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Radiotherapy for NSCLC: Review of conventional and new treatment techniques

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Summary Radiotherapy is an essential modality in the management of lung cancer. It is used as a single modality or in combination with other modalities and aimed at cure or palliation. Recent advances in the simulation techniques or more precise targeting of the tumor made radiotherapy more effective tool in the fight against lung cancer. Using PET scan and better gating for tumor motion are examples of these advances.

This brief review will present summary of the role of radiotherapy in management of lung cancer.

Introduction

Radiotherapy is used for the treatment of NSCLC in many ways. It is the primary treatment modality for locally advanced unresectable tumors, and it is usually given concomitantly with chemotherapy [1].

In the postoperative setting, it used as an adjuvant treatment for stage 3 NSCLC aiming to improve local control. Radiotherapy is also frequently used for the palliation of advanced and metastatic lung cancer.

Radiotherapy for NSCLC is usually delivered using external-beam radiotherapy via a linear accelerator. Newer techniques, such as three-dimensional conformal techniques (3D-CRT) had improved the toxicity profile and allowed to escalate the dose by better protection of normal tissues from unnecessary radiation [2].

Recently 4D-CRT planning techniques accounting for lung motion during radiotherapy treatment had improved precision of dose delivery to intended tumor target.

Definitions

Conventional radiotherapy

Where very large fields of radiation are used to treat the tumor with a margin and regional lymph nodes (LNs) electively.

Conformal radiotherapy

Where limited fields of radiation are used to treat only the primary tumor and involved lymph nodes only.

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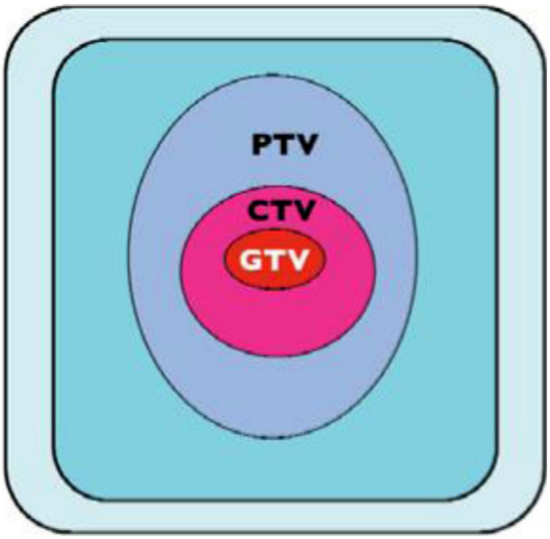

Figure 1 Illustration of various radiation fields for gross tumor volume (GTV), clinical tumor volume (CTV), and planning target volume (PTV).

Brachytherapy is the delivery of radiation inside the airways; it is used mostly for palliative purposes.

The International commission on Radiation units and measurements definitions of target volumes (ICRU 1993, 1999).

Gross tumor volume (GTV)

Macroscopic extent of the malignant growth, e.g. clinically palpable and/or visualized by imaging.

Clinical target volume (CTV)

Anatomical clinical concept that needs to be defined before delineation. It contains GTV and/or subclinical disease which should be eliminated.

Planning target volume (PTV)

Geometrical concept

A 3-D expansion of the CTV to account for all the geometrical uncertainties (for target and organ at risk of motion, set up errors delineation and anatomical changes during treatment) (see Fig. 1).

Conventional radiotherapy

Conventional radiotherapy is two-dimensional (2-D) techniques where AP/PA parallel opposed fields are used to treat the primary tumor and mediastinal LN with a relatively wide margin to account for set up and motion errors due to breathing lung movement.

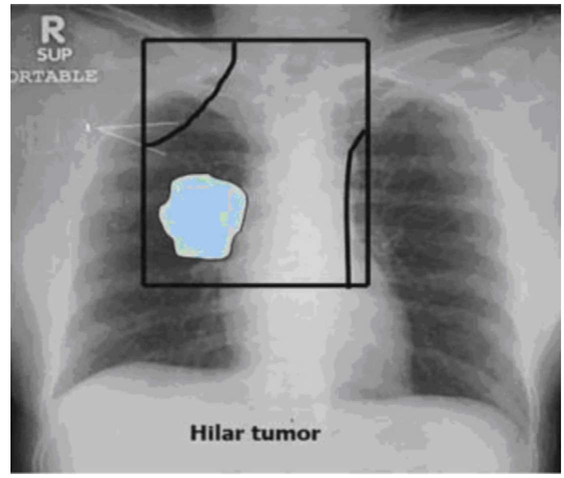

Figure 2 Field borders for hilar tumors.

The field borders are usually defined based on the original location of disease and potentially involved lymph nodes.

Although such techniques are mostly used for palliative setting, it is not advised to use it for curative approach due to poor results in local control, survival and normal tissue toxicity.

Figs. 2 and 3 are examples of field arrangements to treat tumors at different locations.

Conventional definition of radiotherapy curative doses

AP/PA parallel opposed fields can be used until a dose of 46 Gy. Then effort to spare the spinal cord should be made while taking the primary tumor and involved LN to full dose of 60 Gy.

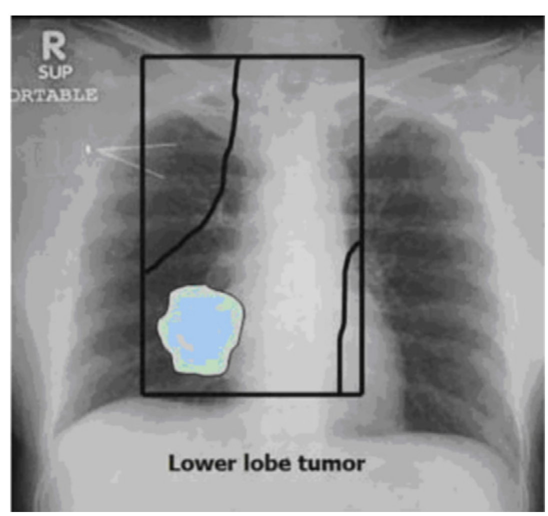

Figure 3 Field borders for lower lobe tumors.

For post portative radiotherapy

- R1 resection (residual microscopic disease); 54 Gy to bronchial stump.
- R2 resection (residual macroscopic disease); 60—66 Gy to Bronchial stump.
- Multiple N2 lymph nodes or extra capsular extension shrinkage field technique after the dose of 46 Gy taking the diseased area to 60—66 Gy.

Daily fractionation of 1.8—2 Gy per day.

Recent advances in radiotherapy for NSCLC

One of the many challenges of lung cancer radiotherapy is conforming radiation to the target due to tumor/organ motion and the need to spare surrounding critical structures.

Control of local disease using conventional two-dimensional (2-D) radiotherapy planning to a total dose of 60—66 Gy, has been poor (only in 30—50% of cases), and dose escalation has been associated with increased toxicity, particularly when concurrent chemotherapy is given [3]

Three main factors contribute to local treatment failure after radiotherapy:

(1) Geographic misses due to inadequacy of imaging tools for staging and radiotherapy planning;
(2) Geographic misses due to respiration-induced tumor motion and anatomic changes during radiation delivery; and
(3) Inadequate radiation dose due to concerns about toxicity.

Recent developments in radiotherapy are for lung cancer can be summarized by the following points:

- Positron emission tomography/computed tomography (PET/CT) has been shown to improve targeting accuracy in 25—50% of cases.
- 4-D planning by accounting for tumor motion.
- Daily on-board imaging reduces treatment set-up uncertainty and provides information about daily organ motion and variations in anatomy.
- Image-guided intensity-modulated radiotherapy (IMRT) may allow for the escalation of radiotherapy dose with no increase in toxicity.
- Image-guided stereotactic radiotherapy can achieve local control rates exceeding 90% through the use of focused, hypo-fractionated, highly biologically effective doses.

These new approaches were considered experimental for many years, but recently accumulating evidence of their potential for significantly improving clinical outcomes is leading to their inclusion in standard treatments for lung cancer at major cancer centers [4].

FDG-PET/CT role in NSCLC radiotherapy treatment

FDG-PET/CT has become an integral component of NSCLC staging because it improves the detection of nodal and distant metastases and frequently alters patient management [5].

Functional imaging is increasingly utilized for treatment planning for patients with NSCLC. Incorporation of FDG PET images into radiation therapy treatment planning resulted in a 15—60% increase or decrease in treated volumes. Ultimately, improvement in outcomes will determine the widespread use of FDG PET/CT in radiation therapy treatment planning [6,7].

Tumor motion management

A major obstacle to radiotherapy in lung cancer has been respiration-induced target motion (also known as intrafractional tumor motion), which can add considerable geometric uncertainty to treatment, particularly for highly conformal radiotherapy treatment delivery techniques such as IMRT or SRBT.

The ideal solution to this problem would be to track the tumor in real time during treatment and correct beam position to match the location of the target.

Internal gross tumor volume (IGTV), which envelops the GTV motion throughout the respiratory cycle, delineating the IGTV from 4-D CT images involves outlining the tumor volume on the expiratory-phase images and then registering the outline to the images from other phases to create a union of target contours enclosing all possible positions of the target.

If 4-D CT is not available, alternative approaches to address tumor motion should be considered; for instance, the IGTV can be delineated by combining volumes on breath-hold spiral CT at the end of expiration and at the end of inspiration, for patients who can comply with this technique.

Stereotactic body radiation therapy (SBRT)

Two important principles of SBRT must be obeyed: (1) An ablative dose (biological effective dose, BED, >100 Gy) is required to achieve >90% local control, and (2) image-guided tumor volume delineation and on-board image-guided radiation delivery (IGRT) are required to ensure that the target is not missed and to avoid normal tissue injury. An ablative dose of SBRT is typically delivered in <5 fractions. With such a small number of fractions, it is critical that patient positioning and target coverage be optimized for each treatment. Toxicity may be severe even fatal if critical normal tissue receives an excess dose of radiation. Conformal SBRT is therefore usually optimized to ensure that at least 95% of the prescribed dose (minimum BED of 100 Gy) is delivered to the PTV which is usually defined as the IGTV plus a small margin to account for set-up uncertainty [8].

It has been shown that this approach can achieve 100% local control with minimal side effects (<grade 3) in centrally located lesions [9].

Conclusion

New technologies are evolving to improve conformality of radiation therapy to help focus the high dose on the target and spare critical normal tissue. Treatment planning based on 4-D CT images and on-board image-guided adaptive treatment delivery helps the radiation oncologist track tumor motion and target the tumor precisely. Improved treatment accuracy and conformality in SBRT enable us to deliver doses high enough to ablate the cancer completely with minimal toxicity in early-stage NSCLC.

For stage III disease, image-guided, individualized IMRT with dose escalation/acceleration can potentially reduce toxicity and increase the cure rate. Further studies to optimize treatment planning, including dose painting in high-risk areas within the target, are still needed [10].

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