Chapter One

Introduction

:Introduction .1.1

even since the discovery of x-ray by roentgen in 1895 . after that , the development of x-ray tube rapidly led to clinical applications , first as a diagnostic tool and later for therapy in patients with malignant disease . the discovery of radium by Marie and Pierre curie in 1898 also resulted in the use of radioactive materials for the approach to cancer. Radiotherapy plays an important role in the treatment of esophageal cancer in the pre-operative, post-operative management. planning target volume is defined base of internal target motion due to respiratory cycle , cardiac motion , and esophageal peristalsis which should be taken into account when planning is carried out, Thus the Determination of the appropriate planning target volume (PTV) is important to minimize locoregional recurrence and limit toxicity of normal surrounding tissues so accurate assessment of esophageal motion is important when determining an appropriate ITV and PTV .This study will use the CT data to measure on maximum esophageal displacement in all direction (Left, right , anterior ,posterior , upper and lower) . When treating .(esophageal malignancies with RT. (Randi J. Cohen.2010

1.2. Problem of study:

The most important issue in radiotherapy of all organ is that management of uncertainties and determination of physiologic motion is not accounted for as in the case when conventional radiotherapy technologies when treatment applied the thoracic and abdominal sites which always managed by increment of field size contributing more dose to normal tissue which lead to more tissue toxicity and therefore minimizing therapeutic ratio of radiotherapy treatment . Therefore measurement of maximum and minimum organ displacement due to respiratory movement is important by using CT planning and therefore improves advances in cancer management using radiotherapy .

:Significant of the Study .1.3

This study will carried to measure esophageal motion in external beam irradiation which lead to increase accuracy of determination of both PTV and ITV resulting in increase and enhancing therapeutic ratio and minimizing toxicity of both neighboring structure and rest volume of esophagus , this is readily carried by much more author in .literature

1.4. General Objective:-

The main aims of this study is to measurement of esophagus motion for external beam irradiation and measure the shaft of esophagus during the respiratory system ,in order to reduce the . exposure of healthy tissue during radiation treatment

1.5. Specific Objective: -

- Measurement of esophagus contour and body contour.
- To find correlation between body contour and esophagus contour.
- To find significant between inspiration and expiration.

1.6. Overview of the thesis:

This study falls into five chapters, Chapter one, which is an introduction, deals with theoretical frame work of the study and (Literature review). It presents the statement of the study problems, objectives of the study, chapter two deals with radiological physics and back ground. Chapter three deal with material and method, Chapter fours deals with results and discussions. Chapter five conclusions, recommendations and references.

Chapter two

Literature review

:Radiation Therapy for Esophageal Cancer .2.1

Radiotherapy (RT) plays an important role in the treatment of esophageal cancer, the three-dimensional conformal radiotherapy (3D-CRT) and intensity-modulated radiotherapy (IMRT) are the most important delivery Precise definition of (RT) fields is crucial for (RT)planning .Variation of target volume and displacement are the sources for RT fields and plan modification, such changes can be intrafractional or interfractional. Intrafractional esophageal motion can be attributed mostly to respiration, cardiac activity, and esophageal peristalsis, which has been well documented. But studies about interfractional esophageal motion were limited. As a consequence of radiation treatment, tumor volumes will change during radiotherapy, significant regression in lung tumor volume can occur by 3 weeks after beginning treatment. But so far, no conclusive data exist as to the nature of the tumor volume changes during radiotherapy for primary esophageal cancer, or the time at which these changes occur .Relative to three-dimensional computed tomography (3DCT), four-dimensional computed tomography (4DCT) Scan could not only obtain the volume of primary tumor GTV without motion information, for example, the GTV delineated on a single phase; but also obtain internal gross tumor volume (IGTV) volume with entire motion .information ,for example, the IGTV combined from 10 phases

In addition, we also can obtain IGTVMIP from the maximum intensity projection (MIP). Therefore, based on repeated4DCT, we can obtain more precise variation after get volume during entire treatment for primary esophageal cancer. In present study, we measured the interfractional displacement of the GTV and variation of GTV/IGTV in conventional fractioned RT during treatment for Primary esophageal cancer using .repeated 4DC

Radiation therapy can be an integral part of the treatment of esophageal cancer. However, since esophageal cancer is not exclusively treated with radiation therapy, it is important for patients to be treated in an environment that can offer multi-modality treatment involving radiation oncologists, surgeons, gastroenterologists, medical oncologists and .nutritionists

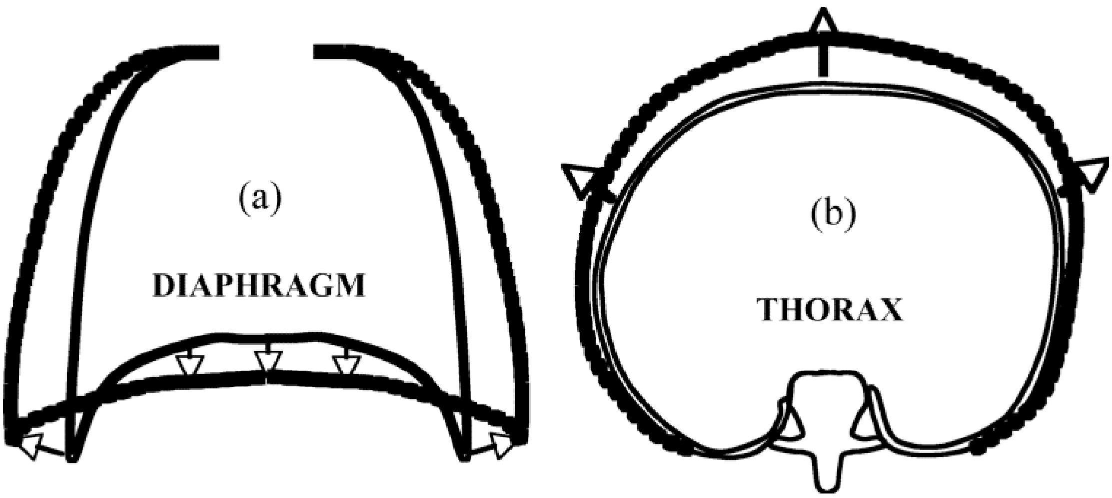
-:Objective of radiation therapy .2.2

The objective of radiation therapy to the esophagus is to kill cancer cells that could otherwise persist after therapy and cause the cancer to relapse locally. Radiation therapy uses high energy x-rays to kill cancer cells that remain in or near the esophagus and surrounding lymph nodes. Radiation therapy can be externally or internally delivered to the esophagus and surrounding lymph nodes. External beam radiation therapy (EBRT) delivers radiation from a machine outside the body, called a linear accelerator. EBRT treatments are typically delivered 5 days a week, for 2-6 weeks, depending on the overall goals of treatment and each treatment lasts between 10-15 minutes. The internal delivery of radiation therapy (brachy therapy) involves the placement of a radioactive isotope, such as .(iridium 192, within the esophagus (Texas Oncology 2014

Radiation therapy is the use of high-energy radiation to kill cancer cells. It is often combined with other types of treatment, such as chemotherapy .(chemo) and/or surgery, to treat esophageal cancer

:The mechanics of breathing .2.3

The primary function of the lung is to facilitate gas (O_2 and CO_2) exchange between blood and air, thus maintaining normal levels of gas pressure (partial pressure of oxygen, PO_2 , and partial pressure of carbon dioxide, PCO_2), in the arterial blood. Respiration is an “involuntary” action; i.e., a person would continue to breathe despite being unconscious. However, within limits, individuals are capable of controlling the frequency and displacement magnitude of their respiration as well as breath-holds. Unlike cardiac motion, the respiratory motion is not rhythmic. The periodic cycle of respiration is regulated through chemoreceptors by the levels of CO_2, O_2, and pH in the arterial blood. Of these, the most important is PCO_2. Reducing PCO_2, as occurs with hyperventilation, is a very effective means for reducing the urge to breathe, or sustaining a breath-hold. Under normal conditions, the O2 and blood pH stimuli play a small role in ventilation control. Anatomically, the lungs are held within the thoracic cavity, encased by the liquid-filled intrapleural space. Inhalation requires active participation of respiration muscles. During the inhalation part of quiet breathing, the increasing volume of the thoracic cavity draws air into the cavity. The most important muscle of inhalation is the diaphragm. As the diaphragm is contracted, it descends and the abdomen is forced inferiorly and interiorly, increasing the superior–inferior (SI) dimension of the chest cavity. The intercostals muscles connect adjacent ribs and also participate in normal inhalation. They contract during inhalation, pulling the ribs –Superiorly and interiorly, thereby increasing both the lateral and anterior .Posterior (AP) diameters of the thorax



(b) (a)

Figure 2.1 show the mechanics of breathing, (a) during inhalation, the diaphragm contracts, the Abdomen is forced down and forward, and the rib cage is lifted. (b) The intercostals muscles also contract to pull and rotate the ribs, resulting in increasing both the lateral and anterior–posterior (AP) diameters of the thorax.

[Reproduced from reference 226: J. B. West, *Respiratory Physiology: The Essentials*, [.Figures 3a,3b. © 1974, with permission from Lippincott Williams, and Wilkins

Exhalation is passive for quiet breathing. The lung and chest walls are .elastic and return passively to their pre-inhalation positions at exhale .Other ventilation muscles are involved only during active exhalation The tendency of the lung to recoil to its deflated volume is opposed by the tendency of the chest cage to bow out. The lung volume at the end of exhale, termed “functional residual capacity,” is at equilibrium or in the most relaxed state. Typically, the time taken to breathe in is longer than the time taken to breathe out. Tran pulmonary pressure, the pressure difference between respired gas at the mouth and the pleural pressure around the lungs, is reduced during inhalation and is recovered during Exhalation. During normal breathing, the deflating lung volume is larger than the inflating volume at the same trans pulmonary pressure. This is called hysteresis, attributable to the complex respiratory Pressure volume relationship of the lung and chest wall. Breathing pattern characterization measurements have been distinguished by posture (upright, prone, supine, lateral deceits), breathing type (chest or abdominal), and depth of respiration (shallow, normal, deep). For example, when the change in abdominal circumference was more than 10 mm greater than the change .in chest circumference, Davies et al.68 classified the breath as abdominal During normal quiet respiration, the lung volume typically changes by 10%3 to 25%; at deep inhale, the increase in lung volume is approximately three to four times that of normal breathing.69 for Radio therapeutic purposes, data measured in the upright posture are relevant only in limited situations (e.g., total body irradiation with the patient standing); therefore, we include only data taken from prone, supine, and .lateral positions

:Types of radiation therapy .2.4

:External-beam radiation therapy .2.4.1

This type of treatment focuses radiation from outside the body on the cancer. This is the type of radiation therapy most often used when trying to cure esophageal cancer. Before your treatments start, the radiation team will take careful measurements to determine the correct angles for aiming the radiation beams and the proper dose of radiation. Radiation therapy is much like getting an x-ray, but the radiation is stronger. The procedure itself is painless. Each treatment lasts only a few minutes, although the setup time – getting you into place for treatment – usually takes longer. Most often, radiation treatments are given 5 days a week for several .(weeks (Texas Oncology2014

:(Internal radiation therapy (brachy therapy .2.4.2

For this type of treatment, the doctor passes an endoscope (a long, flexible tube) down the throat to place radioactive material very close to the cancer. The radiation travels only a short distance, so it reaches the tumor but has little effect on nearby normal tissues. The radioactive source is then removed a short time later. Brachytherapy can be given two :ways

- For *high-dose rate (HDR) brachytherapy*, the doctor leaves the radioactive material near the tumor for a few minutes at a time, .which may require several treatments
- In *low-dose rate (LDR) brachytherapy*, a lower dose of radiation is put near the tumor for longer periods (1 or 2 days) at a time. The patient needs to stay in the hospital during this treatment, but it can .usually be completed in only 1 or 2 sessions

Brachytherapy is most often used with more advanced esophageal cancers to shrink tumors so a patient can swallow more easily. This technique cannot be used to treat a very large area, so it is better used as a way to relieve symptoms (and not to try to cure the cancer). (Texas (Oncology2014

:Measurement of esophagus motion during radiotherapy .2.5

In recent years, there have been significant improvements in the field of radiotherapy. Advances in computer hardware and software, and medical imaging have led to the development of new technology for improving external beam treatment planning, dose delivery and verification or .(radiotherapy. (Saeed Ahmad et al (2013

The principle of treatment planning is based on the attempt to arrange the treatment field so as to conform the high dose region to the target. It also attempts to minimize the radiation dose to normal structures and constrain the dose to critical structures below tolerance. Poor local tumor control or increased normal tissue complications may arise from inaccurate targeting of the tumor, failure to conform the high dose distribution to the target volumes and inaccurately delivered radiation doses. High radiation doses can cause severe health complications or death if delivered to the normal tissues, but these are critical and sometime necessarily needed to be given to a patient for his survival. Delivery of high radiation dose to the tumor without injuring proximal normal tissues requires accuracy and precision in the delivery of radiation to the tumor. Treatment outcome can be improved by improving accuracy and precision in delivering dose to the conformed target with the help of recently developed three dimensional imaging techniques. Confirmation of the accuracy of optimized calculations with verification evaluation techniques is vital in order to assure the quality of treatment. There are different possible errors and uncertainties that may exist in different areas in radiotherapy treatment of a patient. These errors need to be identified, and then removed where possible. The present review discusses in detail about the possible errors and uncertainties in radiotherapy treatment planning, by underscoring the significant areas in accuracy point of view, which broadly are accuracy of immobilization, organ movement, imaging, definition of target volumes, choice of dose distribution, treatment verification, machine checks, and Dosimetry protocols, . planning checks, patient documentation and treatment scheduling .(Saeed Ahmad et al (2013)

:Target volume determination .2.6

Defining the target volume is one of the important steps in treatment planning. Radiation oncologists currently define Planning Target Volume (PTV) empirically. Different problems of tumor localization and geometrical reconstruction has been investigated and solved in research works done previously. For accurate dose reporting, the volume of interest description is a pre-requisite for meaningful 2-D and 3-D ,treatment plans these regions of interests, target and normal structure Delineation should follow the International Commission on Radiation Units and Measurements (ICRU) 50 and 62 Reports. Volumes of interests for target delineation started from grass tumor volume to planning target volume. (Saeed Ahmad et al (2013). A radiation oncologist usually determines these anatomical clinical volumes, often after other relevant specialists such as pathologists or radiologists have been consulted. These entire volumes required different dose levels around their self for the best achievement of goal of radiation therapy. In some cases Grass Tumor

Volume (GTV) and Clinical Target Volume (CTV) are considered as same volume but in other cases these volumes usually differ by different margins as GTV plus very small cm values for regular or irregular GTV. To determine the target volume, any palpable masses are marked with wire and contrast medium may be placed in the bladder, rectum, vagina .or esophagus

The most difficult and subjective step in treatment planning is to quantify margins around grass tumor volume to define clinical target volume. It needs a lot of practice, clinical experience and the knowledge of the patterns of tumor recurrence so that precise data be used to define the margins around GTV. Different factors like age of the patient and considerations of normal tissue tolerance, may influence the maximum .((Saeed Ahmad et al (2013

Volume considered to be appropriate for treatment. The concepts of defining target volumes are also based on the risk of microscopic spread of the disease. There is a chance of error in defining PTV by different Oncologists, and sometimes even by the same oncologist on different occasions. National Cancer Institute (NCI) photon treatment group made efforts to standardize the process of defining PTV and international commission on radiological Units resulted in the definition of the PTV in relationship to the GTV and the clinical target volume (CTV). (Saeed .(Ahmad et al (2013

:Organ at risk (OARs) and normal tissue tolerance .2.7

Tumors arising from different regions of the body vary in pathology, size, shape etc. Added to the fact that there may be different pattern of Organs at Risk (OARs) present in close proximity, a variation of the level of treatment planning difficulties and complexity is expected. As a consequence, the degree of dose conformity to the PTV would also be .affected, where certain tumors are easier to conform than the others

Normal tissues are also irradiated along with the tumor but there is wide variation in the intrinsic radio sensitivity of different normal tissues and susceptibility to changes in fraction size. Therefore, the site and volume of normal tissues must be defined clearly. Increased shielding of Parts of normal organs is now feasible with the use of conformal blocks and multileaf collimators, with calculation of dose volume histograms for description of normal tissue doses. The treatment plans should be evaluated with reliable calculation systems for accurate and optimized outcome. Some of the organs have very small tolerance dose value for example lenses of eye are organs at risk during nasopharyngeal or brain .(tumor treatments. (Saeed Ahmad et al (2013

:Organ movement .2.8

Modern radiotherapy techniques intend to focus on the motion of target volumes, to guarantee the higher degree of accuracy. The treatment Of lung cancer with external beam therapy presents a challenge due to the existence of breathing motion during both the simulation and treatment. The effects of normal breathing on coverage are small on the average, with a less than 4% chance of a 10% or greater decrease in Tumors Control Probability (TCP). However, in patients with large respiration-induced motion, the effect can be significant and efforts to identify such patients are important. Stereotactic body frames are suggested to be used for real-time tumor-tracking, for an effective reduction in respiratory .(intrafractional organ motion. (Saeed Ahmad et al (2013

The driving tenet of conformal radiotherapy is the precise delivery of focal radiation doses to the target, so that an effective dose can be delivered while limiting concomitant normal tissue irradiation and related toxicity risk. Technical advancements, such as three-dimensional (3-D) treatment planning and IMRT (intensity-modulated radiation therapy) have provided significant gains in specifying means to provide such dose distributions. Accurate delivery, so that intended and actual doses agree, is a more complicated matter. The problems of patient positioning and motion have been studied extensively. Although there are currently areas that need further exploration, it is possible to consider the magnitude of various uncertainties in dose delivery due to patient position variation and organ movement, and to discuss rational strategies for dealing with these uncertainties in the context of precision radiotherapy. (Saeed Ahmad et al .((2013

:Description of the Problem of Geometric Variation .2.9

The International Congress on Radiological Units (ICRU) has addressed the relative problem of geometric variations. In reports 50 and 62, concepts are evolved to attempt to standardize means of reporting doses. Some of the concepts presented in these reports have served as the basis for numerous investigations over the past few years, and have been adopted as standards for clinical trials. A brief discussion of the key .concepts as they apply to geometric variation follows

The key structures that are delineated are the gross tumor volume (GTV) and organs at risk (OARs). The GTV is generally defined as the visible target, that is, that can be delineated from imaging or related information. The OARs are tissue structures that are dose limiting due to risk of (radiation-induced toxicity. (Faiz Khan, 2007

The next volume of interest is the clinical target volume (CTV). This target volume ideally expands about the GTV to include a reasonable expectation of the true target extent on a (static) patient model. The basis for CTV expansions includes intraobserver as well as interobserver variations in tumor delineation, as well as a reasonable expectation of the .extent of disease below the sensitive range of the imaging modality

Geometric uncertainty influences both the target volume as well as OARs. To ensure adequate geometric coverage of the target, the CTV is expanded. Internal organ movement is encompassed by an internal margin (IM) about the CTV to make the internal target volume (ITV), and setup error influences a setup margin (SM) about the ITV to yield the (planning target volume (PTV). (Faiz khan, 2007

When the patient is imaged to define the CTV and critical structures, the position is sampled. In general, this sample occurs once, specifically during the computed tomography (CT) scan for treatment planning. To obtain this sample, the patient is immobilized and positioned, with typical reference marks placed on the skin and/or immobilization device at the principal axes of the CT scanner for verification of position and orientation. The sample of the patient serves as the model for treatment planning, and all subsequent targeting and density modeling is based on the information obtained during this session (Faiz Khan, 2007). Determination of the appropriate ITV and PTV. Physiologic esophageal motion results from the respiratory cycle, cardiac motion, and esophageal peristalsis. Motion of the esophagus has been investigated in multiple settings. Using lower esophageal sphincter pressure readings, axial An accurate assessment of esophageal motion is important when determining an motion has been described as approximately 4 mm in the thoracic and 6 mm in the abdominal esophagus . Lateral esophageal motion using digital cine-fluoroscopic imaging performed prior to and after cardiac catheter ablation for a trial fibrillation was documented to be greater than or equal to 2 cm in two-thirds of patients . Computed tomography (CT) scans obtained during inhalation and exhalation phases demonstrate radial displacement of the esophagus on the order of 3 mm in the superior cervical esophagus, 5 mm at the thoracic inlet, 6–7 mm at the carina level, and 10–12 mm at the gastro-esophageal (GE) junction. (Lorchel et al) recommended a 10 mm ITV margin based on their studies using breath hold CT scans performed at inspiration and expiration. In breath hold CT imaging using the optic flow method, esophageal motion was noted to be up to 14 mm with greatest motion at the GE junction. Using 4-dimensional CT (4DCT) during normal respiration, (Dielman et al) determined that a lateral margin encompassing 95% of esophageal motion in the proximal, mid, and caudal esophagus would be 5 mm, 7 mm, and 9 mm, respectively. In the anterior-posterior direction, the reported margins were 5 mm, 6 mm, and 8 mm .Patel et al. recommended 1.5 cm superior-inferior, 0.75 cm left-right, and 0.75 cm anterior-posterior to cover >95% of esophageal primary tumors based on their study of respiratory motion of primary esophageal cancer patients using 4DCT .Inter-fraction esophagus motion during radiation treatment, as measured using daily CT imaging of six patients with a Siemens PRIMATOM (CT-on-rails™) system, supported a margin of 2–5 mm in all directions for esophageal motion, though this was only presented in abstract format. Esophageal motion during radiation therapy has not been well described in our review of the literature. The aim of the present study was to report our results concerning inter- and intra-fraction esophageal motion in patients being treated for cancer of the esophagus and its implications for appropriate (treatment margins. (Cohen et al .2010

:Four-dimensional radiotherapy .2.10

Four-dimensional "4D" radiotherapy is the explicit inclusion of the temporal changes in anatomy during the imaging, planning, and delivery of radiotherapy. Temporal anatomic changes can occur for many reasons, though the focus of the current investigation is respiration motion. The aim of this four dimensional radiotherapy is to develop 4D radiotherapy treatment-planning methodology for DMLC-based respiratory motion tracking. A 4D computed tomography "CT" scan consisting of a series of eight 3D CT image sets acquired at different respiratory phases was used for treatment planning. Deformable image registration was performed to map each CT set from the peak-inhale respiration phase to the CT image sets corresponding to subsequent respiration phases. Deformable registration allows the contours defined on the peak-inhale CT to be automatically transferred to the other respiratory phase CT image sets. Treatment planning was simultaneously performed on each of the eight 3D image sets via automated scripts in which the MLC-defined beam aperture conforms to the PTV !which in this case equaled the GTV due to CT scan length limitations" plus a penumbral margin at each respiratory phase. The dose distribution from each respiratory phase CT image set was mapped back to the peak-inhale CT image set for analysis. The treatment intent of 4D planning is that the radiation beam defined by the DMLC tracks the respiration-induced target motion based on a feedback loop including the respiration signal to a real-time MLC controller. Deformation with respiration was observed for the lung tumor and normal tissues. This deformation was verified by examining the mapping of high contrast objects, such as the lungs and cord, between image sets. For the test case, dosimetric reductions for the cord, heart, and lungs were found for 4D planning compared with 3D planning. 4D radiotherapy planning for DMLC-based respiratory motion tracking is feasible and may offer tumor dose escalation and/or a reduction in treatment-related complications. However, 4D planning requires new planning tools, such as deformable registration and automated treatment planning on multiple .CT image sets

2.11. Previous study:

Wang et al (2013) mentioned in their study of, Detection of interfraction displacement and volume variance during radiotherapy of primary thoracic esophageal cancer based on repeated four-dimensional CT scans, used 4DCT data sets were acquired at the time of treatment simulation and every ten fraction for each of 32 patients throughout treatment. Scans were registered to baseline (simulation) 4DCT scans by using bony landmarks. The gross tumor volumes (GTVs) were delineated on each data set. Coordinates of the GTV centroids were acquired on each respiration phase. Distance between center of the GTV contour on the simulation scan and the centers on subsequent scans were used to assess interfraction displacement between fractions. Volumes were constructed using three approaches: The GTV delineated from the maximum intensity projection (MIP) was defined IGTVMIP, all 10 GTVs were combined to form IGTV 10, GTV mean was the average of all 10 phases of each GTV. Found Interfraction displacement in left-right (LR), anterior-posterior (AP), superior-inferior (SI) directions and 3D vector were 0.13 ± 0.09 cm, 0.16 ± 0.12 cm, 0.34 ± 0.26 cm and 0.43 ± 0.24 cm, respectively between the tenth fraction and simulation 4DCT scan. 0.14 ± 0.09 cm, 0.19 ± 0.16 cm, 0.45 ± 0.43 cm and 0.56 ± 0.40 cm in LR, AP, SI and 3D vector respectively between the twentieth fraction and simulation 4DCT scan. Displacement in SI direction was larger than LR and AP directions during treatment. For distal esophageal cancer, increased interfraction displacements were observed in SI direction and 3D vector (P = 0.002 and P = 0.001, respectively) during radiotherapy. The volume of GTV mean, IGTVMIP, and IGTV10 decreased significantly at the twentieth fraction for middle (median: 34.01%, 33.09% and 28.71%, respectively) and distal (median: 22.76%, 25.27% and 23.96%, respectively) esophageal cancer, but for the upper third, no significant variation were observed during .radiotherapy

Hideomi Yamashita and et al, (2010) stated in their study of Patient setup error and day-to-day esophageal motion error analyzed by cone-beam computed tomography in radiation therapy little has been reported on the errors of setup and daily organ motion that occur during radiation therapy (RT) foresophageal cancer. The purpose of this paper was to determine the margins of esophageal motion during RT. Methods and materials. The shift of the esophagus was analyzed in 20 consecutive patients treated with RT for esophageal cancer from November 2007. CT images for RT planning were used as the primary image series. Computed tomography (CT) images were acquired using an Elekta Synergy System, equipped with a kilovoltage-based cone-beam CT (CBCT) unit. The subsequent CBCT image series used for daily RT setup were compared with the primary image series to analyze esophageal motion. CBCT was performed before treatment sessions a total of 10 times in each patient twice a week. The outer esophageal wall was contoured on the CBCT images of all 200 sets. *Results.* In the 200 sets of CBCT images, the mean (absolute) _ standard deviation (SD) of setup errors were 2 _/– 2 mm (max, 8 mm) in the lateral direction, 4 _/– 3 mm (max, 11 mm) in the longitudinal direction, and 4 _/– 3 mm (max, 13 mm) in the vertical direction. Additionally, the mean _ SD values of daily esophageal motion comparing the CBCT with RT planning CT were 5 _/– 3 mm (max, 15 mm) in the lateral direction and 5 _/– 3 mm (max, 15 mm) in the vertical direction. *Conclusions.* Our data support the use of target margins (between the clinical target volume and planning target volume) of 9 mm for day-to-day esophageal motion and 8 mm for .patient setup in all directions, respectively

Massima et al (2006) mentioned in their study of Use of motion tracking in stereotactic body radiotherapy that Evaluation of uncertainty in off-target dose distribution and optimization strategies spatial accuracy in extracranial radiosurgery is affected by organ motion. Motion tracking systems may be able to avoid PTV enlargement while preserving treatment times, however special attention is needed when fiducial markers are used to identify the target can move with respect to organs at risk (OARs). Ten patients treated by means of the Synchrony system were taken into account. Sparing of irradiated volume and of complication probability were estimated by calculating treatment plans with a motion tracking system (Cyber knife Synchrony, Sunnyvale, CA, USA) and a PTV-enlargement strategy for ten patients. Six patients were also evaluated for possible inaccuracy of estimation of dose to OARs due to relative movement between PTV and OAR during respiration. Dose volume histograms (DVH) and Equivalent Uniform Dose (EUD) were calculated for the organs at risk. In the cases for which the target moved closer to the OAR (three cases of six), a small but significant increase was detected in the DVH and EUD of the OAR. In three other cases no significant variation was detected. Mean reduction in PTV volume was 38% for liver cases, 44% for lung cases and 8.5% for pancreas cases. NTCP for liver reduced from 23.1 to 14.5% on average, for lung it reduced from 2.5 to 0.1% on average. Significant uncertainty may arise from the use of a motion-tracking device in determination of dose to organs at risk due to the relative motion between PTV and OAR. However, it is possible to limit this uncertainty. The breathing phase in which the OAR is closer to the

PTV should be selected for planning. A full understanding of the dose distribution would only be possible by means of a complete 4D-CT .representation

Jacob et al, (2010) stated in their study of Motion of the Esophagus Due to Cardiac Motion, When imaging studies (e.g. CT) are used to quantify morphological changes in an anatomical structure, it is necessary to understand the extent and source of motion which can give imaging artifacts (e.g. blurring or local distortion). The objective of this study was to assess the magnitude of esophageal motion due to cardiac motion. We used retrospective electrocardiogram-gated contrast-enhanced computed tomography angiography images for this study. The anatomic inspiration breath hold with the patients’ arms raised above their shoulders, in a position similar to that used for radiation therapy. The esophagus was delineated on the diastolic phase of cardiac motion, and deformable registration was used to sequentially deform the images in nearest-neighbor phases among the 10 cardiac phases, starting from the diastolic phase. Using the 10 deformation fields generated from the deformable registration, the magnitude of the extreme displacements was then calculated for each voxel, and the mean and maximum displacement was calculated for each computed tomography slice for each patient. The average maximum esophageal displacement due to cardiac motion for all patients was 5.8 mm (standard deviation: 1.6 mm, maximum: 10.0 mm) in the transverse direction. For 21 of 26 patients, the largest esophageal motion was found in the inferior region of the heart; for the other patients, esophageal motion was approximately independent of superior-inferior position. The esophagus motion was larger at cardiac phases where the electrocardiogram R-wave occurs. In conclusion, the magnitude of esophageal motion near the heart due to cardiac motion is similar to that due to other sources of motion, including respiratory motion and intra-fraction motion. A larger cardiac motion will result into larger esophagus .motion in a cardiac Cycle

Randi et al,(2010) stated in their Esophageal Motion During Radiotherapy: Quantification and Margin Implications **,** To evaluate inter- and intra-fraction esophageal motion in the right-left (RL) and anterior-posterior (AP) directions using computed tomography (CT) in esophageal cancer patients. Used Eight patients underwent CT simulation and CT-on-rails imaging before and after radiotherapy. Inter-fraction displacement was defined as differences between pretreatment and simulation images. Intra-fraction displacement was defined as differences between pre- and post-treatment images. Images were fused using bone registries, adjusted to the carina. The mean, average of the absolute, and range of esophageal motion were calculated in RL and AP directions, above and below the carina. Found Thirty-one CT image sets were obtained. The incidence of esophageal inter-fraction motion ≥5 was 24% and ≥10 mm was 3%; intra-fraction motion ≥ 5mm was 13% and ≥10 mm was 4%. The average RL motion was 1.8±5.1 mm, favoring leftward movement, and the average AP motion was 0.6±4.8 mm, favoring posterior movement. Average absolute motion was 4.2 mm or less in RL and AP directions. Motion was greatest in the RL direction above the carina. Coverage of 95% of esophageal mobility requires 12mm left, 8mm right, 10mm posterior, and .9mm anterior margins

Chapter Three

Materials and Methods

3.1Materials:

The data was analyzed with Mat lab program under windows with t-test to assess the Motion of Esophagus in Radiation Therapy. For patient's treatment using external beam radiotherapy machines (linear acceralator and Co 60), the procedure is based on the acquisition of CT scan sequences during simulation before treatment. .

:3.2. Patient

Patients selected criteria if patients with cancer of esophagus s they treated in hospital of radiation and isotopes center of Khartoum (RICK).

3.3. Methods

This study included 30 patients. Patient's data was brought from hospital of radiation and isotopes center of Khartoum (RICK).

3.3.1. Study duration:

This study was done in period from June to December 2014

3.3.2. Study place:

This study carried out in radiation and isotope center of Khartoum (RICK).

3.3.3. Method of data collection

The Data was collected when treated patient is simulated using CT simulator of esophagus and chest organ treatment of cancer where the respiratory gated, three dimensional CT imaging of the full expiratory motion and minimum and maximum displacement was measured based in .CT data

3.3.4. Method of data analysis:

The data will analyze with Mat lab program under windows with t-test to assess the Motion of Esophagus in Radiation Therapy. For patients treatment using external beam radiotherapy machines (linear acceralator and Co 60), the procedure is based on the acquisition of CT scan sequences, followed by an automatic detection of the movement using cross-correlations with matched filters by using image registration technique. Image registration is the process of aligning two or more images of the same scene. Typically, one image, called the base image or reference image, is considered the reference to which the other images, called input images, are compared. The object of image registration is to bring the input image into alignment with the base image by applying a spatial transformation to the input image. The differences between the input image and the output image might have occurred as a result of terrain relief and other changes in perspective when imaging the same scene from different viewpoints. Lens and other internal sensor distortions, or differences between sensors and sensor types, can also cause distortion A spatial transformation maps locations in one image to new locations in another image. (For more details, see Spatial Transformations) Determining the parameters of the spatial transformation needed to bring the images into alignment is a key to the image registration process. Image registration is often used as a preliminary step in other image processing applications. For example, you can use image registration to align satellite images of the earth's surface or images created by different medical diagnostic modalities (MRI and SPECT). After registration, you can compare features in the images to see how a river has migrated, how an area is flooded, or to see .if a tumor is visible in an MRI or SPECT image

3.3.4.1. Image registration:

Image registration is the process of aligning two or more images of the same scene. Typically, one image, called the **base** (inspiration) image or ***reference*** (expiration) image, is considered the reference to which the other images, called ***input*** images, are compared. The object of image registration is to bring the input image into alignment with the base image by applying a spatial transformation to the input image. The differences between the input image and the output image might have occurred as a result of terrain relief and other changes in perspective when imaging the same scene from different viewpoints. Lens and other internal sensor distortions, or differences between sensors and sensor types, can also cause distortion. A spatial transformation maps locations in one image to new locations in another image. Determining the parameters of the spatial transformation needed to bring the images into alignment is key to the image registration process. Image registration is often used as a preliminary step in other image processing applications. For example, it can use image registration to align satellite images of the earth's surface or images created by different medical diagnostic modalities (MRI and SPECT). After registration, researcher will be able

.to see if a tumor is visible in an MRI or SPECT image or not

Point Mapping .3.3.4.2

The Image Processing Toolbox software of Mat Lab program provides tools to support point mapping to determine the parameters of the transformation required to bring an image into alignment with another image. In point mapping, researcher picked points in a pair of images (inspiration and Expiration images) that identify the same feature or landmark in the images. Then, a spatial mapping is inferred from the Positions of these control points. Researcher might need to perform several iterations of this process, experimenting with different types of transformations, before researcher achieve a satisfactory result. In some cases, researcher might perform successive registrations, removing Gross global distortions first, and then removing smaller local distortions in .subsequent passes

The following figure provides a graphic illustration of this process. This (process is best understood by looking at an Example (figure 2

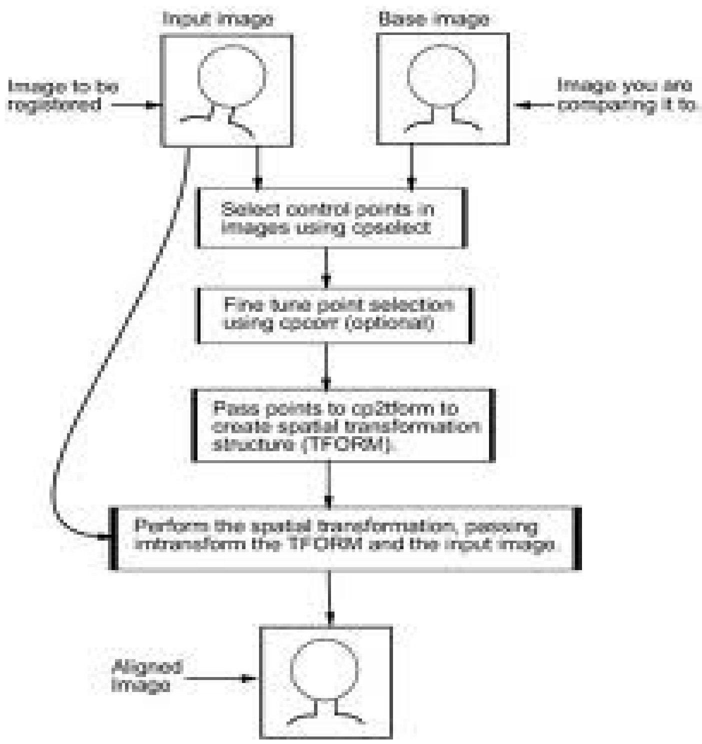


Figure 3.1. Show the illustration image registration

If researcher needs to perform the same kind of registration for many images, researcher automates the process by putting all the steps in a script. For example, researcher could create a script that launches the Control Point Selection Tool with an input and a base image. The script could then use the control points selected to create a TFORM structure and pass the TFORM and the input image to the imtransform function, outputting the registered image. To do this, researcher specifies the 'Wait' option when researcher calls cpselect to launch the Control Point Selection Tool. With the 'Wait' option, cpselect blocks the MATLAB command line until control points have been selected and returns the sets of control points selected in the input image and the base image as a return values. If researcher does not use the 'Wait' option, cpselect returns control immediately and your script will continue without allowing time for control point selection. In addition, without the **'Wait'** option, cpselect .does not return the control points as return values

:Image Registration Steps using Mat Lab .3.3.4.3

Step 1: Read the Images

In this example, the base image is ***inspire1.tif***, the inspiration position. It is a panchromatic (grayscale) image, supplied by the scanning patients using CT scanning which has been orthorectified to remove camera, perspective, and relief distortions (via a specialized image transformation process). The exspire1 is also medical registered the columns and rows of the digital inspire1 image are aligned to the axes of the Massachusetts State Plane coordinate system. In the exspire1, each pixel center corresponds to a definite chest organ location. The image to be registered is ***exspire1.tif***, a digital CT scan radiograph and is a visible-color RGB image. The medical image is geometrically uncorrected: it includes for example camera perspective, terrain and building relief, internal (lens) distortions, and it does not have any particular alignment or registration with respect to the human body. The following example reads both images into the MATLAB workspace and displays them using

(inspire1 = imread ('inspire1.tif'); Figure, imshow (inspire1

;('exspire1 = imread ('exspire1.tif

(Figure, imshow (exspire1) (figure 6

Researcher does not have to read the images into the MATLAB workspace. The cpselect function accepts file specifications for grayscale images. However, if researcher wants to use cross-correlation to tune .control point positioning, the images must be in the workspace

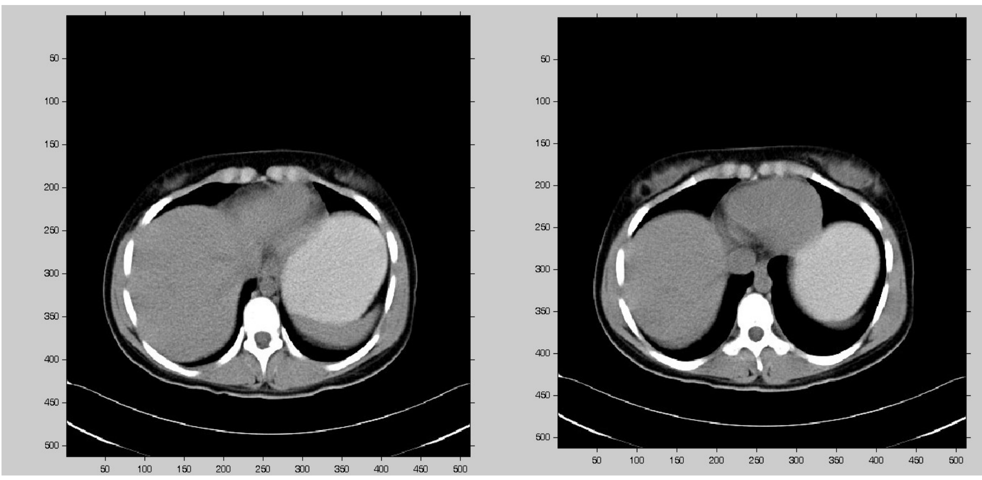


Figure 3.2. Show the Inspiration and Expiration phase images

Step 2: Choose Control Points in the Images

The toolbox provides an interactive tool, called the Control Point Selection Tool, which researcher can use to pick pairs of corresponding control points in both images. Control points are landmarks that you can find in both images, like a road intersection, or a natural feature. To start this tool, researcher enters cpselect at the MATLAB prompt, specifying as (arguments the input and base images. Cpselect (inspire1, expire1 The Control Point Selection Tool displays two views of both the inspiration phase image and the expiration phase image I This was an important step that used cross-correlation to adjust the position of the control points researcher selected with ***cpselect***. To use cross-correlation, features in the two images must be at the same scale and have the same orientation. They could not be rotated relative to each other. Because the ,Concord image was rotated in relation to the base image

cpcorr could not tune the control points

Step 3: Save the Control Point Pairs to the MATLAB Workspace

In the Control Point Selection Tool, a researcher clicked the File menu and chooses the Export Points to Workspace option. the following set of control points in the input image represented spatial coordinates; the left column lists coordinates, the right column lists y-coordinates for different .Organs

Organ: Left Lung

(Input points = (inspiration Phase

180.7870 235.5102

201.7767 213.7709

(Base points= (expiration phase

185.2848 229.5132

206.2745 207.7738

3.3.5. Method of data storage:

The data stored securely in password personal computer (PC)

3.3.6. Ethical issue:-

- Permission from radiotherapy department

Chapter Four

The results

This experimental study was conducted in College of Medical Radiological Science, Sudan University of Science and Technology, radiation Isotopes Center of Khartoum (RICK). The samples were included 30 patients. The main objective of this research was to measure of the esophagus motion for external beam therapy and measure the shaft of esophagus during the respiration system in order to reduce .the exposure of healthy tissue during radiation treatment

For the group of patients where age distribution in sample of study was measured as 3.3 % of patients were within the 25-35 years age range, 16.7 % of patients were within the 36-45 years age range, 53.3 % of patients were within the 46-55 years age range, 26.7 % of patients were within the 56-65 years age range. The key parameters for this group are shown in Table below.

Table show the age distribution for both gender among the study sample

Age Group (years)	***Male***	***Female***
25-35	***1***	***-***
36-45	***3***	***2***
46-55	***12***	***4***
56-65	***6***	***2***

Total geometrical error is built up of many smaller errors, which are presented by systemic and the random deviations can be predicted and use for correction strategy. Systematic errors introduced by target volume delineation, organ motion, and set-up errors should be reduced by clear delineation protocols, multimodality imaging, correct CT scan procedures, and by the application of electronic portal imaging with decision rules (protocols).The results showed the radiation oncologist to take suitable countermeasures in case of significant errors (body contour was equally (7.23 ± 2.47 mm) and for esophagus was (8.42 ± 3.07 mm). In addition, the uses of the image registration technique for automatic position control. When imaging axially, inspiration and expiration phase displacement corresponds to chest organs positions motion were measured. This was measurements and the resulting relative organs position of body contour and esophagus were shown in figure 4-1, figure 4-2 and figure 4-3 respectively showed the breathing wave form of different patients and Cross-correlation between inspiration and expiration phase. The thresholds were set for treatment at end expiration at the beginning of the session; however, the breathing wave form was irregular during the session, resulting in beam enable signals at unintended points in the breathing cycle arrows Figure.4-2 and Figure 4-3 showed a breathing wave form for the same patient in (expiration phase).

There is a difference in average between the body contour position regarding (X-reading) to the inspiration phase which is equal to 9.06 ± 2.48 and 10.5 ±0.92. This difference was significant at p= .05 using t-test with t= 3.91 and p=0.0008. As well as there is differences in average between the body contour positions regarding to (Y-reading) the inspiration phase which is equal to 9.03 ± 2.52 and 11.3 ±3.90. This difference was significant at p= .05 using t-test with t= -2.45 and p‹ 0.001 .((p=0.023

Figure 4-1. Body contour reading during inspiration and expiration phases of body .contour

There is a difference in average between the oesophagus position regarding to (X-reading) of the inspiration phase which is equal to 10.16 ± 3.31 and 10.6 ±3.02. This difference was no significant at p= .05 using t-test with t= -9.74 and p=0.001. As well as here is a difference in average between the oesophagus position regarding to (Y-reading) of the inspiration phase which is equal to 8.6 ± 2.02 and 12.7 ±1.12 This difference was significant at p= .05 using t-test with t= .162 and p=0.87 .as shown in figure 4-2

Figure 4-2. Oesophagus reading during inspiration and expiration phases of body .contour

Contour.Figure 4-3. Correlation between body Contour and oesophagus

Esophagus displacement (mm) ¿ -0.669(body contour displacement) + 11.57

Chapter Five

Discussion, Conclusion and Recommendations

5.1. Discussion:

Organ motion in Radiotherapy induce an error in dose received by the tumour therefore this experimental study conducted to evaluated the organs motion in external beam radiotherapy. Oesophageal cancer accounts for 5% of all GI cancers. There are 16,470 new cases and 14,280 deaths from oesophageal cancer each year globally. It is the sixth leading cause of death from cancer worldwide. Incidence of oesophagus cancer increases with age, peaks at sixth to seventh decade. The male to female ration is 3.5 to 1. In Sudan oesophagus cancer is sixth common cancer. For the group of patients where age distribution in sample of study was measured as 3.3 % of patients were within the 25-35 years age range, 16.7 % of patients were within the 36-45 years age range, 53.3 % of patients were within the 46-55 years age range, 26.7 % of patients were within the 56-65 years age range. The key parameters for this group are shown in Table 4-1. The outcome of the Laser positioning system confirms its potential as tool for patient repositioning and automatic or manual detection of errors caused by breathing or other unpredictable movements. The laser alignment system feedback on the patient's position given by the system provides operator with appropriate visual indices and allows them to take suitable countermeasures in case of significant failures. In addition, the use of system output may be used for automatic control is envisaged. The maintenance of technical condition related errors within known and acceptable limits must be ensured by regular applying of Quality Assurance (QA) procedures for all equipment involved in radiotherapy procedures chain. Total geometrical error is built up of many smaller errors which are presented by systemic and the random deviations can be predicted and use for correction strategy. Systematic errors introduced by target volume delineation, organ motion, and set-up errors should be reduced by clear delineation protocols, multimodality imaging, correct CT scan procedures, and by the application of electronic portal imaging with decision rules (protocols). The mobility of chest structure example esophagus ranged from 3.17 mm up to 14.5 mm with an average of 8.42 mm this movement was appertained between the inspiration and expiration for right and left lung in x, z direction and there are significant difference in the location of the chest structure using t-test at $p = 0.05$ (table 4-1 and table 4-2). Tsukuda et al (2007), Curtin et al (2005), Kauczor and Plathow (2008) studied impaired respiratory mechanics and Respiratory motions of the diaphragm and chest wall (D/CW) using CT and MR imaging in healthy subjects.

5.2. Conclusion:

During a fractionated course of radiotherapy, variations in patient position and in alignment of beams will occur both intra- and inter-fractionally, and a margin for set-up error must be incorporated into the CTV-PTV margin. Errors may be systematic or random. Systematic errors may result from incorrect data transfer from planning to dose delivery, or inaccurate placing of devices such as compensators, shields, etc. Such systematic errors can be corrected. Random errors in set-up may be operator dependent, or result from changes in patient anatomy from day to day which are impossible to correct. Accuracy of set-up may be improved with better immobilization, attention to staff training and/or implanted opaque fiducially markers, such as gold seeds, whose position can be determined in three dimensions at planning, and checked during treatment using portal imaging or IGRT. Translational errors can thereby .be reduced to 1 mm and rotational errors to 1 mm

In conclusion, individualized assessment of tumor mobility can improve the accuracy of target definition in patients who are undergoing SRT for stage I and stage II patients. Definition of the target volume based on a single CT scan with a margin of 10 mm is clearly inappropriate. A single 4DCT scan can replace the use of multiple unmonitored CT scans in defining individualized target volumes more accurately, in particular for highly mobile tumors. This approach can further improve tumor control .and limit the likelihood of treatment-related toxicity

5.3. Recommendations:

The recommendations of this study are:

- Radiotherapy facility should use the respiratory management devices with collaboration with record-and-verify systems
- When deriving CTV–PTV margins for treatment planning specific .to respiratory motion should be taken into account
- The uncertainties of esophagus in radiotherapy planning should be .considered
- Further studies were recommended with more patients and using .more than one breathing measurement technique

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