CONVENTIONAL VERSUS THREE DIMENSIONAL CONFORMAL RADIATION THERAPY AND CONCURRENT CHEMOTHERAPY FOR PATIENTS WITH INOPERABLE, NON-SMALL CELL LUNG CANCER

Thesis
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Ahmed Maamoun Nofal

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LIST OF ABBREVIATIONS

2D	2-dimentional.
3D	3-dimentional
3D-CRT	3-dimentional conformal radiation therapy
4D-CT	4-dimentional computed tomography.
ACR	American college of radiology.
ADL	Activity of daily living.
AG3T	Acute grade 3 toxicity.
AJCC	American joint committee on cancer.
BAC	Broncho-alveolar carcinoma.
CALGB	Cancer and leukemia group B
CCRT	Concurrent chemoradiotherapy.
CHART	Continuous hyperfractionated accelerated radiotherapy.
CR	Complete remission.
CT	Computed tomography.
CTCAE	Common terminology criteria for adverse events.
CTH	Chemotherapy.
CTV	Clinical target volume.
DM	Distant metastases.
ECOG	Eastern cooperative oncology group.

List of abbreviations

EGFR	Epidermal growth factor receptor.
ENI	Elective nodal iradiation.
EORTC	European organization for research and treatment of cancer.
FDA	Food and drug administration.
FDG	Fluorodeoxyglucose.
GTV	Gross target volume
HART	Hyperfractionated accelerated radiotherapy.
HIPPA	Health insurance probability and accountability act.
ICRU	International commission on radiation units.
IGRT	Image-guided radiotherapy.
IMRT	Intensity modulated radiotherapy
LAMP	Locally advanced multimodality protocol.
LF	Local failure.
LRC	Loco-regional control.
LRR	Loco-regional recurrence.
NCCTG	North central cancer treatment group.
NCI	National cancer institute.
NR	No response.
NSCLC	Non-small cell lung cancer.
OR	Overall response.
OS	Overall survival.

PCI	Prophylactic cranial irradiation.
PET	Positron emission tomography.
PR	Partial response.
PS	Performance status.
PTV	Planning target volume.
RT	Radiation therapy.
RTOG	Radiation therapy oncology group
SBRT	Stereotactic body radiotherapy.
SCLC	Small cell lung cancer.
SVC	Superior vena cava.
SWOG	Southwest oncology group.
TBFNA	Transbronchial fine-needle aspiration.
TGF-beta	Transforming growth factor beta
VEGF	Vascular endothelial growth factor.

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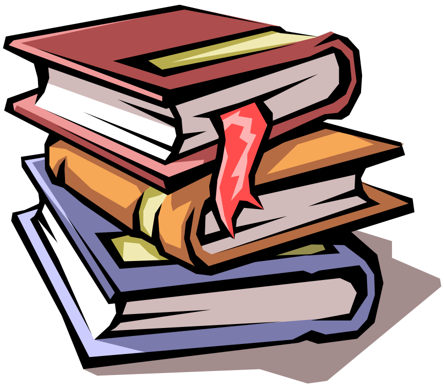

INTRODUCTION AND AIM OF THE WORK

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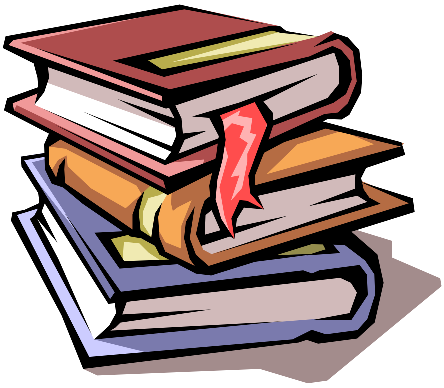
Approximately a third of patients with newly diagnosed non-small cell lung cancer (NSCLC) have locally or regionally advanced disease not amenable for surgical resection. Concurrent chemoradiation is the standard of therapy for patients with unresectable locally advanced NSCLC who have a good performance status and no significant weight loss ***(Govindan et al., 2008)***.

Concurrent chemoradiation (chemo-RT) is the standard treatment for patients with inoperable locally advanced NSCLC ***(Fournel et al., 2005)***. In order to improve the outcome obtained with concurrent chemo-RT, clinical research is focusing on additional combination chemotherapy administered in the induction or consolidation setting in addition to the standard concurrent chemo-RT ***(Choy et al., 2002)***.

Improved radiation therapy techniques using precise targeting of the tumors have played a key role in achieving more favorable overall outcome with less toxicity in patients with locally advanced NSCLC. Moreover, it has been shown that higher than conventional doses of thoracic radiation can be administered safely in combination with chemotherapy. Omission of elective nodal irradiation (ENI) was associated with a very low incidence of isolated nodal failure (INF), and allowed for more radiation dose escalation with acceptable therapeutic ratio. The integration of functional imaging with FDG-PET for radiotherapy treatment planning is an important advance that will further mitigate the potential impact of ENI in locally advanced NSCLC. PET imaging may also refine radiotherapy target volumes by displaying the extent of “active” disease, including differentiating tumor from postobstructive atelectasis ***(Govindan et al., 2008)***.

This prospective study was designed to try to answer the question whether or not the advent of the 3-dimentinal conformal radiation treatment (3D-CRT) made a difference as regards to more preferable outcome and less toxicity compared to the conventional 2-dimentional radiation treatment (2D-RT), when given concurrently with weekly paclitaxel/carboplatin and followed by 2 cycles of the same chemotherapeutic agents in full systemic doses, in patients with inoperable locally advanced non-small cell lung cancer. The study primary endpoints were overall survival (OS) and progression free survival (PFS). Secondary endpoints included toxicity, objective response (OR), locoregional control (LRC), pattern of failure, and isolated nodal failure (INF).



REVIEW OF LITERATURE

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Epidemiology

Worldwide, lung cancer is the most common (1.35 million of 10.9 million new cases) and the deadliest (1.18 million of 6.7 million cancer-related deaths) form of cancer ***(Ozols et al., 2007)***. The United States 2006 cancer statistics showed that lung cancer is the second most common cancer for both men and women (92,700 or 13% of all cases, and 81,770 or 12% of all cases, respectively), but the number-one cancer killer in both sexes (90,330 men, 31% of all cancer-related deaths; and 72,300 women, 26% of all cancer-related deaths). In fact, more people in the United States die of lung cancer than of the next three causes of cancer-related death prostate cancer, breast cancer, and colorectal cancer combined ***(Jamal et al., 2006)***.

Between 1991 and 2002, the lung cancer incidence decreased 19.8% in men (1.8% reduction per year), but it increased 8% in women between 1990 and 1998 (1% increase per year) and subsequently decreased 2% between 1998 and 2002 (0.5% reduction per year). Lung cancer death rates for men have dropped by 19% during the past decade, whereas these rates continued to increase in women up to the year 2002 ***(Ozols et al., 2007)***.

Lung cancer is rapidly emerging as a major cause of mortality in the Middle East, Africa, and Asia as well. For instance, an estimated 71,228 annual cancer-related deaths will be attributed to lung cancer in Japan within 2 years ***(Kaneko et al., 2003)***.

The global rise in lung cancer incidence, together with the fact that the overall 5-year survival of patients with this disease is less than 15%, underscores the magnitude of the lung cancer epidemic ***(Ferlay et al., 2006)***.