) หน่วยตรวจคลินิกโรคปอดอุดกั้นเรื้อรัง สาขาวิชาโรคระบบการหายใจและวัณโรค ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล ตึกอัษฎางค์ ชั้น 2 โรงพยาบาลศิริราช เขตบางกอกน้อย กรุงเทพฯ

2) หน่วยตรวจคลินิกผู้ป่วยนอก กลุ่มงานคลินิกพิเศษและงานกายภาพบำบัดเพื่อการฟื้นฟู สมรรถภาพปอด ณ สถาบันโรคทรวงอก อ.เมือง จ.นนทบุรี

3) หน่วยเวชศาสตร์นิวเคลียร์ ภาควิชารังสีวิทยา คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี โทรศัพท์ 0-2201-1157 ต่อ 104, 105 (หน่วยตรวจ), 0-2246-1037-87 ต่อ 1149 (ภาควิชา)

โดยข้าพเจ้าได้รับทราบเกี่ยวกับรายละเอียดของการศึกษาที่ 1 ดังต่อไปนี้

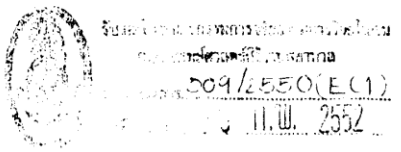
เทคนิคการขจัดเสมหะในทางเดินหายใจด้วยวิธีการทางกายภาพบำบัด มีบทบาทสำคัญในการช่วยลดปัญหาในผู้ป่วยโรคปอดอุดกั้นเรื้อรังและผู้ป่วยโรคหลอดลมโป่งพองที่มีอาการไอเรื้อรังมีเสมหะคั่งค้าง ซึ่งอาการดังกล่าวถือเป็นปัญหาสำคัญที่พบได้ในทางคลินิกและมักจะเป็นสาเหตุนำไปสู่อัตราการเสื่อมถอยของโรคที่เพิ่มขึ้น การเกิดภาวะแทรก ซ้อน ความถี่ของอาการกำเริบของโรคมากขึ้น รวมทั้งส่งผลต่อคุณภาพชีวิตของผู้ป่วยแย่ลง



ฉบับแก้ไขล่าสุด 7 มกราคม 2552

ดังนั้น การช่วยเพิ่มการเคลื่อนเสมหะในทางเดินหายใจ ลดการคั่งค้างของเสมหะ ลดการอุดกั้นของท่อทางเดินหายใจ รวมทั้งเพิ่มการระบายอากาศและการแลกเปลี่ยนก๊าซภายในปอด จึงถือเป็นแนวทางการรักษาที่สำคัญอย่างหนึ่ง อย่างไรก็ตาม เทคนิคการขจัดเสมหะที่ดี ควรจะเป็นเทคนิคที่ง่ายในการนำไปปฏิบัติด้วยตนเอง สะดวกและไม่ยุ่งยากสำหรับผู้ป่วย อีกทั้งไม่ต้องสูญเสียค่าใช้จ่ายในการรักษา ดังนั้นการศึกษาครั้งนี้ จึงทำการศึกษาผลของเทคนิคการหายใจแบบห่อริมฝีปากร่วมกับการหายใจออกอย่างแรง และเทคนิคการหายใจแบบวงจรด้วยตนเองต่อการขจัดเสมหะของทางเดินหายใจในกลุ่มคนปกติด้วยเทคนิคการตรวจวัดละอองสารเภสัชรังสีร่วมกับการถ่ายภาพปอดเพื่อเปรียบเทียบประสิทธิภาพของเทคนิคทั้งสองรูปแบบต่อการเคลื่อนของเสมหะในทาง เดินหายใจโดยตรง

ข้าพเจ้าได้รับเชิญให้เข้าร่วมการวิจัยนี้ เพราะเป็นกลุ่มคนปกติที่มีคุณสมบัติเหมาะสมผ่านเกณฑ์คัดเข้าและคัดออกของการศึกษานี้ที่จะทำการศึกษาวิจัย ซึ่งการศึกษานี้จะมีผู้เข้าร่วมวิจัยทั้งสิ้น 5 คน และใช้เวลาเข้าร่วมการศึกษารวม 4 วันต่อหนึ่งคน โดยมีขั้นตอนการวิจัยดังนี้



1. ขั้นเตรียมการ

ผู้วิจัยทำการอธิบายวัตถุประสงค์, ขั้นตอนการวิจัยและประโยชน์ของการวิจัยให้ข้าพเจ้าทราบ จากนั้นข้าพเจ้าลงนามในหนังสือแสดงเจตนายินยอมเข้าร่วมโครงการวิจัย

2. ขั้นตอนการเก็บข้อมูล

1) ผู้วิจัย จะทำการศึกษาประวัติจากเวชระเบียน, ซักประวัติ ตรวจวัดสมรรถภาพปอดและตรวจวัดด้วยภาพถ่ายรังสีทรวงอก (chest x-ray) ของข้าพเจ้า
2) ข้าพเจ้าจะได้รับการแนะนำ อธิบายรายละเอียดและฝึกปฏิบัติเทคนิคการขจัดเสมหะสองเทคนิค คือ 1) เทคนิคการหายใจแบบห่อริมฝีปากร่วมกับการหายใจออกอย่างแรง , 2) เทคนิคการหายใจแบบวงจรด้วยตนเอง จนเข้าใจและสามารถปฏิบัติเทคนิคได้ถูกต้อง
3) ข้าพเจ้าจะต้องเข้าร่วมเก็บข้อมูลวิจัย จำนวน 3 ครั้งการศึกษารวม 3 วัน เพื่อศึกษาผลของเทคนิคการขจัดเสมหะต่อการเคลื่อนระบายเสมหะในทางเดินหายใจด้วยเทคนิคการตรวจวัดละอองสารเภสัชรังสีร่วมกับการถ่ายภาพปอด ณ หน่วยเวชศาสตร์นิวเคลียร์ ภาควิชารังสีวิทยา คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี เขตราชเทวี กรุงเทพฯ
4) ลำดับการศึกษา คือ วันที่ 1 ปฏิบัติการหายใจแบบปกติ (กลุ่มควบคุม), วันที่ 2 และ 3 จะสุ่มลำดับการปฏิบัติเทคนิคการขจัดเสมหะ คือ เทคนิคการหายใจแบบห่อริมฝีปากร่วมกับการหายใจออกอย่างแรง และ เทคนิคการหายใจแบบวงจรด้วยตนเอง โดยระยะเวลาการเก็บข้อมูลวิจัยในหนึ่งครั้ง นาน 70 นาที แบ่งเป็น 3 ช่วง คือ ช่วง 10 นาทีแรก (พัก), ช่วงปฏิบัติเทคนิคการขจัดเสมหะ คือนาทีที่ 10-40 (นาน 30 นาที), ช่วง 30 นาทีหลัง (พัก)

5) ข้าพเจ้าได้ทราบถึงวิธีการของเทคนิคการตรวจวัดละอองสารเภสัชรังสีร่วมกับการถ่ายภาพปอด ซึ่งจะอยู่ภายใต้การควบคุมดูแลและดำเนินการโดยแพทย์เฉพาะทางด้านรังสีนิวเคลียร์ เจ้าหน้าที่เฉพาะทาง นักรังสีวิทยาจากหน่วยเวชศาสตร์นิวเคลียร์ ภาควิชารังสีวิทยา คณะแพทยศาสตร์โรงพยาบาลรามาธิบดีและมีหลักเกณฑ์มาตรฐานด้านเวชศาสตร์นิวเคลียร์สากลในการควบคุม ดังนี้

5.1 ข้าพเจ้าจะได้รับการพ่นละอองสารเภสัชรังสี คือ ^{99m}Technetium-human serum albumin aerosol จำนวน 25-35 mCi (900-1,300 MBq) จากอุปกรณ์ระบบพ่นละอองสารเภสัชรังสีมาตรฐานสากลที่ใช้ร่วมกับอัตราการไหลของออกซิเจน 10 ลิตรต่อนาที ซึ่งจะหายใจปกติ 4 ครั้งสลับกับหายใจเข้าลึกและค้างไว้ 5 วินาที อีก 1 ครั้งการหายใจ ทำสลับกันจนกว่าละอองสารที่พ่นจะหมด โดยใช้เวลาประมาณ 5- 8 นาที หลังจากนั้นข้าพเจ้าจะได้รับน้ำดื่มกลั้วคอและบ้วนปาก รวมทั้งดื่มน้ำเพื่อล้างสารที่ตกค้างในลำคอและช่องปากออก ทั้งนี้ ข้าพเจ้าจะได้รับปริมาณละอองสารเภสัชรังสีอยู่ในบริเวณปอดเฉลี่ย 0.5-1.0 mCi (20-40 MBq)

5.2 หลังการพ่นละอองสาร ข้าพเจ้าจะนั่งตรงอยู่ในตำแหน่งที่วางกล้องแกรมม่าเพื่อถ่ายภาพปอดด้านหลังและได้รับการถ่ายภาพปอดเมื่อเริ่มต้น, ข้าพเจ้าจะต้องหายใจในลักษณะปกติในช่วงพัก 10 นาทีแรก, ปฏิบัติเทคนิคขจัดเสมหะในนาทีที่ 10-40 และหายใจในลักษณะปกติในนาทีที่ 50-70 ทั้งนี้ จะได้รับการบันทึกภาพปอดจำนวนอีก 7 ภาพในทุก 10 นาที ตั้งแต่นาทีที่ 10 จนถึงนาทีที่ 70 ของการศึกษา

6) ข้าพเจ้าจะได้รับการประเมินระดับความรู้สึกเหนื่อยหอบด้วยการบอกระดับคะแนน 0-10, วัดค่าความเร็วลมหายใจออกด้วยการเป่าเครื่องวัดทั้งก่อนและหลังการศึกษา ได้รับการวัดอัตราการเต้นของหัวใจและค่าออกซิเจนในเลือดแดงตลอดเวลาการศึกษาด้วยเครื่อง ช่วงการศึกษา 70 นาที

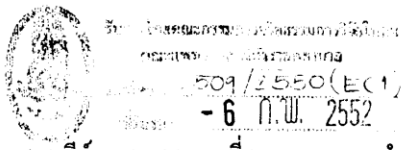
ทั้งนี้ ข้าพเจ้าได้รับทราบข้อมูลทางวิชาการเกี่ยวกับความเสี่ยงต่ออันตรายหรือความไม่สุขสบายที่อาจจะได้รับจากการเข้าร่วมการวิจัย คือ ในการปฏิบัติเทคนิคการขจัดเสมหะทั้งสองเทคนิค จะไม่มีความเสี่ยงใดในคนปกติ ผู้ป่วยโรคปอดอุดกั้นเรื้อรังและในผู้ป่วยโรคหลอดลมโป่งพอง แต่ข้าพเจ้าจะได้รับการฝึกสอนและปฏิบัติเทคนิคอย่างถูกต้องมีประสิทธิภาพ อาจต้องใช้ระยะ เวลาในการฝึกปฏิบัติพอสมควร ซึ่งผู้วิจัยคาดว่าอาจส่งผลให้ข้าพเจ้าเกิดความอ่อนล้าหรือความเครียดจากการฝึกปฏิบัติเทคนิค ส่วนในด้านเทคนิคการตรวจวัดละอองสารเภสัชรังสีร่วมกับภาพถ่ายปอดนั้น มีการศึกษาวิจัยด้วยเทคนิคดังกล่าวมากกว่า 30 การศึกษา ซึ่งไม่พบความเสี่ยงใดที่เกิดขึ้นกับผู้เข้าร่วมการวิจัย นอกจากนี้ รายงานสถิติเกี่ยวกับการเกิดอาการไม่พึงประสงค์จากการใช้สารรังสีเภสัชเพื่อตรวจวินิจฉัยและรักษา พบว่าในประเทศสหรัฐอเมริกา จะมีอาการไม่พึงประสงค์เกิด ขึ้นร้อยละ 0.0023 ของจำนวน 783,525 ครั้งการตรวจด้วยสารเภสัชรังสี โดยอัตราการเกิดผลไม่พึงประสงค์จะน้อยกว่าการรายงานผลของการถ่ายภาพรังสีเอ็กซเรย์ถึง 1,000 เท่า ส่วนที่ประเทศอังกฤษ มีรายงานอาการไม่พึงประสงค์ ร้อยละ 0.011 ของจำนวนการตรวจด้วยสารเภสัชรังสี 71,046 ครั้ง ซึ่งทั้งสองรายงาน พบว่า อาการไม่พึงประสงค์เป็นอาการที่ไม่รุนแรง ไม่ต้อง

เข้ารับการรักษาในโรงพยาบาลและกว่าครึ่งหนึ่งของอาการที่เกิดขึ้นนั้นเป็นผื่นบริเวณผิวหนัง ในปัจจุบันการใช้สารเภสัชรังสี ชนิด ^{99m} Technetium--human serum albumin ด้วยการพ่นเป็นละอองสารยังไม่มีรายงานพบอาการไม่พึงประสงค์เกิดขึ้นแต่อย่างใด นอกจากนี้ การศึกษานี้ได้กำหนดการใช้ชนิดและปริมาณสารเภสัชรังสีรวมทั้งเครื่องมืออุปกรณ์ที่มีประสิทธิภาพและคุณภาพมาตรฐานสากล อีกทั้งการดำเนินการตรวจวัดอยู่ภายใต้การปฏิบัติของแพทย์ผู้เชี่ยวชาญเฉพาะทาง ซึ่งมีประสบการณ์ทำงานโดยตรง ผู้วิจัยจึงเชื่อมั่นว่าจะมีความเสี่ยงน้อยที่สุดที่อาจจะเกิดเหตุ การณ์ไม่พึงประสงค์ต่อประชากรที่เข้าร่วมการศึกษา

ข้าพเจ้าได้รับทราบถึงประโยชน์โดยตรงที่ข้าพเจ้าจะได้รับ คือ จะได้ทราบถึงประสิทธิภาพของการเคลื่อนระบายเสมหะในทางเดินหายใจของตนเองในสภาพการทำงานทั่วไป, ทราบถึงประสิทธิภาพในการเคลื่อนระบายเสมหะในทางเดินหายใจด้วยเทคนิคการขจัดเสมหะทั้งสองเทคนิค อันจะเป็นข้อมูลพื้นฐานในการนำไปพิจารณาเลือกใช้เทคนิคขจัดเสมหะด้วยตนเองในชีวิตประจำวันได้อย่างมีประสิทธิภาพ อีกทั้งข้าพเจ้าจะสามารถปฏิบัติเทคนิคการขจัดเสมหะทั้งสองเทคนิคได้อย่างถูกต้องและมีประสิทธิภาพ ทั้งนี้ ประโยชน์โดยรวมของการศึกษานี้จะได้ทราบถึงประสิทธิภาพของเทคนิคการหายใจแบบห่อริมฝีปากร่วมกับการหายใจออกอย่างแรงและเทคนิคการหายใจแบบวงจรด้วยตนเองต่อการเคลื่อนระบายเสมหะในทางเดินหายใจ ผลการศึกษาที่ได้จะเป็นข้อมูลทางวิชาการที่สามารถเผยแพร่ แนะนำและเป็นแนวทางในการเลือกใช้เทคนิคการขจัดเสมหะด้วยตนเองสำหรับผู้ป่วยได้อย่างมีประสิทธิภาพ อีกทั้งเป็นข้อมูลสนับสนุนการนำเทคนิคการขจัดเสมหะด้วยตนเองไปใช้ในทางคลินิก ซึ่งย่อมส่งผลต่อด้านงบประมาณค่าใช้จ่ายเพื่อการดูแลรักษาของผู้ป่วยและรัฐบาลน้อยลง ลดภาวะแทรกซ้อน อาการกำเริบของโรค หรือความถี่ของการเข้ารับการรักษาตัวในโรงพยาบาล ทำให้เกิดผลดีในระยะยาวต่อผู้ป่วย และประโยชน์โดยรวมของประเทศไทยได้

ข้าพเจ้าได้รับทราบถึงสิทธิ์ที่จะได้รับข้อมูลเพิ่มเติมทั้งทางด้านประโยชน์และโทษที่เกี่ยวข้องกับการวิจัยอย่างรวดเร็วโดยไม่ปิดบัง และสามารถถอนตัวหรืองดเข้าร่วมการวิจัยได้ทุกเมื่อ โดยจะไม่มีผลกระทบต่อการบริการและการรักษาพยาบาลที่ข้าพเจ้าสมควรจะได้รับต่อไปในอนาคต อีกทั้งข้อมูลส่วนตัวของข้าพเจ้าจะถูกเก็บรักษาไว้ ไม่เปิดเผยต่อสาธารณะเป็นรายบุคคล แต่จะรายงานผลการวิจัยเป็นข้อมูลโดยรวม ทั้งนี้ข้อมูลเป็นรายบุคคลอาจมีคณะบุคคลบางกลุ่มเข้ามาตรวจสอบได้ เช่น สถาบันหรือองค์กรของรัฐที่มีหน้าที่ตรวจสอบ, คณะกรรมการจริยธรรมฯ เป็นต้น

หากเกิดผลข้างเคียงที่ไม่พึงประสงค์จากการวิจัย ข้าพเจ้าจะได้รับการช่วยเหลือจากผู้วิจัยและส่งปรึกษาแพทย์ผู้เชี่ยวชาญต่อไป โดยจะได้รับการรักษาพยาบาลอย่างถูกต้อง เหมาะสม ทั้งนี้ผู้วิจัยจะเป็นผู้รับผิดชอบค่าใช้จ่ายนั้น ข้าพเจ้าจะได้รับค่าชดเชยสำหรับการเดินทางในการเข้าร่วมการศึกษา ครั้งละ 200 บาท, จำนวน 4 ครั้ง รวม 800 บาทตลอดการศึกษา และหากข้าพเจ้ามีข้อข้องใจเกี่ยวกับขั้นตอนของการวิจัย หรือเกิดผลข้างเคียงที่ไม่พึง



5

ประสงค์จากการวิจัย ข้าพเจ้าจะสามารถติดต่อกับนางสาวเสาวณีย์ วรวุฒางกูร ที่คณะกายภาพบำบัดและวิทยาศาสตร์การเคลื่อนไหวประยุกต์ ตึกคณะกายภาพบำบัดและวิทยาศาสตร์การเคลื่อนไหวประยุกต์ วิทยาเขตศาลายา มหาวิทยาลัยมหิดล เลขที่ 999 ถนนพุทธมณฑล สาย 4 ตำบลศาลายา อำเภอพุทธมณฑล จังหวัดนครปฐม 73170 โทรศัพท์ 0-2441-5450 , โทรสาร 0-2441-5454 หรือ 081-770-1284 (มือถือ)

หากข้าพเจ้าได้รับการปฏิบัติที่ไม่ตรงตามที่ได้ระบุไว้ในเอกสารชี้แจงนี้ ข้าพเจ้าจะสามารถแจ้งให้ประธานคณะกรรมการจริยธรรมการวิจัยในคนทราบได้ที่ สำนักงานคณะกรรมการจริยธรรมการวิจัยในคน ตึกอดุลยเดชวิกรม ชั้น 6 ร.พ.ศิริราช เบอร์โทรศัพท์ 0-2419-6405-6

ข้าพเจ้าได้รับทราบข้อมูลของโครงการข้างต้น ตลอดจนข้อดี ข้อเสีย ที่จะได้รับจากการเข้าร่วมโครงการในครั้งนี้และข้าพเจ้ายินยอมที่จะเข้าร่วมในโครงการดังกล่าว โดยขอให้ผู้วิจัยงดการเปิดเผยชื่อ ประวัติ ตลอดจนข้อมูลที่เกี่ยวข้องกับข้าพเจ้า แก่ผู้อื่นได้รับทราบแต่จะนำเสนอข้อมูลจากการวิจัยเป็นข้อมูลโดยรวม

ลงชื่อ..... ผู้ให้ความยินยอม/ผู้แทน

(.....) โดยชอบธรรม(ระบุความเกี่ยวข้อง)

วันที่.....

ลงชื่อ..... ผู้ให้ข้อมูลและขอความยินยอม/หัวหน้าโครงการวิจัย

(.....)

วันที่.....

ในกรณีที่ผู้เข้าร่วมการวิจัยอ่านหนังสือไม่ออก ผู้ที่อ่านข้อความทั้งหมดแทนผู้เข้าร่วมการวิจัย คือ ..... จึงได้ลงลายมือชื่อไว้เป็นพยาน

ลงชื่อ.....พยาน/วันที่.....

(.....)

CONSENT FORM OF THE SECOND STUDY

หนังสือแสดงเจตนายินยอมเข้าร่วมโครงการวิจัย

สำหรับการศึกษาที่ 2

วันที่.....เดือน.....พ.ศ .....

ข้าพเจ้า ..... อายุ ..... ปี อาศัยอยู่บ้านเลขที่ .....

ถนน.....ตำบล.....อำเภอ.....

จังหวัด.....รหัสไปรษณีย์.....โทรศัพท์.....

ขอแสดงเจตนายินยอมเข้าร่วมโครงการวิจัยเรื่อง ผลของเทคนิคการหายใจแบบห่อริมฝีปากร่วมกับการหายใจออกอย่างแรงและเทคนิคการหายใจแบบวงจรด้วยตนเองต่อการขจัดเสมหะของทางเดินหายใจในผู้ป่วยโรคปอดอุดกั้นเรื้อรังและผู้ป่วยโรคหลอดลมโป่งพอง ในการศึกษาที่ 2 คือ การศึกษาเปรียบเทียบประสิทธิผลระยะสั้นของเทคนิคการหายใจแบบห่อริมฝีปากร่วมกับการหายใจออกอย่างแรงและเทคนิคการหายใจแบบวงจรด้วยตนเองต่อการขจัดเสมหะของทางเดินหายใจในผู้ป่วยโรคปอดอุดกั้นเรื้อรังและผู้ป่วยโรคหลอดลมโป่งพองทางคลินิก

ชื่อผู้วิจัย นางสาวเสาวณีย์ วรวุฒางกูร

สถานที่ทำวิจัย 1) หน่วยตรวจคลินิกโรคปอดอุดกั้นเรื้อรัง สาขาวิชาโรคระบบการหายใจและวัณโรค ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล ตึกอัษฎางค์ ชั้น 2 โรงพยาบาลศิริราช เขตบางกอกน้อย กรุงเทพฯ

2) หน่วยตรวจคลินิกผู้ป่วยนอก กลุ่มงานคลินิกพิเศษและงานกายภาพบำบัดเพื่อการฟื้นฟูสมรรถภาพปอด ณ สถาบันโรคทรวงอก อ.เมือง จ.นนทบุรี

โดยข้าพเจ้าได้รับทราบเกี่ยวกับรายละเอียดของการศึกษาที่ 2 ดังต่อไปนี้

ในผู้ป่วยโรคปอดอุดกั้นเรื้อรังและผู้ป่วยโรคหลอดลมโป่งพอง อาการไอเรื้อรังมีเสมหะถือเป็นปัญหาสำคัญที่พบได้ในทางคลินิกและมักจะเป็นสาเหตุนำไปสู่อัตราการเสื่อมถอยของโรคที่เพิ่มขึ้น การเกิดภาวะแทรกซ้อน ความถี่ของอาการกำเริบของโรคมากขึ้น รวมทั้งส่งผลต่อคุณภาพชีวิตของผู้ป่วยแย่ลง ดังนั้น เทคนิคการขจัดเสมหะในทางเดินหายใจ จึงมีบทบาทสำคัญในการลดปัญหาดังกล่าวในผู้ป่วย เพื่อช่วยเพิ่มการเคลื่อนเสมหะในทางเดินหายใจ ลดการคั่งค้างของเสมหะ ลดการอุดกั้นของท่อทางเดินหายใจ รวมทั้งเพิ่มการระบายอากาศและการแลกเปลี่ยนก๊าซภายในปอด อย่างไรก็ตาม เทคนิคการขจัดเสมหะที่ดี ควรจะเป็นเทคนิคที่ง่ายในการนำไปปฏิบัติด้วยตนเอง สะดวกและไม่ยุ่งยากสำหรับผู้ป่วย อีกทั้งไม่ต้องสูญเสียค่าใช้จ่ายในการรักษา ดังนั้นการ ศึกษาครั้งนี้ จึงทำการศึกษาเปรียบเทียบประสิทธิผลระยะสั้นของเทคนิคการหายใจแบบห่อริมฝีปาก

ร่วมกับการหายใจออกอย่างแรง และเทคนิคการหายใจแบบวงจรด้วยตนเองต่อการขจัดเสมหะของทางเดินหายใจในผู้ป่วยโรคปอดอุดกั้นเรื้อรัง

ข้าพเจ้าได้รับเชิญให้เข้าร่วมการวิจัยนี้ เพราะเป็นผู้ที่ได้รับการวินิจฉัยจากแพทย์ทางอายุรศาสตร์ สาขาวิชาโรคระบบการหายใจและวัณโรคว่าเป็นผู้ป่วยโรคปอดอุดกั้นเรื้อรังหรือจากหน่วยตรวจคลินิกผู้ป่วยนอก กลุ่มงานคลินิกพิเศษและงานกายภาพบำบัดเพื่อการฟื้นฟูสมรรถภาพปอด ณ สถาบันโรคทรวงอก อ.เมือง จ.นนทบุรี ซึ่งมีคุณสมบัติเหมาะสมที่จะทำการศึกษาวิจัย ซึ่งการศึกษานี้จะมีผู้เข้าร่วมวิจัยทั้งสิ้น 40 คน และใช้เวลาเข้าร่วมการศึกษารวม 2 สัปดาห์ต่อหนึ่งคน โดยมีขั้นตอนการวิจัยดังนี้

1. ขั้นเตรียมการ

ผู้วิจัยทำการอธิบายวัตถุประสงค์, ขั้นตอนการวิจัยและประโยชน์ของการวิจัยให้ข้าพเจ้าทราบ จากนั้นข้าพเจ้าลงนามในหนังสือแสดงเจตนายินยอมเข้าร่วมโครงการวิจัย

2. ขั้นตอนการเก็บข้อมูล

1) ผู้วิจัยจะทำการศึกษาเวชระเบียน, ซักประวัติ และตรวจวัดสมรรถภาพปอดของข้าพเจ้า
2) ข้าพเจ้าจะได้รับการสุ่มอิสระเพื่อเลือกกลุ่มการศึกษา คือ กลุ่มที่ได้รับการรักษาด้วยเทคนิคการหายใจแบบห่อริมฝีปากร่วมกับการหายใจออกอย่างแรง และกลุ่มที่ได้รับการรักษาด้วยเทคนิคการหายใจแบบวงจรด้วยตนเอง หลังจากนั้น ข้าพเจ้าจะได้รับคำอธิบาย แนะนำเทคนิค และสอนปฏิบัติเทคนิคดังกล่าว จนเกิดความเข้าใจและสามารถปฏิบัติเทคนิคได้ถูกต้อง ซึ่งจะดำเนินการภายใน 2 วันแรกของการเข้าร่วมการศึกษา
3) ข้าพเจ้าจะต้องปฏิบัติเทคนิคขจัดเสมหะ ครั้งละ 30 นาที วันละ 2 ครั้ง ในเวลาเช้าและเย็น ทุกวันตลอด 2 สัปดาห์ เพื่อศึกษาประสิทธิผลระยะสั้นของเทคนิคการขจัดเสมหะ โดยมีรายละเอียดของการปฏิบัติเทคนิคดังนี้
   3.1 เทคนิคการหายใจแบบห่อริมฝีปากร่วมกับการหายใจออกอย่างแรง : ปฏิบัติการหายใจแบบห่อริมฝีปาก 5 ครั้งการหายใจ ร่วมกับการหายใจออกอย่างแรง 1 ครั้ง ต่อชุดการหายใจ ปฏิบัติเทคนิคนานประมาณ 4 นาที พัก 1 นาที ต่อรอบ ทำซ้ำ 6 รอบ ใช้เวลาประมาณ 30 นาทีต่อครั้งการปฏิบัติเทคนิค
   3.2 เทคนิคการหายใจแบบวงจรด้วยตนเอง : ประกอบด้วย 1) การหายใจแบบควบคุม , 2) การหายใจเน้นการขยายทรวงอก เป็นการหายใจเข้า ลึก ช้าๆ ค้างไว้ 3 วินาที และหายใจออกปกติ และ 3) การหายใจออกแรง เริ่มปฏิบัติรูปแบบการหายใจเป็นวงจรต่อเนื่อง คือ การหายใจแบบควบคุม 3- 4 ครั้งการหายใจ (หรือจนกว่ารู้สึกผ่อนคลาย) ตามด้วยการหายใจเน้นการขยายทรวงอก 4 ครั้งการหายใจ และการหายใจออกแรง 1 ครั้ง และเริ่มต้นทำซ้ำใหม่ ปฏิบัติเทคนิคนานประมาณ 4 นาที พัก 1 นาที ต่อรอบ ทำซ้ำ 6 รอบ ใช้เวลาประมาณ 30 นาทีต่อครั้งการปฏิบัติเทคนิค
4) ข้าพเจ้าจะได้รับการตรวจวัดค่าของสมรรถภาพปอด ในวันที่ 1, 7 และ 14 ของการศึกษา รวมจำนวน 3 ครั้ง

5) ข้าพเจ้าจะตอบแบบสอบถามเกี่ยวกับการประเมินอาการด้วยตนเองของผู้ป่วย ในวันที่ 1, 7 และ 14 ของการศึกษา รวมจำนวน 3 ครั้ง

6) ข้าพเจ้าจะต้องบันทึกค่าความเร็วลมหายใจออกด้วยการเป่าเครื่อง, ปริมาณเสมหะและคะแนนระดับความรู้สึกเหนื่อยหอบของแต่ละวันลงในแบบบันทึกประจำวันของการศึกษาครั้งนี้ในตลอดระยะเวลา 2 สัปดาห์ของการศึกษา ทั้งนี้ผู้วิจัยจะนำเครื่องมือและอุปกรณ์การวิจัยครั้งนี้มาสอนและแนะนำการใช้งาน และข้าพเจ้าจะคืนเครื่องมืออุปกรณ์ต่างๆ เมื่อเสร็จสิ้นการศึกษาครั้งนี้

7) ข้าพเจ้าจะตอบแบบสอบถามเกี่ยวกับความพอใจในเทคนิคการรักษาเมื่อสิ้นสุดการศึกษา

ทั้งนี้ ข้าพเจ้าได้รับทราบข้อมูลทางวิชาการเกี่ยวกับความเสี่ยงต่ออันตรายหรือความไม่สุขสบายที่อาจจะได้ รับจากการเข้าร่วมการวิจัย คือ ในการปฏิบัติเทคนิคการขจัดเสมหะทั้งสองเทคนิค จะไม่มีความเสี่ยงใดในผู้ป่วยโรคปอดอุดกั้นเรื้อรังและผู้ป่วยโรคหลอดลมโป่งพอง แต่ข้าพเจ้าจะได้รับการฝึกสอนและปฏิบัติเทคนิคอย่างถูกต้องมีประสิทธิภาพ อาจต้องใช้ระยะ เวลาในการฝึกปฏิบัติพอสมควร ซึ่งอาจส่งผลให้ข้าพเจ้าเกิดความอ่อนล้าหรือความเครียดจากการฝึกปฏิบัติเทคนิคได้ อีกทั้งการศึกษานี้ข้าพเจ้าจะต้องปฏิบัติเทคนิคการขจัดเสมหะด้วยตนเองที่บ้าน วัดและบันทึกค่าตัวแปรการศึกษาจำนวน 3 ตัวแปรในแต่ละวัน จึงอาจเป็นภาระที่จะต้องรับผิดชอบเพิ่มขึ้น อย่างไรก็ตาม ผู้วิจัยเชื่อมั่นว่า การศึกษาครั้งนี้ จะมีผลด้านความเสี่ยงต่ออันตรายหรืออาการไม่พึงประสงค์น้อยที่สุด

ข้าพเจ้าได้รับทราบถึงประโยชน์โดยตรงที่ข้าพเจ้าจะได้รับ คือข้าพเจ้าสามารถปฏิบัติเทคนิคการขจัดเสมหะหนึ่งเทคนิคในการศึกษาครั้งนี้ได้อย่างถูกต้องและมีประสิทธิภาพ และทราบถึงประสิทธิผลระยะสั้นของเทคนิคการขจัดเสมหะว่ามีประสิทธิภาพในการเคลื่อนระบายเสมหะในทางเดินหายใจของตนเองอย่างไร อีกทั้งการศึกษานี้ จะส่งผลทางอ้อมให้ข้าพเจ้าเกิดความตระหนักและใส่ใจต่อการดูแลรักษาตนเองมากยิ่งขึ้น ซึ่งจะเป็นผลดีในการดูแลรักษาโรคด้วยตนเองในระยะยาว และการขจัดเสมหะในทางเดินหายใจที่มีประสิทธิภาพย่อมส่งผลให้ข้าพเจ้าลดการเกิดภาวะแทรกซ้อน ความถี่ของอาการกำเริบของโรค อีกทั้งจะส่งผลดีต่อคุณภาพชีวิตของข้าพเจ้าอีกด้วย ทั้งนี้ประโยชน์โดยรวมของการศึกษานี้ จะได้ทราบถึงผลของเทคนิคการหายใจแบบห่อริมฝีปากร่วมกับการหายใจออกอย่างแรงและเทคนิคการหายใจแบบวงจรด้วยตนเองในผู้ป่วยโรคปอดอุดกั้นเรื้อรังและผู้ป่วยโรคหลอดลมโป่งพอง ผลการศึกษาที่ได้จะเป็นข้อมูลทางวิชาการที่สามารถเผยแพร่ แนะนำและเป็นแนวทางในการเลือกใช้เทคนิคการขจัดเสมหะด้วยตนเองสำหรับผู้ป่วยได้อย่างมีประสิทธิภาพ อีกทั้งเป็นข้อมูลสนับสนุนการนำเทคนิคการขจัดเสมหะด้วยตนเองไปใช้ในทางคลินิก ซึ่งย่อมส่งผลต่อด้านงบประมาณค่าใช้จ่ายเพื่อการดูแลรักษาของผู้ป่วยและรัฐบาลน้อยลง ลดภาวะ แทรกซ้อน อาการกำเริบของโรค หรือความถี่ของการเข้ารับการรักษาตัวในโรงพยาบาล ทำให้เกิดผลดีในระยะยาวต่อผู้ป่วย และประโยชน์โดยรวมของประเทศไทยได้

ข้าพเจ้าได้รับทราบถึงสิทธิ์ที่จะได้รับข้อมูลเพิ่มเติมทั้งทางด้านประโยชน์และโทษที่เกี่ยวข้องกับการวิจัยอย่างรวดเร็วโดยไม่ปิดบัง และสามารถถอนตัวหรืองดเข้าร่วมการวิจัยได้ทุกเมื่อ โดยจะไม่มีผลกระทบต่อการบริการและการรักษาพยาบาลที่ข้าพเจ้าสมควรจะได้รับต่อไปในอนาคต อีกทั้งข้อมูลส่วนตัวของข้าพเจ้าจะถูกเก็บรักษาไว้ ไม่เปิดเผยต่อสาธารณะเป็นรายบุคคล แต่จะรายงานผลการวิจัยเป็นข้อมูลโดยรวม ทั้งนี้ข้อมูล

เป็นรายบุคคลอาจมีคณะบุคคลบางกลุ่มเข้ามาตรวจสอบได้ เช่น สถาบันหรือองค์กรของรัฐที่มีหน้าที่ตรวจสอบ, คณะกรรมการจริยธรรมฯ เป็นต้น

หากเกิดผลข้างเคียงที่ไม่พึงประสงค์จากการวิจัย ข้าพเจ้าจะได้รับการช่วยเหลือจากผู้วิจัยและส่งปรึกษาแพทย์ผู้เชี่ยวชาญต่อไป โดยจะได้รับการรักษาพยาบาลอย่างถูกต้อง เหมาะสม ทั้งนี้ผู้วิจัยจะเป็นผู้รับผิดชอบค่าใช้จ่ายนั้น ข้าพเจ้าจะได้รับค่าชดเชยการเดินทางในการเข้าร่วมการศึกษาครั้งละ 200 บาท, 2 ครั้ง รวม 400 บาทตลอดการศึกษาและหากข้าพเจ้ามีข้อข้องใจเกี่ยวกับขั้นตอนของการวิจัย หรือเกิดผลข้างเคียงที่ไม่พึงประสงค์จากการวิจัย ข้าพเจ้าจะสามารถติดต่อกับนางสาวเสาวณีย์ วรวุฒางกูร ที่คณะกายภาพบำบัดและวิทยาศาสตร์การเคลื่อนไหวประยุกต์ ตึกคณะกายภาพบำบัดและวิทยาศาสตร์การเคลื่อนไหวประยุกต์ วิทยาเขตศาลายา มหาวิทยาลัยมหิดล เลขที่ 999 ถนนพุทธมณฑล สาย 4 ตำบลศาลายา อำเภอพุทธมณฑล จังหวัดนครปฐม 73170 โทรศัพท์ 0-2441-5450 , โทรสาร 0-2441-5454 หรือ 081-770-1284 (มือถือ)

หากข้าพเจ้าได้รับการปฏิบัติที่ไม่ตรงตามที่ได้ระบุไว้ในเอกสารชี้แจงนี้ ข้าพเจ้าจะสามารถแจ้งให้ประธานคณะกรรมการจริยธรรมการวิจัยในคนทราบ ได้ที่สำนักงานคณะกรรมการจริยธรรมการวิจัยในคน ตึกอดุลยเดชวิกรม ชั้น 6 ร.พ.ศิริราช เบอร์โทรศัพท์ 0-2419-6405-6

รับรองโดยคณะกรรมการจริยธรรมการวิจัยในคน
คณะแพทยศาสตร์ศิริราชพยาบาล
รหัสโครงการ 509/2550(EC1)
วันที่รับรอง - 5 ก.ค. 2551

ข้าพเจ้าได้รับทราบข้อมูลของโครงการข้างต้น ตลอดจนข้อดี ข้อเสีย ที่จะได้รับจากการเข้าร่วมโครงการในครั้งนี้และข้าพเจ้ายินยอมที่จะเข้าร่วมในโครงการดังกล่าว โดยขอให้ผู้วิจัยงดการเปิดเผยชื่อ ประวัติตลอดจนข้อมูลที่เกี่ยวข้องกับข้าพเจ้า แก่ผู้อื่นได้รับทราบแต่จะนำเสนอข้อมูลจากการวิจัยเป็นข้อมูลโดยรวม

ลงชื่อ..... ผู้ให้ความยินยอม/ผู้แทน

(.....) โดยชอบธรรม(ระบุความเกี่ยวข้อง)

วันที่.....

ลงชื่อ..... ผู้ให้ข้อมูลและขอความยินยอม/

(.....) หัวหน้าโครงการวิจัย

วันที่.....

ในกรณีที่ผู้เข้าร่วมการวิจัยอ่านหนังสือไม่ออก ผู้ที่อ่านข้อความทั้งหมดแทนผู้เข้าร่วมการวิจัยคือ ..... จึงได้ลงลายมือชื่อไว้เป็นพยาน

ลงชื่อ.....พยาน/วันที่.....

(.....)

DATA COLLECTION FORM

แบบบันทึกข้อมูลของผู้เข้าร่วมการวิจัย

Code Number..... (กรอกโดยผู้วิจัย)

Date .....

Part I: Personal History

Gender ☐F ☐M **Age**.....yrs

Weight.....kg **Height**.....cm **Race** .....

Diagnosis : .....

Chief Complaint : .....

.....

History of present illness : .....

.....

.....

.....

.....

Clinical signs and symptoms of COPD (1)

..... Chronic coughs / Coughs for at least 3 months in year at least 2 consecutive years *

..... Persistent cough with production of sputum *

..... General decreased breath sound

..... Crepitation/ Rhonchi / Wheezing

..... Cyanosis (blue discoloration of skin and mucous membranes)

..... Decreased exercise tolerance

Medical treatment & medications :

β2 –agonist (short-acting) ☐ Fenoterol (4-6 h) ☐ Salbutamol /albuterol (4-6 h)
☐ Terbutaline (4-6 h)

(long-acting) ☐ Formoterol (12+h) ☐ Salmeterol (12+h)

Anticholinergics (short-acting) ☐ Ipratropium bromide (6-8 h)

(long-acting) ☐ Tiotropium (24+ h)

Combination short-acting β2 –agonist plus anticholinergics in one inhaler

☐ Fenoterol/Ipratropium (6-8 h) ☐ Salbutamol/Ipratropium (6-8 h)

Methylxanthines ☐ Aminophylline (24+ h) ☐ Theophyline (24+ h)

Inhaled glucocorticosteriods

☐ Beclomethasone ☐ Budesonide ☐ Fluticasone ☐ Triamcinolone

Combination long-acting β2 –agonist plus glucocorticosteriods in one inhaler

☐ Formoterol/Budesonide ☐ Salmeterol/Fluticasone

Systemic glucocorticosteriods ☐ Prednisone ☐ Methyl-prednisolone

☐ Influenza vaccines

☐ Mucolytic (ambroxol, erdosteine, carbocysteine, iodinated glycerol)

Other medications : .....

.....

.....

Past medical history :

Disease / conditions	Y	N	Note	Disease / conditions	Y	N	Note
Cancer				Allergies			
Diabetes				Asthma			
Hypertension or high BP				Ulcers/ stomach problems			
Heart disease				Depression			
Angina or chest pain				Anxiety			
Tuberculosis				Other (please describe)			
Arthritis/ gout				.....			
Kidney disease				.....			

General Health :

1. Are you taking any prescription or over-the-counter medications? Y / N
   If yes, please list : .....(Antitussives , Narcotics)
2. Have you had any illnesses within the last 4 weeks (e.g., colds, influenza, infection) Y / N
3. Have you had any unexplained weight gain or loss in the last month? Y / N
4. Do you smoke or chew tobacco ? How many packs a day..... Y / N
5. Do you drink alcohol ? How much do you drink in the course of a week? Y / N
6. Are you on any special research study in recent? Y / N
   If yes, please list : .....
7. Do you have a pacemaker, transplanted organ, metal implants? Y / N
8. Have you had any surgical in the past ? Y / N
   If yes, please list : .....

รับรองโดย คณะกรรมการจริยธรรมการวิจัยในคน
คณะแพทยศาสตร์ศิริราชพยาบาล
รหัสโครงการ Si 1/2551 (EC1)
วันที่รับรอง 11 ก.พ. 2551

Part II: Physical examination

Vital signs: **BP**.....mmHg **HR**.....bpm (❑ **regular** ❑ **irregular**)

RR.....breaths/min

Shape of chest ❑ Normal ❑ Barrel chest ❑ increased AP diameter ❑ Funnel chest

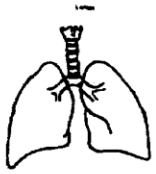
❑ Thoracic Kyphoscoliosis ❑ Others .....

Auscultation : .....

.....

.....

O_2 saturation (SpO_2) .....%



Front

Chest X-ray Date .....

Spirometry :

Variable	Actual value	% Predict
FVC		
FEV_1		
FEV_1/FVC		
FEF_{25-75}		
PEF		

Classification of severity of COPD by GOLD in the 2006 report :

Stage	Severity	Characteristic
I	Mild	* FEV_1/FVC < 70% , $FEV_1 \geq$ 80% predicted * With or without chronic symptom
II	Moderate	* FEV_1/FVC < 70% , 50% $\leq FEV_1$ < 80% predicted * With or without chronic symptom
III	Severe	* FEV_1/FVC < 70% , 30% $\leq FEV_1$ < 50% predicted * With or without chronic symptom
IV	Very severe	* FEV_1/FVC < 70% , FEV_1 < 30% predicted or presence of respiratory failure or right heart failure

Patient Stage : .....

แบบบันทึกข้อมูลสำหรับการศึกษาที่ 1

(กรอกโดยคณะผู้วิจัย)

Code Number: ..... **Test date :** .....

Gender □ F □ M **Age**.....yrs **Weight**.....kg

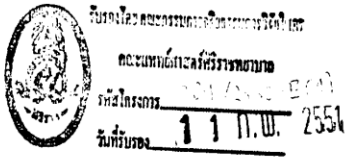
Height.....cm**Intervention** .....

Variables		rest		intervention			rest			Note
		0	10th	20th	30th	40th	50th	60th	70th	
		R1	R2	R3	R4	R5	R6	R7	R8	
1. No. of count (Rt.Lung)	Central									
	Intermediate									
	Peripheral									
	Total .									
2. % of Retention (Rt.Lung)	Central									
	Intermediate									
	Peripheral									
	Total .									
3. Heart rate										
4. SaO2										

Varibles	Before	After
1. PEFR		
2. Modified Borg score		
3. Sputum volume		

Time collecting data .....

Investigator .....



แบบบันทึกข้อมูลสำหรับการศึกษาที่ 2

(กรอกโดยผู้วิจัย)

Code No: ..... **Test date :** .....

Gender □ F □ M **Group intervention** .....

Variables		Actual value	% predict
1. PFT	FEV_1		
	FVC		
	FEV_1/FVC		
	FEF_{25-75}		
2. Modified patient evaluation questionnaire			

Mean variables from daily logbook : .....

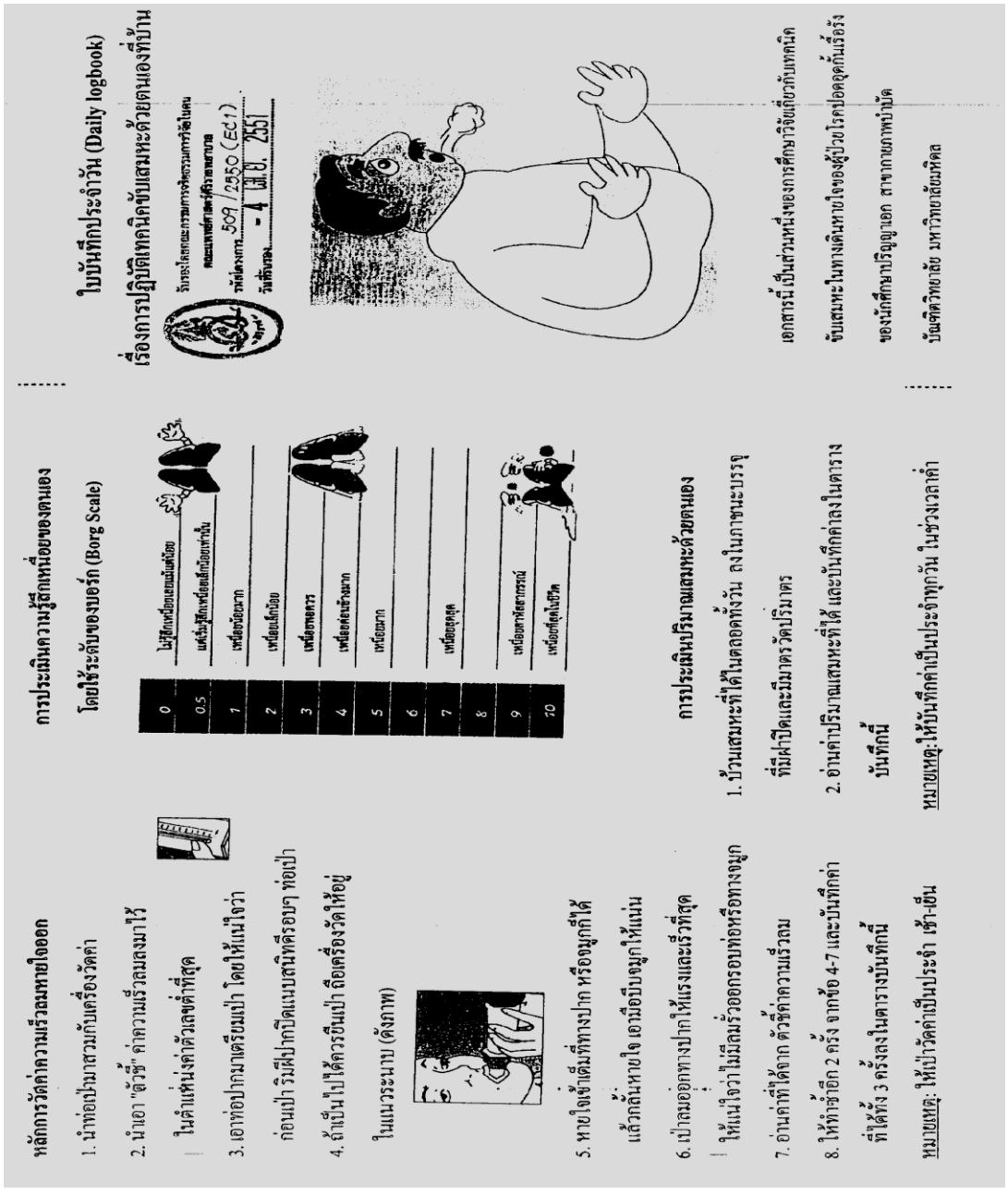
Variables	1st	2nd	3rd	4th	5th	6th	7th
1. PEFR							
2. Modified Borg score							
3. Sputum volume							

Variable for termination of the study

Variable	Score
1. Modified patient preference questionnaire	

DAILY LOGBOOK

(filled in by patient)



ใบบันทึกประจำวัน (Daily logbook)

เรื่องการปฏิบัติเทคนิคขับเสมหะด้วยตนเองที่บ้าน

รับรองโดยคณะกรรมการจริยธรรมการวิจัยในคน
คณะเทคนิคการแพทย์ มหาวิทยาลัยมหิดล
รหัสโครงการ 509/2550 (EC1)
วันที่รับรอง - 4 ก.ค. 2551

ของนักศึกษาปริญญาเอก สาขาการแพทย์ทางเลือก

มหาวิทยาลัยมหิดล

เอกสารนี้เป็นส่วนหนึ่งของการศึกษาวิจัยเกี่ยวกับเทคนิค

ขับเสมหะในทางเดินหายใจของผู้ป่วยโรคปอดอุดกั้นเรื้อรัง

การประเมินความรู้สึกหนักของตนเอง

โดยใช้ระดับของบอร์ก (Borg Scale)

0	ไม่รู้สึกหนักเลยแม้แต่น้อย
0.5	แทบไม่รู้สึกหนักเลยแม้แต่น้อย
1	เหนื่อยน้อยมาก
2	เหนื่อยนิดน้อย
3	เหนื่อยพอควร
4	เหนื่อยค่อนข้างมาก
5	เหนื่อยมาก
6	
7	เหนื่อยหนัก
8	
9	เหนื่อยหนักอย่างยิ่ง
10	เหนื่อยที่สุดในชีวิต

หลักการวัดค่าความเร็วลมหายใจออก

1. นำท่อปากลมกับเครื่องวัดค่า

2. นำเอา "ตัวชี้" ค่าความเร็วลมลงมาให้

ในตำแหน่งค่าตัวเลขต่ำที่สุด

3. เอาท่อปากเตรียมเป่า โดยให้แน่ใจว่า

ก่อนเป่า ริมฝีปากปิดแนบสนิทรอบๆ ท่อเป่า

4. ถ้าเป็นไปได้ควรยืนเป่า ถือเครื่องวัดให้อยู่

ในแนวระนาบ (ดังภาพ)

5. หายใจเข้าเต็มที่ทางปาก หรือจมูกก็ได้

แล้วกลั้นหายใจ เอามือบีบจมูกให้แน่น

6. เป่าลมออกทางปากให้แรงและเร็วที่สุด

ให้แน่ใจว่าไม่มีลมรั่วออกรอบท่อหรือทางจมูก

7. อ่านค่าที่ได้จาก ตัวชี้ค่าความเร็วลม

8. ให้ทำซ้ำอีก 2 ครั้ง จากข้อ 4-7 และบันทึกค่า

ที่ได้ทั้ง 3 ครั้งลงในตารางบันทึกนี้

หมายเหตุ: ให้ป่าวัดค่านี้เป็นประจำ เช้า-เย็น

การประเมินปริมาณเสมหะด้วยตนเอง

1. ปริมาณเสมหะที่ได้ในตลอดทั้งวัน ลงในภาชนะบรรจุ

ที่มีฝาปิดและมีมาตรวัดปริมาตร

2. อ่านค่าปริมาณเสมหะที่ได้ และบันทึกค่าลงในตาราง

บันทึกนี้

หมายเหตุ: ให้บันทึกค่านี้เป็นประจำทุกวัน ในช่วงเวลาค่ำ

ตารางบันทึกประจำวันต่อการปฏิบัติเทคนิคขับเสมหะด้วยตนเองที่บ้าน

C N: .....

สัปดาห์ที่ ..... ระหว่างวันที่ .....

ลำดับ	วันที่	การปฏิบัติเทคนิคขับเสมหะ	ค่าความเร็วลมหายใจออก			ระดับความรู้สึกเหนื่อย (0-10)	ปริมาณเสมหะ (มิลลิลิตร)	หมายเหตุ
			ครั้งที่1	ครั้งที่ 2	ครั้งที่ 3			
1		เช้า						
		เย็น						
2		เช้า						
		เย็น						
3		เช้า						
		เย็น						
4		เช้า						
		เย็น						
5		เช้า						
		เย็น						
6		เช้า						
		เย็น						
7		เช้า						
		เย็น						

หมายเหตุ: หากท่านไม่สามารถปฏิบัติเทคนิคหรือมีอาการผิดปกติในขณะฝึกปฏิบัติ กรุณาบันทึกข้อมูลลงในส่วนหมายเหตุ หรือ

หากมีข้อสงสัยใด กรุณาติดต่อ คุณเสาวณีย์ วรวุฒางกูร ที่หมายเลขโทรศัพท์ 081-770-1284

MODIFIED PATIENT EVALUATION QUESTIONNAIRE

English version of Modified patient evaluation questionnaire (90)

1. Cough episodes : Frequency – throughout the day

   How frequency were your cough episodes on a typical day during the past week:

   1) None – Unaware of coughing
   2) Rare – Cough now-and-then
   3) Occasional-Less than hourly
   4) Frequent –One or more times an hour
   5) Almost constant-Never free of cough or feeling free of the need to cough

2. Cough episodes : Severity – on arising and throughout the day

   How severe were your coughing episodes on a typical day during the past week :

   1) None – Unaware of coughing
   2) Mild – Did not interfere with usual morning or daily activity
   3) Moderate- Must stop activity during coughing episode
   4) Marked – Must stop activity during and for a brief period after coughing episode
   5) Severe- Stops all activity for some time and is exhausting ; may be accompanied by dizziness, headache, and/or pain in chest or abdomen

3. Chest discomfort: Tightness and/or congestion – on arising and throughout the day

   How much chest discomfort did you have on a typical day during the past week:

   1) None – Unaware of any discomfort
   2) Mild – Noticeable now-and-then but is not bothersome and passes quickly; does not limit activity.
   3) Moderate-Noticeable less than hourly; limits and is aggravated or brought on by moderate activity

(continued)

4) Marked-Noticeable one or more times an hour; may be accompanied by dyspnea;limits and is aggravated or brought on by normal activity, such as walking
5) Severe- Almost constant; accompanied by dyspnea; present even when resting; limits all activity

4. Difficulty breathing : Dypsnea (short of breath)- on arising and throughout the day
   How much difficulty did you have breathing on a typical day during the past week:
   1) None – Unaware of any difficulty
   2) Mild – Noticeable during more strenuous activity; such as morning exercise;walking more than one block or up more than one flight of stairs without stopping
   3) Moderate-Noticeable during light activity; such as making beds or taking out the garbage, walking one block or up one flight of stairs, or running or jogging
   4) Marked-Noticeable when washing or dressing in the morning; after slowly walking less than one block or up one flight of stairs
   5) Severe- Almost constant; present even when resting (sitting on bed or chair)

5. Ease in bringing up sputum – on arising and throughout the day.
   Indicate any change in the ease with which you brought up sputum, on a typical day during the past week:
   1) Marked Improvement
   2) Moderate Improvement
   3) Slight Improvement
   4) No Change
   5) Slightly worse
   6) Moderately worse
   7) Markedly worse

THE SCORING SYSTEM

Precoded and Final Values for Items 1 - 4

Response Choices	Precoded Value	Final Value
None	1	1
Rare/ Mild	2	2
Occasional/ Moderate	3	3
Frequent / Marked	4	4
Almost constant /Severe	5	5

Precoded and Final Values for Items 5

Response Choices	Precoded Value	Final Value
Marked Improvement	1	1
Moderate Improvement	2	2
Slight Improvement	3	3
No Change	4	4
Slightly worse	5	5
Moderately worse	6	6
Markedly worse	7	7

The questionnaire was developed by Petty et al in 1990 (90). The lowest possible raw scores is 5 and the highest scores is 27 in this questionnaire. In this scoring system, higher scores represent worse disease and lower scores suggest on improvement.

Thai version of Modified patient evaluation questionnaire

แบบสอบถามเกี่ยวกับการประเมินอาการด้วยตนเองของผู้ป่วย สำหรับการศึกษาที่ 2

(กรอกโดยผู้เข้าร่วมการวิจัย)

Code Number …….. กลุ่มที่ .....
วันที่ ..... ครั้งที่ .....

คำชี้แจง : แบบสอบถามนี้ ประกอบด้วย 5 ข้อคำถาม โดยมีวัตถุประสงค์เพื่อให้ท่านประเมินอาการไอและการมีเสมหะเรื้อรังด้วยตนเอง โปรดทำเครื่องหมาย X ในตัวเลือกแต่ละข้อ ตามอาการที่ท่านมีอยู่

1. การไอ: ความถี่ของการไอตลอดทั้งวัน
   ท่านมีอาการไอบ่อยแค่ไหน คิดโดยรวมตลอดทั้งวันในช่วงสัปดาห์ที่ผ่านมา
   1) ไม่มี – ไม่มีอาการไอ
   2) น้อยมาก – ไอนาน ๆ ครั้ง
   3) เป็นครั้งคราว-ไอน้อยกว่า 1 ครั้งต่อชั่วโมง
   4) บ่อยครั้ง – ไอหนึ่งครั้งหรือมากกว่า 1 ครั้งต่อชั่วโมง
   5) เกือบตลอดเวลา – รู้สึกไอเกือบตลอดเวลา, ไอไม่หยุด
2. การไอ: ความรุนแรงของอาการไอที่เกิดขึ้นในขณะตื่นนอนและตลอดทั้งวัน
   ท่านมีอาการไอรุนแรงมากแค่ไหน คิดโดยรวมตลอดทั้งวันในช่วงสัปดาห์ที่ผ่านมา
   1) ไม่มี – ไม่มีอาการไอ
   2) น้อย – อาการไอไม่ส่งผลต่อกิจกรรมที่ทำในแต่ละวัน
   3) ปานกลาง-ต้องหยุดทำกิจกรรมนั้นๆ ระหว่างมีอาการไอ
   4) มากชัดเจน – ต้องหยุดทำกิจกรรมนั้นๆ ระหว่างมีอาการไอและต้องพักช่วงสั้น ๆ หลังมีอาการไอ
   5) รุนแรงมาก – ต้องหยุดทุกกิจกรรมในบางช่วงเวลา และมีอาการเหนื่อยจากการออกแรงไอ รวมทั้งอาจมีอาการวิงเวียน ปวดศีรษะและ/หรือเจ็บบริเวณทรวงอกหรือท้อง
3. อาการไม่สบายบริเวณทรวงอก: อาการขึดตึงและ/หรือ แน่นขัดที่เกิดขึ้นขณะตื่นนอนและตลอดทั้งวัน
   ท่านรู้สึกหรือมีอาการไม่สบายบริเวณทรวงอกมากน้อยแค่ไหน คิดโดยรวมตลอดทั้งวันในช่วงสัปดาห์ที่ผ่านมา
   1) ไม่มี – ไม่มีอาการใด
   2) น้อย – รู้สึกเป็นครั้งคราว แต่อาการไม่รบกวนและหายไปอย่างรวดเร็ว โดยไม่จำกัดต่อการทำกิจกรรมใด

(ต่อ)

3) ปานกลาง- รู้สึกอาการได้น้อยกว่า 1 ครั้งต่อชั่วโมง จำกัดกิจกรรม และถูกกระตุ้นหรือมีอาการเมื่อทำกิจกรรมในระดับปานกลาง
4) มากชัดเจน – รู้สึกอาการได้มากกว่าหรือเท่ากับ 1 ครั้งต่อชั่วโมง อาจเกิดร่วมกับอาการหายใจหอบเหนื่อย อาการจะเพิ่มขึ้นชัดเจนหรือเกิดขึ้นเมื่อทำกิจกรรมปกติ เช่น การเดิน
5) รุนแรงมาก – มีอาการเกือบตลอดเวลา ซึ่งเกิดร่วมกับอาการหายใจหอบเหนื่อย แสดงอาการแม้ในขณะพัก และมีการจำกัดการทำกิจกรรมต่างๆ

4. การหายใจลำบาก: อาการหายใจลำบากที่เกิดขึ้นขณะตื่นนอนและตลอดทั้งวัน
ท่านมีการหายใจลำบากมากน้อยแค่ไหน คิดโดยรวมตลอดทั้งวันในช่วงสัปดาห์ที่ผ่านมา
1) ไม่มี – ไม่รู้สึกว่าหายใจลำบาก
2) เล็กน้อย – รู้สึกได้ขณะทำกิจกรรมที่ออกแรงมาก เช่น ออกกำลังกายตอนเช้า เดินด้วยระยะไกลกว่า 500 เมตร หรือขึ้นบันไดมากกว่า 1 ชั้นโดยไม่หยุดพัก
3) ปานกลาง- รู้สึกได้ขณะทำกิจกรรมเบาๆ เช่น การเดิน 500 เมตร หรือขึ้นบันได 1 ชั้น
4) มากชัดเจน – รู้สึกได้ขณะอาบน้ำหรือแต่งกาย หรือเกิดอาการหลังการเดินช้าๆ ระยะทางน้อยกว่า 500 เมตร หรือการขึ้นบันได 1 ชั้นอย่างช้าๆ
5) รุนแรงมาก – มีอาการเกือบตลอดเวลา แม้ในขณะพัก นั่งบนเตียงหรือเก้าอี้

5. ความง่ายของการขับเสมหะขณะตื่นนอนและตลอดทั้งวัน
โปรดระบุการเปลี่ยนแปลงของความง่ายในการขับเสมหะของท่านที่เกิดขึ้นตลอดวันในช่วงสัปดาห์ที่ผ่านมา
1) ดีขึ้นอย่างชัดเจน
2) ดีขึ้นปานกลาง
3) ดีขึ้นเล็กน้อย
4) ไม่เปลี่ยนแปลง
5) แย่ลงเล็กน้อย
6) แย่ลงปานกลาง
7) แย่ลงอย่างชัดเจน

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MODIFIED PATIENT SATISFACTION QUESTIONNAIRE

English version

Please indicate the overall satisfaction of technique you have experienced during the study

Items	5 (Excellent)	4 (Good)	3 (Fair)	2 (Poor)	1 (Very poor)
1) Ease of technique					
2) Comfort					
3) Secretion clearance					
4) Recommendation to a friend					

THE SCORING SYSTEM

Modified patient satisfaction questionnaire is a five-point, four-item questionnaire. The patients will be asked to rate the treatment mode for 1) ease of technique; 2) comfort; 3) secretion clearance; and 4) recommendation to a friend. The scale is assigned a point value concerning the patients' level of satisfaction. The rating scale are from 5 to 1 (5 = excellent, 4 = good, 3 = fair, 2 = poor, 1 = very poor).

Precoded and Final Values for Items 1 - 4

Response Choices	Precoded Value	Final Value
Excellent	5	5
Good	4	4
Fair	3	3
Poor	2	2
Very poor	1	1

The lowest possible raw scores is 4 and the highest is 20 in this questionnaire. In this scoring system, higher scores represent high satisfaction of the technique and lower scores suggest on unsatisfaction (79).

Thai version

แบบสอบถามเกี่ยวกับความพอใจในเทคนิคการรักษา สำหรับการศึกษาที่ 2

(กรอกโดยผู้เข้าร่วมการวิจัย)

Code Number …….. กลุ่มที่ ..... วันที่ .....

โปรดระบุความพึงพอใจโดยรวมต่อเทคนิคการขับเสมหะที่ท่านได้ฝึกปฏิบัติจากการศึกษาครั้งนี้

หัวข้อ	5 มากที่สุด	4 มาก	3 ปานกลาง	2 น้อย	1 น้อยที่สุด
1) ความง่ายของเทคนิค					
2) ความสะดวกสบายของการปฏิบัติเทคนิค					
3)ประสิทธิภาพในการขับเสมหะของเทคนิค					
4) ความรู้สึกที่อยากจะแนะนำเทคนิค การรักษานี้ให้ผู้ป่วยท่านอื่น					

ข้อเสนอแนะ (ถ้ามี)

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TEST VALIDITY

Measurement validity concerns the extent to which an instrument measures what it is intended to measure. Validity implies that a measurement is relatively free from error. Therefore, the purpose of this study was to define the instrument measures, which were modified patient evaluation questionnaire and modified patient preference questionnaire, that intend to measure and free from error by translation from English version to Thai version. Validation procedures were based on the face validity. There were considered subjective judgments and indicated that the questionnaires appeared to be serving its intended purpose.

The face validity of both questionnaires were assessed by three physical therapists with experienced 6, 7 and 8 years respectively, two experts of chest physical therapist with experienced 25 and 29 years (Assist. Prof. Vipawan Chewachutirung-ruang, Assoc.Prof. Suwannee Jarungjitaree) and one clinical physical therapist with experienced 13 years (Assist. Prof. Mantana Vongsirinavarat, Ph.D.) to make judge ment about the clarify and comprehensiveness of the questionnaires. This process was performed three revisions. When all physical therapists agreed with the content domain of questionnaire, face validity was supported.

AIRWAY CLEARANCE TECHNIQUES OF THE STUDY

I. Active Cycle of Breathing Technique (ACBT)

ACBT is an airway clearance technique that used to mobilize and clear excess bronchial secretions. This technique combines three breathing methods to move mucous out of the lungs:

1. **Breathing control** (gentle relaxed breathing)
2. **Thoracic expansion exercises** (deep breaths, often with a three-second-breath hold and quiet unforced breath out)
3. **Forced expiration technique** (breathing out one or two huffs which uses "huffing" from various lung volumes to assist in removal of secretions).

Breathing control (breathing at normal tidal volume**)**

3-4 Thoracic expansion exercise

Deep inhalation with relaxed exhalation at vital capacity

with or without chest percussion

Breathing control

3-4 Thoracic expansion exercise

Breathing control

Forced expiration technique

1 - 2 Huffs at mid to low lung volume

Abdominal muscle contraction to produce forced exhalation

Breathing control

These three steps are done in sequence to loosen and expel the mucous. This method encourages active participation of the patient and has been shown to be as effective when performed by patient alone. Postural drainage positions may be used in conjunction with ACBT. One advantage is that you can do it on your own with no equipment. Patient can also perform it even if they have poor lung function

Procedure of ACBT

Position : Patient should be in a comfortable well-supported position either sitting or side lying position

1. Breathing control : Breath in a gentle relaxed manner with normal tidal volume and rate, using the lower chest and abdomen. Relaxation of the upper chest and shoulders. Expiration is unforced. You shouldn't feel that you are working at breathing and you should allow your tummy to rise as you breathe in and fall as you breaths out. The phase should last as long as the patient requires to relax and to prepare for the next phases, usually 5 to 10 seconds. In patient with bronchospasm or unstable airways, the breathing control phase may be as long as 10 to 20 seconds.
2. Thoracic expansion exercise : The emphasis during this phase is on inspiration. The patient is instructed to take in a deep breath to inspiratory reserve; expiration is passive and relaxed. The patient may place a hand over the area of the thorax being treated to further encourage increased chest wall movement.

    - Take a slow, relaxed deep breath in, as far as you can. To allow maximum air into the lungs by deep breathing
    - Now hold your breath for the count of 3 (the deepest breath you can comfortably hold, usually 3 second)
    - Followed by a quiet relaxed breath out (passive relaxed expiration)
    - Repeat 3 – 4 times.

4. Forced expiration technique : It is defined as 1-2 huffs from mid to low lung volume followed by a period of relaxed breathing control. A huff is a rapid, forced exhalation but not with maximal effort, requires the glottis to remain open. The

muscles of the abdomen should contract to provide greater expiratory force.

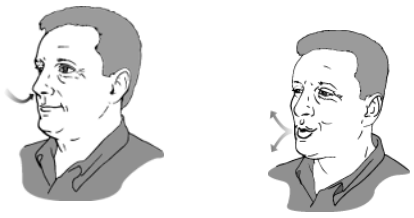
- Take a normal breath in and then with your mouth open, squeeze the air out forcibly. Making a “huffing” sound. You should feel your stomach muscles contract strongly.
- Keep “huffing out” until you can’t breathe out any more. (the huff should be long enough to move secretions from the smaller airways)
- Repeat 1-2 huffs then pause
- Do breathing control in the pause to avoid wheeziness. The length of the pause will depend on how you are feeling. You may find you tire easily, so 20 seconds rest between each huff should give you enough time to recover. If you are well, pauses can be shorter
- Repeat as necessary
- When the secretions reach the large airways, take a deep breath and huff again to get the sputum into your mouth to clear out.

II. Pursed Lips breathing (PLB)

PLB is one of the simplest ways to control shortness of breath. It provides a quick and easy way to slow your pace of breathing, making each breath more effective. This breathing are improves ventilation, releases trapped air in the lungs, keeps the airways open longer and decreases the work of breathing, prolongs exhalation to slow the breathing rate, improves breathing patterns by moving old air out of the lungs and allowing for new air to enter the lungs, relieves shortness of breath and causes general relaxation

Procedure of PLB

1. Relax your neck and shoulder muscles.



2. Breathe in (inhale) slowly through your nose for two counts, keeping your mouth closed. Don't take a deep breath; a normal breath will do. It may help to count to yourself: inhale, one, two.

3. Pucker or "purse" your lips as if you were going to whistle or gently flicker the flame of a candle.

4. Breathe out (exhale) slowly and gently through your pursed lips while counting to four. It may help to count to yourself: exhale, one, two, three, four or to six.

Verbal instructions of PLB are as follows : Breathe in through your nose, not a deep breath, just a normal inhalation. Count to two in your head. Your breath out should take two or three times as long as you breathe in. Keep your lips firmly together except for the very center. When exhaling, blow the air out in a firm, steady stream through the center of your lips. Remember to breathe out slowly; Do not blow too hard, but do keep the stream of air firm by blowing through the small opening left between your lips in the center of your mouth while counting to four or six" .

III. The forced expiration technique (FET)

FET is a forced expiration, or huff, combined with periods of relaxed diaphragmatic breathing (breathing control). One or two huffs from mid lung volume to low lung volume (this being the range at which more peripheral secretions are mobilized) are followed by breathing control. The forced expiration technique utilizes the physiology of the huff combined with a recovery phase to reduce the possibility of airway closure, desaturation or fatigue and lower intrathoracic pressures than a cough.

To produce effective breathing control, the patient takes a gentle breathing using the lower chest at normal tidal volume and at a natural rate. Unforced expiration.

To produce an effective huff, the patient takes a short breath in and then breathes out forcefully through the mouth, contracting the abdominal muscles.

- Mouth open, O-shaped, to keep the back of the throat (glottis) open
- Two different levels of huffing

  a) A forced expiration from mid-lung volume to low lung volume
    - for move the more peripheral secretions

  b) A forced expiration from high-lung volume to mid-lung volume
    - for move the more proximal secretions
- Muscles of the chest wall and abdomen contract.

  Sound is like a sigh, but forced.

RELIABILITY TEST OF SPIROMETRY MEASUREMENT

Spirometry is a medical test that measures the air volume an individual inhales or exhales as a function of time. Spirometry is an effort-dependent test that requires careful instruction and the cooperation of the subject. Because this test is not routine and the researcher performed the measurement on all patients; then the researcher needed to present the reliability for recording the values of pulmonary function test in the study. The test-retest reliability was performed prior to the data collection.

Procedure :

1. Operation, set up procedure of spirometry test

Autospiro AS-500 device was used for this pilot study. Spirometry includes the measurement of forced vital capacity (FVC), forced expiratory volume in the first second (FEV_1) and other forced expiratory flow measurement such as $FEF_{25-75\%}$. There was performed calibration procedure before operation and set up for reliable data. Interpreting the data and the curve displayed on the LCD or printed out.

2. Subject

Ten healthy subjects who are naïve to spirometry test. No relative contraindication to performing spirometry.

3. Measurement procedures of spirometry

Procedure of spirometry test in this pilot study was based on Standardisation of spirometry by American Thoracic Society (ATS) and European Respiratory Society (ERS), update 2005 and American Thoracic Society in 1996. After additional instruction and demonstration of spirometry, each subject performed 2 series of testing in standing position with 15 minutes resting period. For each sery measurement, the highest value was recorded and used in analysis between the first and second series. The test-retest reliability was calculated.

4. Data analysis

The level of statistical significance was set at probability level less than 0.05 ($p<0.05$) for all analyses. Results were presented as mean ± SD in descriptive statistics on subject characteristics. Intraclass correlation coefficient (ICC3,1) was used to determine the test-retest reliability of the values of pulmonary function for all parameters between 2 trials.

Results of Reliability test

Ten female subjects were included in the reliability study. The characteristics of subjects are shown in Table C.1. The results of test-retest reliability are shown in Table C.2.

Table C .1 Characteristic of subjects for reliability testing (n=10)

Characteristics	**Mean ± SD**
Age (yr)	21.70 ± 0.48
Body weight (kg)	51.50 ± 6.38
Height (cm)	159.00 ± 8.41

Table C.2 Intraclass correlation coefficients of spirometry (n = 10)

Parameters	**ICC value**
FVC (L)	0.9345
FEV_1 (L)	0.8894
FEV_1 / FVC (%)	0.9243
$FEF_{25-75\%}$ (L/S)	0.9060

The ICC ranged between 0.8894 and 0.9345. All spirometric parameters were indicated good reliability with ICC values above 0.75. Therefore, this pilot study found that a test-retest reliability was good and to express confidence in the obtained spirometry measurement in research study.

CALCULATION OF SAMPLE SIZE

The purpose of the first study is to compare the efficacy of PLB&FETs and ACBT on pulmonary mucus clearance in healthy subjects. In this study, mucociliary transport and mucus clearance are measured by quantifying the removal of an inhaled radiolabeled aerosol deposited on the bronchial mucosa in a radioaerosol technique. The radioaerosol technique is a sensitive technique to quantify changes in bronchial mucus transport, especially when mucus production is low. So, there is high monitoring precision. Moreover, most of the previous studies were within-subjects designs with small sample size (range from 4 to 10) (92, 93, 95-98, 105). Group of subjects was tested under all conditions and each subject acted as his own control. Thus, the differences among airway clearance techniques are more likely to reflect treatment effects and not variability between subjects. Therefore, this study requires the sample size of 3 subjects for data collection to represent the trend of lung zone clearance by PLB&FETs and ACBT in healthy subjects.

The purpose of the second study is to investigate the effectiveness of PLB&FETs and ACBT in patients with chronic obstructive pulmonary disease. Recently, there are no studies of COPD patients using PLB&FETs focus on the improvement of airway clearance. Therefore, the sample size was calculated according to the result of preliminary study in our study from n = 5 in each group. The determination of sample size by G* Power version 3.0.10 by F test with repeated measures, within-between interaction, ANOVA-approach. Analysis with a priori for compute required sample size was used. From the result of preliminary study, input parameter were effect size (f) of PEF parameter between groups (f = 0.29) set $\alpha = 0.05$, power (1-β) =0.80, number of groups = 2 and repetitions = 3. Finally, the output of total sample size were 22 with actual power = 0.82

RAW DATA OF THE FIRST STUDY

Table E.1 Characteristics of the subjects in the first study

No.	Age (y)	Weight (kg)	Height (cm.)	BMI	Spirometer parameter (%predicted values) FVC	FEV_1	FEV_1/ FVC	$FEF_{25-75\%}$	PEF
1	34	80	170	27.68	88	89	81	71	67
2	33	82	174	27.08	99	99	82	79	90
3	35	64	160	25.00	103	106	86	99	89

Table E.2 Percentage retention of radioactivity in the central right lung zone among three intervention at the difference of time for individual data (Decay-corrected data)

		Percentage retention of radioactivity in each time							
No	**Interventions**	**0^{th}**	**10^{th}**	**20^{th}**	**30^{th}**	**40^{th}**	**50^{th}**	**60^{th}**	**70^{th}**
N1	Control	100.00	101.87	102.81	99.79	100.43	96.06	95.27	92.11
	PLB&FETs	100.00	96.37	96.83	98.50	97.93	94.10	93.40	92.71
	ACBT	100.00	101.22	101.12	100.09	100.12	100.30	99.48	101.00
N2	Control	100.00	100.75	99.64	100.12	101.26	102.42	103.51	100.42
	PLB&FETs	100.00	100.83	102.02	103.19	102.78	103.88	103.40	103.30
	ACBT	100.00	100.15	100.89	96.32	92.20	92.43	91.37	89.43
N3	Control	100.00	101.01	98.97	98.70	99.30	100.50	97.50	92.86
	PLB&FETs	100.00	96.97	95.47	93.31	90.39	90.89	86.15	86.03
	ACBT	100.00	101.37	100.55	97.84	99.52	98.75	97.78	98.16

Table E.3 Percentage retention of radioactivity in the intermediate right lung zone among three intervention at the difference of time for individual data (Decay-corrected data)

		Percentage retention of radioactivity in each time							
No	**Interventions**	**0th**	**10th**	**20th**	**30th**	**40th**	**50th**	**60th**	**70th**
N1	Control	100.00	96.55	96.08	94.34	94.85	96.08	94.87	92.49
	PLB&FETs	100.00	98.55	99.93	96.41	92.23	87.99	86.63	88.01
	ACBT	100.00	101.22	95.98	93.45	94.40	92.33	93.76	86.29
N2	Control	100.00	99.76	97.58	97.54	97.35	98.10	99.32	100.48
	PLB&FETs	100.00	97.44	97.72	94.60	90.69	91.01	88.98	86.99
	ACBT	100.00	96.30	95.54	90.93	89.78	88.81	87.44	86.10
N3	Control	100.00	99.99	100.55	100.45	98.13	94.98	95.87	92.64
	PLB&FETs	100.00	98.27	90.30	86.83	83.04	83.27	79.94	77.73
	ACBT	100.00	96.61	89.35	89.94	83.50	81.37	81.57	78.89

Table E.4 Percentage retention of radioactivity in the peripheral right lung zone among three intervention at the difference of time for individual data (Decay-corrected data)

		Percentage retention of radioactivity in each time							
No	**Interventions**	**0th**	**10th**	**20th**	**30th**	**40th**	**50th**	**60th**	**70th**
N1	Control	100.00	101.65	100.43	97.82	99.58	101.28	102.53	97.88
	PLB&FETs	100.00	100.90	100.28	98.75	94.11	89.15	88.88	90.05
	ACBT	100.00	94.43	90.55	89.10	89.42	90.50	87.87	81.23
N2	Control	100.00	101.00	98.41	92.28	86.86	86.67	87.31	87.98
	PLB&FETs	100.00	94.95	94.26	92.01	84.14	80.93	80.53	80.69
	ACBT	100.00	93.00	88.70	89.93	87.71	85.99	86.75	84.63
N3	Control	100.00	100.20	99.66	96.21	96.64	96.82	91.95	87.28
	PLB&FETs	100.00	100.65	96.22	91.77	86.03	84.57	82.42	79.49
	ACBT	100.00	98.11	89.51	87.70	87.69	83.69	81.12	80.28

Table E.5 Percentage retention of radioactivity in the whole right lung zone among three intervention at the difference of time for individual data (Decay-corrected data)

		Percentage retention of radioactivity in each time							
No	**Interventions**	**0th**	**10th**	**20th**	**30th**	**40th**	**50th**	**60th**	**70th**
N1	Control	100.00	100.02	99.81	97.35	98.30	97.71	97.42	94.05
	PLB&FETs	100.00	98.55	98.97	97.88	94.81	90.48	89.70	90.29
	ACBT	100.00	99.14	96.21	94.56	94.98	94.69	94.06	90.14
N2	Control	100.00	100.52	98.62	96.86	95.52	96.13	97.12	96.52
	PLB&FETs	100.00	97.87	98.16	96.89	92.97	92.43	91.49	90.88
	ACBT	100.00	96.69	95.36	92.62	90.02	89.26	88.68	86.87
N3	Control	100.00	100.46	99.66	98.53	98.17	97.72	95.39	91.19
	PLB&FETs	100.00	98.41	94.01	90.79	86.80	86.67	83.11	81.53
	ACBT	100.00	98.92	93.84	92.45	91.03	88.92	87.88	86.93

Table E.6 The values of heart rate among the control, PLB&FETs and ACBT in the experimental period for individual data

		Heart rate in each time (BPM)							
No	**Interventions**	**0th**	**10th**	**20th**	**30th**	**40th**	**50th**	**60th**	**70th**
N1	Control	85	85	84	83	70	75	75	84
	PLB&FETs	84	81	78	84	72	75	71	74
	ACBT	94	90	84	73	73	71	70	75
N2	Control	78	87	87	88	87	83	82	80
	PLB&FETs	78	75	80	78	80	76	79	75
	ACBT	82	83	80	79	75	82	77	82
N3	Control	79	82	79	80	79	81	82	82
	PLB&FETs	89	88	82	85	86	89	79	82
	ACBT	87	87	93	98	93	83	87	87

Table E.7 The values of oxygen saturation (%) among the control, PLB&FETs and ACBT in the experimental period for individual data and the group mean values

		Oxygen saturation (%) in each time							
No	**Interventions**	**0th**	**10th**	**20th**	**30th**	**40th**	**50th**	**60th**	**70th**
N1	Control	98	97	97	97	97	97	97	97
	PLB&FETs	97	99	98	99	99	97	98	98
	ACBT	97	96	99	99	99	95	96	98
N2	Control	99	99	99	98	98	99	98	99
	PLB&FETs	98	98	99	99	98	97	99	99
	ACBT	99	98	100	100	99	99	99	98
N3	Control	97	97	97	98	98	97	97	98
	PLB&FETs	98	99	98	99	99	97	98	98
	ACBT	97	97	98	98	99	97	96	97

Table E.8 The values of peak expiratory flow rate among the control, PLB&FETs and ACBT at before and immediate after the experimental period for individual data

		PEFR (L/min)	
Subject No.	Interventions	Before	Immediate after
N1	Control	500	480
	PLB&FETs	550	500
	ACBT	520	520
N2	Control	500	570
	PLB&FETs	500	560
	ACBT	530	550
N3	Control	450	450
	PLB&FETs	470	470
	ACBT	450	450

Table E.9 The values of Modified Borg scores of dyspnea among the control, PLB&FETs and ACBT at before and immediate after the experimental period for individual data

		Borg Scores	
Subject No.	Interventions	Before	Immediate after
N1	Control	0	0
	PLB&FETs	0	0.5
	ACBT	0	0
N2	Control	0	0
	PLB&FETs	0	0
	ACBT	0	0
N3	Control	0	0
	PLB&FETs	0	0
	ACBT	0	0

RAW DATA OF THE SECOND STUDY

Table E.10 Characteristics of the subjects in the second study

Subject	Age (yr)	Weight (kg)	Height (cm)	Smokeing history (pack year)	Ex-smoke (yr)	COPD Stage	Others
P1	80	55.00	165	40	20	1	BPH, IIH,HT, DLP
P2	68	65.50	163	17	15	3	Allergic rhinitis, HT
P3	71	71.20	173	24	20	3	senile cataract
P4	72	64.20	170	75	2	1	BPH
P5	84	50.00	165	70	14	2	Abnormal PVC during exercise
P6	75	43.20	172	18.5	20	2	
P7	60	54.40	170	37.5	0.5	2	Cataract, DLP
P8	76	47.30	158	63	35	3	HT
P9	59	56.70	161	52.5	1	3	HT
P10	68	74.70	165	42	1	1	DLP
P11	64	58.70	167	41	8	2	
A1	79	44.10	155	0	0	2	HT
A2	80	61.50	163	50	12	2	HT, BPH
A3	67	50.80	165	18	7	2	Lt.empyema thoracic , DLP
A4	64	54.00	161	140	4	2	hypertriglyceri ne, HT. DLP
A5	72	58.60	158	20	30	3	Both OA knee
A6	65	70.00	178	100	1	3	Thyrotoricosis
A7	78	59.50	162	20	5	3	IIH, BPH
A8	75	58.70	166	49.5	24	3	HT
A9	70	58.00	162	104	7	3	Psoriasis, HT
A10	55	49.50	159	26.25	1	1	
A11	62	78.00	171	20	22	2	Gout, HT

Table E.11 The percent predicted values of pulmonary function parameters at the 1st day

Subject	FVC	FEV_1	FEV_1/FVC	$FEF_{25-75\%}$	PEF
P1	99.00	86.00	88.00	41.66	81.00
P2	52.60	33.10	59.90	13.43	25.70
P3	48.60	44.30	86.10	28.76	48.40
P4	76.80	75.50	92.80	48.05	86.50
P5	130.10	107.10	78.20	48.97	103.50
P6	84.20	60.10	66.90	28.89	58.90
P7	73.90	56.50	72.90	24.86	42.80
P8	61.20	31.90	49.40	11.00	26.30
P9	66.10	39.90	56.70	10.74	47.10
P10	88.70	80.30	86.10	45.09	56.20
P11	109.20	69.00	57.70	23.64	27.80
A1	72.00	72.00	93.00	43.50	78.00
A2	92.50	70.70	65.30	19.77	64.10
A3	90.00	63.00	65.00	24.97	39.00
A4	89.80	63.70	67.70	27.48	42.20
A5	78.00	50.00	61.10	14.43	21.20
A6	79.20	52.60	62.90	25.99	31.20
A7	75.50	69.20	86.40	37.57	58.50
A8	73.00	37.50	48.40	13.26	32.50
A9	65.20	36.00	52.50	13.57	33.00
A10	98.00	85.00	83.23	42.19	76.12
A11	85.90	56.50	66.40	20.53	69.30

P = PLB&FETs group, A = ACBT group

Table E.12 The percent predicted values of pulmonary function parameters at the 7th day

Subject	FVC	FEV_1	FEV_1/FVC	$FEF_{25-75\%}$	PEF
P1	90.00	90.00	95.00	59.80	104.00
P2	61.10	39.40	61.50	17.78	20.40
P3	51.00	47.10	87.20	32.35	53.30
P4	79.30	75.90	90.30	44.41	88.90
P5	116.60	90.60	72.40	40.52	95.50
P6	77.90	56.60	65.80	27.11	56.30
P7	74.50	55.90	70.90	29.58	60.30
P8	64.50	33.00	48.50	12.00	27.20
P9	64.00	35.30	52.70	11.05	48.20
P10	96.40	85.10	84.00	45.82	80.80
P11	104.20	71.90	65.90	30.05	51.80
A1	65.00	71.00	104.00	47.98	81.00
A2	88.90	63.80	66.80	19.29	66.20
A3	86.00	63.00	69.00	25.68	41.00
A4	96.50	67.90	69.20	31.21	52.70
A5	80.30	51.00	60.40	16.38	56.10
A6	60.50	44.70	64.70	20.73	70.40
A7	78.60	62.30	74.70	23.99	57.30
A8	82.30	45.70	52.40	18.81	50.40
A9	66.00	38.20	55.20	14.32	34.90
A10	92.20	95.80	99.20	44.31	100.80
A11	77.30	56.70	71.20	24.11	74.70

P = PLB&FETs group, A = ACBT group

Table E.13 The percent predicted values of pulmonary function parameters at the 14th day

Subject	FVC	FEV_1	FEV_1/FVC	$FEF_{25-75\%}$	PEF
P1	79.00	103.00	122.00	60.29	115.00
P2	66.30	42.40	61.00	18.15	16.60
P3	58.70	46.70	75.10	26.36	52.50
P4	75.00	74.20	93.30	48.45	75.70
P5	83.20	83.80	105.30	63.04	93.80
P6	83.00	57.40	64.90	29.34	54.50
P7	73.60	55.60	70.00	26.12	57.20
P8	65.40	32.60	47.30	11.00	27.60
P9	52.00	28.40	50.30	8.21	40.00
P10	105.40	96.60	83.80	49.09	97.10
P11	105.50	69.10	63.30	28.03	42.10
A1	71.00	59.00	115.00	63.23	81.00
A2	85.30	69.50	76.40	29.41	73.20
A3	85.90	61.50	68.10	27.11	43.60
A4	98.70	77.50	74.90	40.03	62.60
A5	61.10	41.80	65.20	13.26	52.20
A6	68.30	50.70	70.40	33.72	52.90
A7	82.20	63.20	72.50	24.44	55.10
A8	84.90	43.90	51.50	17.53	55.70
A9	49.80	29.50	51.90	10.93	29.00
A10	90.50	98.60	104.50	54.33	102.70
A11	77.90	56.40	69.10	21.83	81.20

P = PLB&FETs group, A = ACBT group

Table E.14 The values of peak expiratory flow rate in daily logbook record in the first week (L/min)

Subject	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
	Mo	Ev	Mo	Ev	Mo	Ev	Mo	Ev	Mo	Ev	Mo	Ev	Mo	Ev
P1	300	300	352	352	330	350	350	305	350	330	310	380	360	350
P2	150	150	200	200	245	180	170	170	170	200	170	180	160	140
P3	200	200	240	250	260	230	260	230	260	260	230	220	270	240
P4	380	380	370	380	430	400	440	380	440	370	430	420	400	380
P5	350	350	350	350	350	350	340	320	330	350	340	350	350	330
P6	230	230	260	230	240	230	240	240	240	240	236	240	240	240
P7	300	300	280	300	310	330	290	310	280	320	285	300	290	300
P8	116	116	120	116	118	116	116	120	116	118	116	120	116	120
P9	150	150	170	200	180	190	210	240	240	230	230	210	220	240
P10	320	320	300	300	300	340	300	280	300	350	350	380	400	380
P11	110	110	110	120	120	130	150	180	170	210	200	200	200	180
A1	270	270	270	280	280	290	290	300	290	300	300	300	300	300
A2	160	160	210	180	200	180	154	180	260	220	180	220	200	200
A3	200	200	200	200	220	200	220	200	200	200	200	210	200	210
A4	250	250	250	250	250	250	250	250	250	250	250	250	250	250
A5	120	120	150	150	200	150	170	150	170	160	170	180	190	190
A6	300	300	300	270	350	280	320	290	280	300	300	290	270	280
A7	200	200	210	200	200	200	200	200	200	200	200	200	220	220
A8	240	240	240	250	240	240	230	250	250	250	240	230	240	240
A9	100	100	90	110	110	140	130	150	150	160	150	130	130	140
A10	440	440	450	480	520	470	500	480	490	510	480	480	510	490
A11	350	350	370	390	440	380	420	380	400	380	380	380	380	350

P = PLB&FETs group, A = ACBT group, Mo = Morning, Ev = Evening

Table E.15 The values of peak expiratory flow rate in daily logbook record in the second week (L/min)

Subject	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
	Mo	Ev	Mo	Ev	Mo	Ev	Mo	Ev	Mo	Ev	Mo	Ev	Mo	Ev
P1	330	330	340	330	350	355	355	340	320	340	355	350	350	360
P2	200	200	190	200	190	170	170	200	180	160	160	190	190	180
P3	260	260	270	260	270	260	290	260	260	260	280	280	310	260
P4	390	380	380	360	370	400	410	380	370	380	380	370	370	360
P5	350	330	330	330	350	350	330	330	350	330	330	350	330	330
P6	240	240	250	240	250	240	240	240	230	240	240	240	230	230
P7	300	300	280	310	280	290	280	320	300	310	310	300	300	310
P8	180	180	180	190	190	190	180	190	190	180	200	200	200	200
P9	230	230	250	220	240	230	230	260	260	250	240	230	240	240
P10	380	380	380	350	350	370	350	370	450	400	350	380	350	350
P11	200	190	240	220	220	240	250	200	220	220	220	240	220	230
A1	280	280	280	280	290	290	300	270	280	300	300	290	300	280
A2	240	240	180	200	220	200	180	260	220	220	250	200	280	200
A3	200	200	210	200	200	210	210	200	210	210	210	200	210	210
A4	250	250	250	250	250	250	250	250	250	250	250	250	250	250
A5	180	200	180	170	200	170	200	190	200	200	200	190	180	180
A6	250	270	250	320	280	260	260	270	300	280	290	250	260	290
A7	200	200	190	200	200	210	200	210	200	200	210	200	200	190
A8	250	250	250	250	250	250	250	240	250	250	250	250	250	240
A9	200	200	120	120	120	150	160	140	130	130	130	130	120	130
A10	200	200	510	510	500	510	510	530	520	510	530	530	540	560
A11	370	380	370	370	380	370	370	380	400	380	360	370	350	360

P = PLB&FETs group, A = ACBT group, Mo = Morning, Ev = Evening

Table E.16 The values of sputum volume in daily logbook record in the first week (milliliters)

Subject	Day1 *	Day2	Day3	Day4	Day5	Day6	Day7	Mean	Range
P1	10	15	15	15	10	10	15	12.86	10 -15
P2	10	30	45	35	40	30	40	32.86	10 – 45
P3	12.5	15	15	17.5	15	15	15	15.00	12.5 – 17.5
P4	5	10	12.5	10	12.5	10	17.5	11.07	5 – 17.5
P5	10	22.5	30	40	40	20	10	24.64	10 – 40
P6	10	25	20	20	20	15	15	17.86	10 – 25
P7	27.5	45	40	40	30	40	37.5	37.14	27.5 – 40
P8	5	10	20	12.5	10	10	10	11.07	5 – 20
P9	10	15	15	10	15	10	15	12.86	10 – 15
P10	20	35	30	25	20	10	10	21.43	10 – 35
P11	12.5	12.5	12	12	12.5	10	10	11.64	10 – 12.5
A1	7.5	10	10	10	10	10	10	9.64	7.5-10
A2	10	20	20	10	20	30	20	18.57	10 - 30
A3	10	35	32.5	30	30	35	30	28.93	10 - 35
A4	15	35	30	30	25	25	20	25.71	15 - 35
A5	15	20	25	25	10	10	10	16.43	10 - 25
A6	17.5	15	20	17.5	20	15	17.5	17.50	15 - 20
A7	10	10	25	10	20	25	10	15.71	10 - 25
A8	10	15	15	15	15	15	10	13.57	10 - 15
A9	20	17.5	12.5	10	0	0	0	8.57	0 - 20
A10	17.5	40	45	27.5	20	35	35	31.43	17.5 - 45
A11	10	10	10	10	10	10	7.5	9.64	7.5 - 10

P = PLB&FETs group, A = ACBT group, * = half day record

Table E.17 The values of sputum volume in daily logbook record in the second week (milliliters)

Subject	Day1 *	Day2	Day3	Day4	Day5	Day6	Day7	Mean	Range
P1	5	10	5	15	5	5	5	7.14	5 – 15
P2	15	25	20	35	30	30	25	25.71	15 – 35
P3	10	12.5	10	10	10	12.5	10	10.71	10 – 12.5
P4	10	15	12.5	10	15	12.5	15	12.86	10 – 15
P5	0	0	10	10	20	0	0	5.71	0 – 20
P6	10	20	10	15	15	10	20	14.29	10 – 20
P7	20	30	25	25	30	20	25	25.00	20 – 30
P8	5	5	5	5	7.5	7.5	7.5	6.07	5 – 7.5
P9	12.5	12.5	15	15	5	12.5	12.5	12.14	5 – 15
P10	10	0	0	0	0	0	0	1.43	0 – 10
P11	7.5	5	10	12.5	10	7.5	7.5	8.57	5 – 12.5
A1	5	5	5	5	5	5	5	5.00	5
A2	10	20	20	20	20	20	20	18.57	10 - 20
A3	30	35	32.5	30	30	32.5	30	31.43	30 - 35
A4	5	15	15	10	10	5	5	9.29	5 - 15
A5	10	10	10	10	10	10	10	10.00	10
A6	10	15	20	10	15	10	10	12.86	10 - 20
A7	10	10	10	10	10	10	10	10.00	10
A8	20	20	27.5	22.5	22.5	22.5	20	22.14	20 - 27.5
A9	0	0	0	0	0	0	0	0.00	-
A10	37.5	27.5	20	35	35	35	40	32.86	20 - 40
A11	10	10	10	10	10	10	10	10.00	10

P = PLB&FETs group, A = ACBT group, * = half day record

Table E.18 The values of Modified Borg scores of dyspnea in daily logbook record in the first week

Subject	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
	Mo	Ev	Mo	Ev	Mo	Ev	Mo	Ev	Mo	Ev	Mo	Ev	Mo	Ev
P1	3	3	2	3	3	3	3	3	3	3	3	3	3	3
P2	0.5	0.5	2	2	1	2	2	2	2	2	2	2	2	2
P3	2	2	2	2	0.5	2	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
P4	0	0	0	0	0	0	0	0	0	0	0	0	0	0
P5	5	5	5	4	5	4	3	4	4	3	4	3	3	2
P6	1	1	2	1	1	1	1	1	1	1	1	1	1	1
P7	1	1	2	1	2	2	2	2	2	2	2	2	2	2
P8	2	2	2	2	2	2	2	2	2	2	2	2	2	2
P9	2	2	1	3	2	2	2	3	3	3	2	3	2	3
P10	2	2	2	2	2	2	2	2	2	2	2	2	2	2
P11	2	2	2	2	2	2	2	2	2	2	2	2	2	2
A1	-	4	4	3	3	3	2	2	3	2	2	2	2	2
A2	-	4	4	4	4	4	3	4	4	4	4	4	4	3
A3	-	0.5	0.5	1	1	0.5	0.5	0.5	1	0.5	0.5	1	0.5	0.5
A4	-	2	2	2	2	2	2	2	2	2	2	2	2	2
A5	-	2	1	2	1	2	2	2	1	1	1	1	1	1
A6	-	0.5	0.5	1	0.5	0.5	0.5	1	0.5	0.5	1	0.5	0.5	1
A7	-	0	0	0	0	0	0.5	1	1	1	0	0	0	0
A8	-	3	3	3	3	3	3	3	3	3	3	3	3	3
A9	-	2	3	3	3	3	3	3	2	2	1	1	1	1
A10	-	1	2	2	2	2	2	1	2	2	2	2	1	1
A11	-	0	0	0	0	0	0	0	0	0	0	0	0	0

P = PLB&FETs group, A = ACBT group, Mo = Morning, Ev = Evening

Table E.19 The values of Modified Borg scores of dyspnea in daily logbook record in the second week

Subject	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
	Mo	Ev	Mo	Ev	Mo	Ev	Mo	Ev	Mo	Ev	Mo	Ev	Mo	Ev
P1	3	3	3	3	3	3	3	3	3	3	3	3	3	3
P2	0.5	0.5	2	2	2	2	2	2	2	2	2	2	2	2
P3	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
P4	0	0	0	0	0	0	0	0	0	0	0	0	0	0
P5	3	3	3	3	3	3	3	3	3	3	3	3	3	3
P6	1	1	1	1	1	1	1	1	2	1	1	1	1	1
P7	2	2	2	2	2	2	2	2	2	2	2	2	2	2
P8	1	1	0	1	0	1	0	1	0	1	0	1	0	1
P9	2	2	3	3	2	2	3	3	3	3	2	3	2	3
P10	0	0	0	0	0	0	0	0	0	0	0	0	0	0
P11	2	2	2	2	2	2	2	2	2	2	2	2	2	2
A1	-	3	2	2	2	2	2	2	2	2	2	1	1	2
A2	-	4	3	4	3	4	4	3	3	3	4	3	3	3
A3	1	0.5	0.5	1	1	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
A4	-	2	2	2	2	2	2	2	2	2	2	2	2	2
A5	0.5	1	1	1	1	1	1	1	1	1	1	1	1	1
A6	-	1	0.5	1	0.5	0.5	1	1	0.5	0.5	0.5	0.5	0.5	1
A7	1	1	1	1	1	1	1	1	1	1	1	1	1	1
A8	3	3	3	3	3	3	3	3	3	3	2	2	2	2
A9	-	1	1	2	1	2	2	1	2	1	2	2	1	2
A10	-	2	2	2	2	2	2	2	1	1	1	1	1	1
A11	0	0	0	0	0	0	0	0	0	0	0	0	0	0

P = PLB&FETs group, A = ACBT group, Mo = Morning, Ev = Evening

Table E.20 The scores of Modified patient evaluation questionnaire at the 1st day

Subject	Frequency Cough (Score 1-5)	Severity Cough (Score 1-5)	Chest discomfort (Score 1-5)	Dyspnea (Score 1-5)	Ease expectorate (Score 1-7)	Total scores (0-27)
P1	3	2	1	3	2	11
P2	2	2	1	3	4	12
P3	3	2	2	2	1	10
P4	2	3	2	2	1	10
P5	2	2	2	2	2	10
P6	4	2	1	2	4	12
P7	2	2	2	2	4	12
P8	2	3	2	3	5	15
P9	2	2	2	2	3	11
P10	4	5	4	2	6	21
P11	3	2	1	2	3	11
A1	2	3	3	2	4	14
A2	4	3	2	2	6	17
A3	3	2	1	2	4	12
A4	4	2	2	1	4	13
A5	2	2	2	2	4	12
A6	2	2	1	2	4	11
A7	2	2	2	3	5	14
A8	4	4	2	2	4	16
A9	5	2	2	3	1	13
A10	2	2	2	2	3	11
A11	2	2	2	1	5	12

P = PLB&FETs group, A = ACBT group

Table E.21 The scores of Modified patient evaluation questionnaire at the 7th day

Subject	Frequency Cough (Score 1-5)	Severity Cough (Score 1-5)	Chest discomfort (Score 1-5)	Dyspnea (Score 1-5)	Ease expectorate (Score 1-7)	Total scores (0-27)
P1	2	2	1	2	3	10
P2	3	2	1	2	3	11
P3	2	2	1	1	1	7
P4	2	2	1	2	3	10
P5	2	2	1	2	1	8
P6	4	2	1	2	3	12
P7	2	2	1	1	2	8
P8	2	3	2	2	1	10
P9	2	1	2	2	3	10
P10	2	1	2	2	1	8
P11	2	2	1	2	2	9
A1	2	3	3	1	2	11
A2	4	2	1	1	5	13
A3	3	2	1	1	3	10
A4	2	2	1	1	2	8
A5	2	2	2	2	3	11
A6	3	2	1	1	3	10
A7	2	2	2	2	2	10
A8	3	2	2	2	2	11
A9	2	2	1	2	1	8
A10	2	2	1	1	2	8
A11	1	1	1	1	2	6

P = PLB&FETs group, A = ACBT group

Table E.22 The scores of Modified patient evaluation questionnaire at the 14th day

Subject	Frequency Cough (Score 1-5)	Severity Cough (Score 1-5)	Chest discomfort (Score 1-5)	Dyspnea (Score 1-5)	Ease expectorate (Score 1-7)	Total scores (0-27)
P1	2	2	2	3	3	12
P2	4	2	1	2	2	11
P3	1	1	2	1	1	6
P4	2	2	1	1	4	10
P5	1	1	1	1	1	5
P6	3	2	1	2	1	9
P7	1	1	1	1	3	7
P8	2	2	1	2	3	10
P9	2	2	1	2	2	9
P10	2	1	1	2	3	9
P11	2	1	1	2	2	8
A1	2	2	2	2	3	11
A2	3	2	1	2	4	12
A3	2	2	1	1	2	8
A4	2	2	1	2	1	8
A5	2	2	2	1	1	8
A6	2	2	1	1	2	8
A7	2	2	1	2	1	8
A8	3	2	1	2	2	10
A9	1	1	1	2	2	7
A10	2	1	1	1	3	8
A11	2	1	1	1	2	7

P = PLB&FETs group, A = ACBT group

Table E.23 The scores of Modified patient satisfaction questionnaire at the 14th day of the study

Subject	Ease of technique (Score 1-5)	Comfort (Score 1-5)	Secretion clearance (Score 1-5)	Recommendation to a friend (Score 1-5)	Total scores (0-20)
P1	4	4	4	5	17
P2	5	4	5	4	18
P3	4	4	4	4	16
P4	4	5	4	5	18
P5	5	5	5	5	20
P6	5	5	4	5	19
P7	3	4	5	5	17
P8	5	4	5	5	19
P9	4	3	3	4	14
P10	3	3	2	3	11
P11	4	4	4	5	19
A1	3	4	3	3	13
A2	5	5	5	4	19
A3	4	3	4	4	15
A4	4	4	4	4	16
A5	5	5	5	5	20
A6	3	4	2	3	12
A7	4	5	3	4	16
A8	3	4	5	5	17
A9	5	5	3	5	18
A10	4	5	4	4	17
A11	5	5	4	5	19

P = PLB&FETs group, A = ACBT group

BIOGRAPHY

NAME	Miss.Saowanee Woravutrangkul
DATE OF BIRTH	17 February 1973
PLACE OF BIRTH	Bangkok, Thailand
INSTITUTIONS ATTENDED	Mahidol University, 1991-1994 : Bachelor of Science (Physiotherapy) Mahidol University, 1995-1997 : Master of Science (Physiotherapy) Mahidol University, 2005-2009 : Doctor of Philosophy (Physiotherapy)
EDUCATION FUND	Faculty of Physical Therapy, Huachiew Chalermprakiet University Affairs 2005-2009
HOME ADDRESS	18 Chan rd. Tungwatdon Sathron Bangkok, Thailand