



بسم الله الرحمن الرحيم

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بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى

مسئولية عن محتوى هذه الرسالة.

ملاحظات: لا يوجد



## INTRODUCTION

Cancer, in general, is still a leading cause of death worldwide. Breast cancer is one of the most common malignant tumors in females worldwide. In Egypt, cancer breast is not only the commonest malignancy in females (about 32% of cancers in women) but it is also the primary cause of cancer-related mortality (*Yehia Ibrahim et al., 2019*).

There is increased attention to women in our country. For example, the Egyptian Women's Health Initiative, launched by President Abdel Fattah Elsisi, which aims to promote women's health nationwide. The main objectives of this initiative, regarding breast cancer, are to promote breast cancer awareness and the importance of early diagnosis, screening for breast cancer, and treatment of diagnosed cases according to the recent protocols. Suspected cases are referred for further investigation and treatment at no cost to the participants (*Alorabi & Elghazawy, 2021*).

Radiation therapy or radiotherapy (RT) is an important part of the multidisciplinary management of breast cancer. It is a treatment with radiation, as high energy x-rays or particles, to destroy cancer cells and the radiation is produced from x-ray machine. RT can be used in almost all stages of cancer breast. In the early stages, after surgery, used to remove any remaining cancer cells and that improves recurrence. It even may be used intra-operative as one high dose to tumor or tumor bed with

breast-conserving surgery in early-stage patients. It may be used also in the late stages when the breast cancer is unresectable or metastatic to bones, lungs, brain, and liver. In that stage, RT is used to reduce complications e.g. to reduce pain, decrease bleeding risk, improve breathing and relieve spinal cord pressure symptoms (*Hennequin et al., 2016*).

RT is quite painless to have and can kill cancer cells, also it damages normal cells, but the normal cells can recover from the injury much better whereas the cancer cells go on and die, so it has a high success rate in treating cancer in the area that is shown at. Damage to normal cells can cause some side effects. The main short-term side effects are fatigue, breast swelling, and skin changes like redness, soreness, skin peeling, or darkening of the skin (*Emami, 2013*).

Most of the side effects gradually disappear in the weeks or months after treatment, but long term side effects can continue or might start some months or even years later on such as lymphedema (arm swelling), breast shrinking, breastfeeding problems, breathing problems, heart problems, ribs fracture and very rarely development of another cancer (*Hennequin et al., 2016*).

Breathing problems of RT occur due to inflammation of lung tissue causing Radiation pneumonitis (RP) which manifests a few weeks after getting radiotherapy. In some cases, there are no symptoms of RP, and it was discovered

accidentally on radiographs. Common symptoms of RP include shortness of breath, cough, chest pain, blood-tinged sputum, low-grade fever, and generalized weakness. Frequently symptoms go away on their own, although steroids treatment is required in some patients. Most cases respond well and recover with steroids, but if the condition persists that means pulmonary fibrosis unfortunately developed (*Hanania et al., 2019*).

There is no definite tool to diagnose radiation pneumonitis, so it mainly depends on clinical suspicion. For further assessment of the condition chest radiographs, pulmonary function tests, and other laboratory tests act a vital role to confirm the diagnosis or differentiate it from other diseases (*Hanania et al., 2019*).

Evaluation of pulmonary function is an important issue in many clinical situations, both when the patient has a history and/or symptoms suggesting lung disease and when any risk factor for lung disease is present, such as radiation exposure. Pulmonary functions tests present a great window for the assessment of the respiratory system. There are many types of PFTs, but spirometry is still the most common one (*Robbins et al., 2012*).

Spirometry, as a tool, is non-invasive, objective, reproducible, and sensitive to early changes, besides measuring lung volumes and capacities. It also presents information about

the responsiveness of airways, the influence of disease on lung function, the prognosis of the disease, and response to therapeutic interventions (*Graham et al., 2019*).

There are numerous studies on the changes in pulmonary function post-radiotherapy for breast cancer. In general, the studies have shown a reduction in most pulmonary function parameters including Forced Vital Capacity (FVC), Forced Expiratory Volume in the first second (FEV<sub>1</sub>), Total Lung Capacity (TLC), and Functional Residual Capacity (FRC) within the first six months, but these parameters tend to be normal within one year. FEV<sub>1</sub>/FVC ratio is usually within normal limits or slightly decreased, coping with the restrictive type of lung disease (*Jeba et al., 2015*).

## **AIM OF THE WORK**

The aim of this study is to evaluate the effect of hypofractionated radiotherapy in breast cancer patients on pulmonary functions (spirometry).

## Chapter One

# SPIROMETRY

Pulmonary function tests (PFTs) have a long and diverse history. Since the time of old Greece, great work has been done to understand the method that regulates our breathing in health and disease. There are many extensive published histories of lung function and physiology to extend this understanding (*Wu et al., 2018*).

PFTs give an accurate, reproducible assessment of the functional state of the respiratory system. It is worth underlying that PFTs do not diagnose specific diseases. Different diseases cause different patterns of abnormalities in PFTs. These patterns allow us to assess the severity of respiratory disease, which enables us to detect disease early and characterize the natural history and response to treatment. It also aids in the preoperative assessment of certain patients. It is important to remember that these conclusions are based on inferences, not specific proofs. The accuracy of our inferences depends on a complete knowledge of the physiologic basis of the functions tested, properly validated equipment, and appropriate protocols (*Gold & Koth, 2016*).

The main roles of PFTs are aiding in the diagnosis, assessing disease severity, and monitoring the progress and effects of treatment. It also has a role in clearing the cause of symptoms in patients who are diseased and clinically normal

(early detection) as well as measuring lung damage due to occupational injury and pre-operative assessment (*Tojo, 2014*).

Many different types of PFTs may be used. Spirometry is the most common type of PFTs; however, other commonly employed PFTs include lung volume measurement, lung diffusion capacity, and oxygen level tests. The main lung function test that measures the air that is inspired and expired is the Spirometer (*Types of Pulmonary Function Tests, n.d.*).

## **SPIROMETRY**

The spirometer is objective, non-invasive, reproducible, and sensitive to early change tool. There are three primary related measurements: volume, time, and flow. With the presence of portable meters, it can be performed almost anywhere, and it can be performed by anybody with the right training (*Graham et al., 2019*).

### **➤ DEFINITION**

Spirometry is a physiological test to assess the functional aspect of the lungs using an objective indicator by calculating the amount of air that a patient can inhale and exhale to the maximum (*Consortium, 2005*).



## ➤ INDICATIONS

Spirometry is a high-value tool that provides important information to physicians which helps together with history, symptoms, and physical findings, to reach a proper diagnosis. A spirometer enables us to assess airway responsiveness, measure the effect of a disease on pulmonary function, monitor disease course, evaluate the result of therapeutic interventions, assess preoperative risk, and determine the prognosis for many respiratory conditions (*Graham et al., 2019*). See figure (1)

**Diagnostic**

- To evaluate symptoms, signs or abnormal laboratory tests
- To measure the effect of disease on pulmonary function
- To screen individuals at risk of having pulmonary disease
- To assess pre-operative risk
- To assess prognosis
- To assess health status before beginning strenuous physical activity programmes

**Monitoring**

- To assess therapeutic intervention
- To describe the course of diseases that affect lung function
- To monitor people exposed to injurious agents
- To monitor for adverse reactions to drugs with known pulmonary toxicity

**Disability/impairment evaluations**

- To assess patients as part of a rehabilitation programme
- To assess risks as part of an insurance evaluation
- To assess individuals for legal reasons

**Public health**

- Epidemiological surveys
- Derivation of reference equations
- Clinical research

**Figure (1)**

Indications for Spirometry (*Graham et al., 2019*)

## ➤ CONTRAINDICATIONS

Although performing spirometry can be physically challenging there is no absolute contraindication. The forced expiratory maneuver used in spirometer increases intra-thoracic, intra-abdominal, and intracranial pressures and that causes the potential risks to thoracic and abdominal organs like pneumothorax or effect on recent thoracic or abdominal surgery. The physical effort required can increase myocardial demand or change blood pressure. Caution must be used for patients with medical conditions that could be adversely affected by the increased intracranial/intraocular pressure, sinus and middle ear pressure associated with spirometry. Although such risks are likely to be minimal for spirometry in most patients, the potential risks associated with testing should always be weighed against the benefit of obtaining information about lung function (*Cooper, 2011*).

Infection control issues must be considered, including active or suspected transmissible respiratory or systemic infections including tuberculosis, or physical conditions predisposing to the transmission of infections such as hemoptysis, significant secretions or oral lesions, and bleeding (*Cooper, 2011*).

## ➤ LUNG VOLUMES & LUNG CAPACITIES

***Tidal volume (TV):*** Amount of air inhaled or exhaled with each breath under resting conditions with a normal value about 500ml.

***Inspiratory reserve volume (IRV):*** The amount of air that can be forcefully inhaled after a normal tidal volume inhalation and the normal value is about 3000 ml.

***Expiratory reserve volume (ERV):*** Amount of air that can be forcefully exhaled after a normal tidal volume exhalation and in normal about 1000 ml.

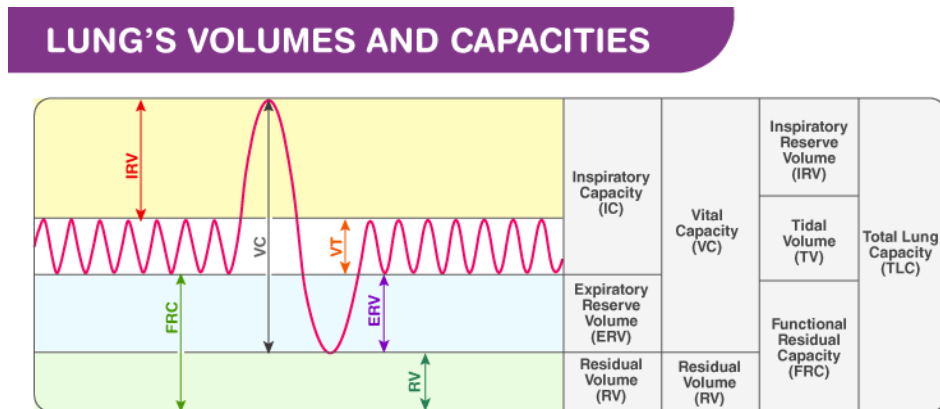
***Residual volume (RV):*** The amount of air that remains in the lungs after a forced exhalation and normally it is about 1200 ml.

***Total lung capacity (TLC):*** Maximum amount of air contained in lungs after a maximum inspiratory effort, about 5700 ml.

***Vital capacity (VC):*** Maximum amount of air that can be expired after a maximum inspiratory effort, about 4500 ml.

***Inspiratory capacity (IC):*** Maximum amount of air that can be inspired after a normal expiration, about 3500 ml.

***Functional residual capacity (FRC):*** Volume of air remaining in the lungs after normal tidal volume expiration, about 2200 ml (Soliman, 2020).



**Figure (2)**

Lung Volumes and Lung Capacities (*Delgado & Bajaj, 2019*)

### ➤ THE MEASURES

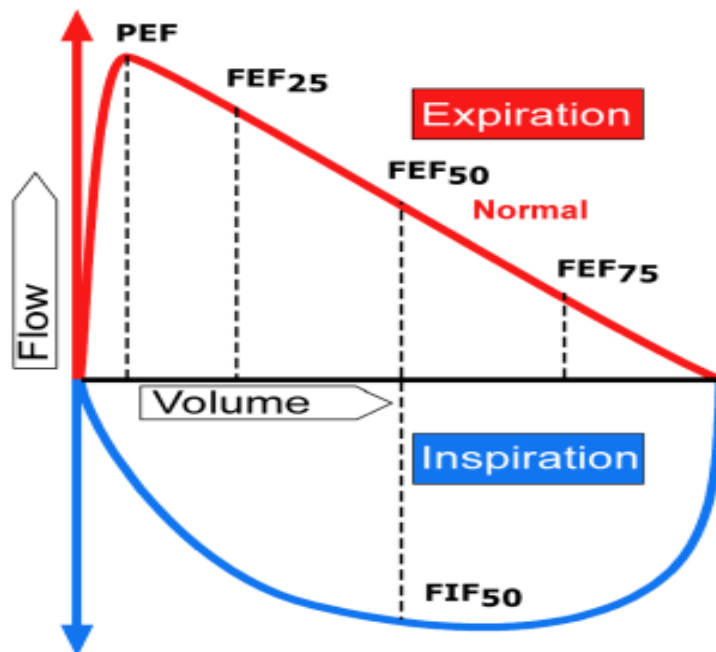
***Forced vital capacity (FVC):*** It's the maximum volume of air that is expired with the greatest force and speed after maximal inspiration to total lung capacity. The normal value is about 4.8 L in an adult person.

***Forced expiratory volume in 1<sup>st</sup> second (FEV<sub>1</sub>):*** It's the maximum volume of air expired by greatest force and speed after maximum inspiration to TLC at the first second. The normal value is 75-85%.

***FEV<sub>1</sub>/FVC ratio:*** Relation between both parameters. Normal values are approximately 75%.

**Maximal mid expiratory flow/ Forced expiratory flow at 25-75% of forced vital capacity ( $FEF_{25-75\%}$ ):** The amount of air expelled from the lungs during the middle half of the forced vital capacity.

**Mid expiratory flow/ Forced expiratory flow at 50% of forced vital capacity ( $FEF_{50\%}$ ):** Amount of air that was forcibly expelled in the first 50% of the total forced vital capacity (Moore, 2012).



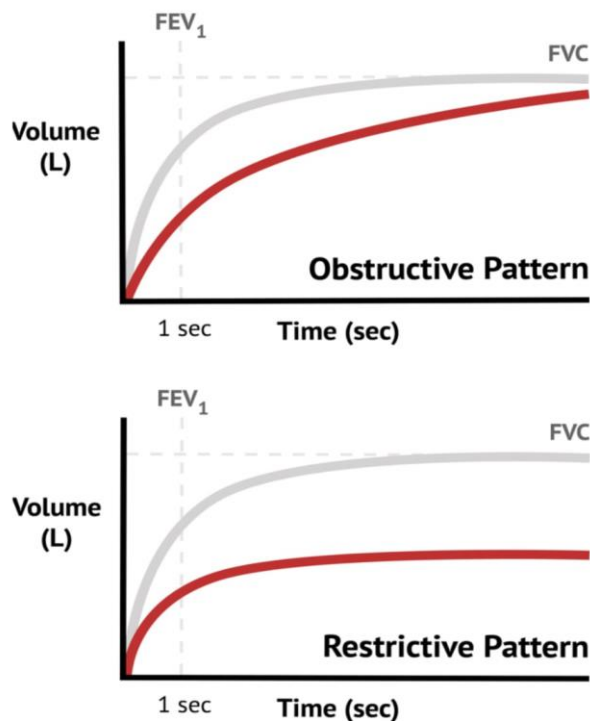
**Figure (3)**

Flow volume loop (Graham et al., 2019)

PEF=Peak Expiratory flow,  $FEF_{25}$ =Forced Expiratory flow at 25%,  $FEF_{50}$ = Forced Expiratory flow at 50%,  $FEF_{75}$ = Forced Expiratory flow at 75%,  $FIF_{50}$ =Forced Inspiratory Flow at 50%

## ➤ VOLUME TIME GRAPH

It represents spirometry results. In obstructive diseases, the flow is reduced (reduced  $FEV_1$ ) however the patient eventually almost meets a normal forced vital capacity as in Chronic Obstructive Pulmonary Disease (COPD). When the forced vital capacity is overall reduced, as is the  $FEV_1$ , this is suggestive of restrictive disease (*D'Urzo et al., 2011*).



**Figure (4)**

Obstructive & Restrictive Patterns of Volume-Time Graphs (*D'Urzo et al., 2011*)

L=Liter, sec=second

## ➤ FLOW VOLUME LOOP

It is usually done as a part of spirometry. The flow-volume loop is a plot of inspiratory and expiratory flow (on the Y-axis) against volume (on the X-axis) during the performance of maximally forced inspiratory and expiratory maneuvers. The patient is instructed to take a full inspiration (to total lung capacity), exhale forcefully and completely into the mouthpiece (to residual volume), and then inspire forcefully and fully back to total lung capacity (*Johnson & Theurer, 2014*).

In normal loop, the inspiratory limb is convex and symmetrical, with the linear expiratory limb. The obstructive loop shows a dipping or steeple pattern, with reduced flow and expiratory prolongation as in COPD, asthma, bronchiectasis, cystic fibrosis, bronchiolitis, and  $\alpha_1$ -antitrypsin deficiency. The restrictive pattern has reduced overall volume, with grossly normal shape e.g. pulmonary fibrosis, sarcoidosis, chest wall deformity, and neuromuscular diseases. Fixed upper airway obstruction has flattening of inspiratory and expiratory limbs like in Tracheal stenosis and goiter. Variable extra-thoracic obstruction shows flat inspiratory limb only, with no impairment of expiration as unilateral vocal cord paralysis, while variable intrathoracic obstruction has diminished expiratory limb with no impairment of inspiration for example Tracheomalacia (*Johnson & Theurer, 2014*).