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Case report Free Access

Management of oligometastatic triple-negative breast cancer with lung metastasis using 4DCT: a case report

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Abstract

Introduction: Breast cancer remains the most prevalent disease in women. Oligometastatic breast cancer (OMBC), is defined by a limited disease burden. 40% of Triple negative breast cancer are associated with Lung metastasis. Stereotactic body radiotherapy is used for lung metastasis. We report a case of oligometastatic triple-negative breast cancer with lung metastasis treated with the deep inspiratory breath hold technique via four-dimensional (4D) respiratory correlated CT imaging (4DCT).

Case presentation: A 77-year-old Asian Indian female patient presented with breathing difficulty. Evaluation revealed it as Oligometastatic breast carcinoma with solitary lung metastasis. She was treated with SBRT to her lung lesion using 4DCT after her primary management.

Discussion: 4DCT has revolutionized the radiotherapy planning for gated radiotherapy delivery. Retrospective 4DCT allows the reconstruction of a number of breathing phases that demonstrate the motion of the tumor and surrounding tissue. Despite its limits, the addition of this technology has been beneficial to the overall sector.

Conclusion: A total dose of 50 Gy in 5 fractions (BED10: 100 Gy) via volumetric modulated arc therapy (VMAT) was delivered to solitary lung metastasis. During surveillance imaging with PET/CT, there was no sign of progression or distant failure, and the treated lesion responded almost completely after 3 months beyond evidence of pneumonitis**.**

Keywords: Oligometastatic, CyberKnife, Breast cancer, Four-dimensional computed tomography (4DCT), Lung metastasis

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Introduction

Survival of patients with metastatic breast cancer has improved. Oligometastatic breast cancer (OMBC), is an independent prognostic factor (1, 2). The most common definition uses up to five metastases (3). The optimal treatment for OMBC has yet to be determined, yet systemic therapy remains key. Lung metastasis is commonly diagnosed in TNBC. Stereotactic body radiotherapy (SBRT) is an advancement over traditional conventional radiotherapy and is delivered in fewer fractions. It is commonly used for lung, liver, or adrenal metastasis (4). Respiratory motion management is useful for targets moving beyond 5 mm, especially those in the lungs and liver. Marker blocks on the chest or abdomen (RPM respiratory gating), have been widely used. The traditional wider gating has been reduced to a very low gating amplitude. A tool used to measure breathing motion is 4DCT. 4DCT is a motion-encompassing method introduced in the early 2000s. Its goal is to depict the temporal dynamics of a 3D sample with high temporal and spatial precision. 4DCT will often use a gating approach, such as breathing tracking, to automatically initiate picture acquisition at predetermined points. Additionally, the radiation beam is only activated during specific breathing cycle points (e.g., the deep inspiration breath-hold technique). We report a case of oligometastatic triple-negative breast cancer with lung metastasis. The solitary lung metastasis was treated with the deep inspiratory breath hold technique via 4DCT. The reports talk about the 4DCT technique, its advantages over conventional free breathing technique and 3DCRT and its disadvantages.

Case presentation

A 77-year-old Asian Indian female patient presented with a lump in her right breast in the outer quadrant. On examination, an ulceroproliferative mass measuring 7.5 cm x 7.5 cm was felt in the right outer quadrant; the base and the nipple-areola complex were uninvolved. The nipple was not retracted. A single palpable node was felt in the right axillary region measuring 1 cm by 1 cm. Core biopsy from the lump revealed invasive breast cancer (no special type), Nottingham grade II (overall score of 7). The IHC-4 panel suggests that there are negative estrogen receptors, negative progesterone receptors, and equivocal human epidermal growth factor receptor 2 (Her2neu) with a Ki67-30--40%. Fluorescent in situ hybridization (FISH) was negative for Her2neu. PET-CT revealed a faintly metabolically active soft tissue nodule is seen in the posterior basal segment of the left lung lower lobe of the left lung measuring 1.1 × 1.4 cm in addition to the primary segment. SBRT was planned to treat her solitary metastatic lesion in her lung with 4D CT. (Figures 1, 2).

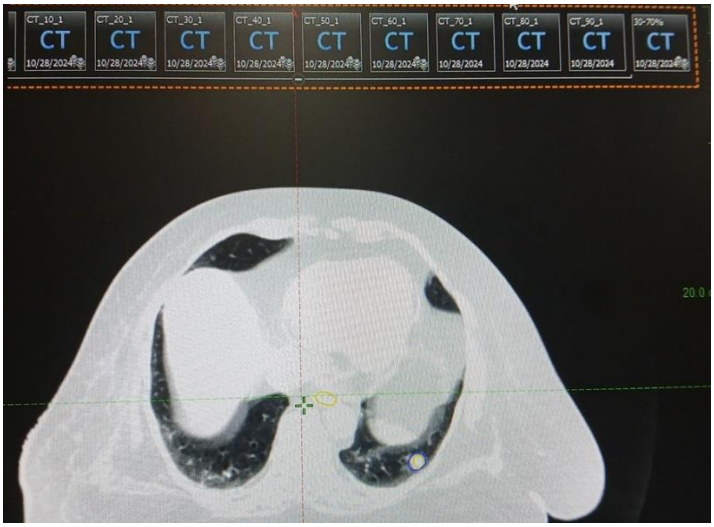

Figure 1. 4DCT acquisition - average RPM (Respiration Per Minute) for at least 10 breathing cycles.

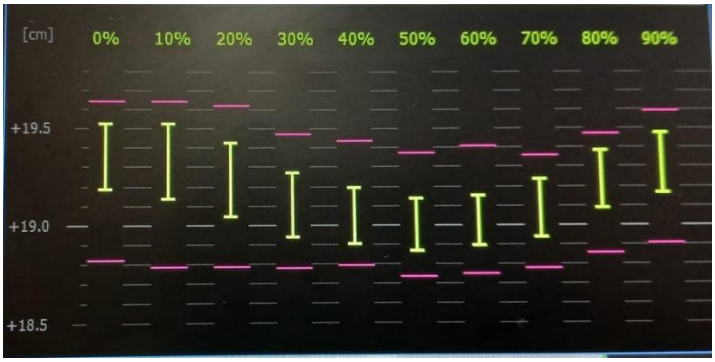

Figure 2. 4DCT waveform (showing highest Tumor velocity and tumor stability between 30-70% phases).

Plans were calculated with 6MV FFF (Figure 3).

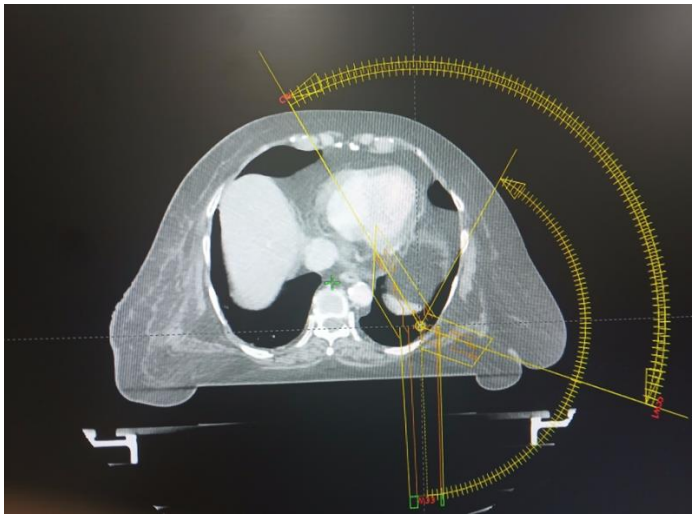

Figure 3. Arc offsets (use of 3 arcs, including a partial arc).

Discussion

Lung metastases have very devastating clinical presentations and consequences, in addition to the poor prognosis associated with metastatic breast cancer. Metastatic breast cancer to lung presents with constant cough, pain, difficulty breathing or shortness of breath, wheezing, fatigue, recurring infections in the chest, coughing up blood or unintentional weight loss. 5-year survival rate as per The Surveillance, Epidemiology, and End Results (SEER) database such as lung is 30 %. According to gene expression study, the luminal B and basal subtypes had the highest numbers of lung recurrence patients. Despite receiving chemotherapy, targeted therapy, and endocrine therapy based on molecular receptor profiles, patients with lung metastases from breast cancer still have a poor prognosis. Early diagnosis is now the best and only way to prevent lung metastases from breast cancer. Therefore, in order to develop more effective treatment plans, we need to completely comprehend the mechanism of breast cancer lung metastases. According to studies, patients with low volume OMBC may see an improvement in progression-free survival or long-term disease remission.

Since the mid-1980s, efforts have been made to improve outcomes through escalating radiotherapy doses. SBRT is low morbidity non-invasive option or metastasis-directed curative intent therapy. SBRT is an advanced type of external beam radiation therapy that uses a small number (one to five) of high-dose fractions. SBRT is being utilized in oligometastatic disease and in patients who have oligoprogressive disease. SBRT can also be used for patients with limited lung metastases or limited metastases to other body sites (5). Prospective series have shown similar overall survival and cancer-specific survival between SBRT and lobectomy. Deep Inspiration Breath Hold (DIBH) SBRT is an improvement over the existing free breathing (FB) SBRT. Free breathing computed tomography (CT) scans in the treatment planning process, capture the random position of a tumour and/or artefacts. Extensive literature has shown the efficacy and safety of SBRT for peripheral and central tumors. A 2-year local control range of 88% to 100% was noted by systematic reviews. 50 Gy in 5 fractions is often used for ultracentral tumors, whereas RTOG 0813 is a dose escalation study of 5-fraction SBRT up to 12 Gy/fraction for central tumors.

The challenge

The respiratory motion is an important challenge for patients with moving targets (6,7). The challenge frequently encountered during a radiation planning session is how to design an appropriate plan for a moving target such as the lung. This motion should be taken into consideration clinically to ensure that the target receives the right dosage. This helps to minimize the toxicity associated with irradiation of surrounding healthy tissue. Conventionally, larger margins are used when creating a planning target volume from the clinical target volume. Larger margins result in increased irradiated healthy tissue, possibly leading to increased toxicity. The internal target volume defined during treatment planning may not accurately cover the target range of motion during treatment delivery. In free breathing CT scanning, respiratory organ motion can result in significant geometrical distortion. The target may become longer or shorter due to distortions along the axis of motion. The center of the imaged object may be shifted by as much as the motion's amplitude in addition to shape distortion.

What is 4DCT

A tool used to measure the breathing motion is four-dimensional (4D) respiratory correlated CT imaging (4DCT). It uses a gating mechanism. This gating can also be used during treatment, such as when the deep inspiration breath-hold technique is used, in which the

radiation beam is only activated during specific breathing cycle points (8, 9). Multiple CT images are produced by the 4D-CT, each of which shows the location and size of the tumor at a certain breathing phase. Various available 4DCT methods practiced include slow CT, prospective gated or breath hold CT, and retrospective 4DCT, each having their own advantages. The tumor position with respect to the patient's respiratory cycle can be determined via the respiratory gating technique. The process involves the use of an infrared tracking camera and a reflective marker placed on the patient. The patient's respiratory pattern and range of motion are displayed as a waveform. Gating thresholds can be set along the waveform. This allows patient-specific margins. Gating can be prospective or retrospective. For retrospective image acquisition, continuous images are acquired. Retrospective sorting can be done in either sinogram space (before reconstruction) or image space (after reconstruction). Images can be sorted using either the breathing phase or the amplitude phase.

To develop a comfortable frequency and amplitude of breathing, it is crucial to remember that the patient must get coaching. Compliance was defined as ability to hold her breath for 20– 30 seconds. Understanding the movement of a tumor within a patient can help customize treatment or even use tumor tracking or gating technology to further limit normal tissue exposure and improve clinical outcomes. The gross tumor volume (GTV) was defined as the lung tumor volume on the basis of the planning 4D CT (with intravenous contrast) and fused PET images. Tumor contouring is typically carried out during each breathing phase, followed by the establishment of an internal target volume (ITV) that accounts for the full movement cycle. Contouring was completed by multiphase Maximum intensity projection (4D-MIP). The highest tumor velocity and tumor stability is between 30-70% phases. Similarly, the internal target volume (ITV) was defined using the 30% to 70% respiratory phase. A uniform 5 mm prescription target volume (PTV) margin was expanded from the ITV. Planning uses the ECLIPSE algorithm and the analytical anisotropic algorithm (AAA) for dose calculation. Image guidance was based on CBCT during treatment.

Treatment was prescribed for a total dose of 50 Gy in 5 fractions (BED10: 100 Gy) via volumetric modulated arc therapy (VMAT). All critical structures were contoured according to the RTOG 0915 guidelines. She was offered the adjuvant capecitabine but did not comply. During surveillance imaging with PET/CT, there was no sign of progression or distant failure, and the treated lesion responded almost completely after 3 months beyond evidence of pneumonitis. Approximately 10% of patients have reported grade 3 or above toxicity, with fatal effects, including hemorrhage, airway necrosis, and fistula formation. Our patient developed grade 1 pneumonitis. She is being kept on regular follow-up and advised to undergo lung physiotherapy and incentive spirometry.

Advantages and disadvantages of 4DCT

4DCT advantages: 1. It allows a potential decrease in the patient-specific ITV that corresponds to a respiratory component.

2. The 4DCT approach divides the CT data into distinct breathing stages, which decreases or eliminates the irregularity.

3. This approach benefits from free-breathing CT-based target delineation, which assumes that the target is constant.

4. Typically, the procedure involves defining the target volume for each phase, the average intensity projection data sets, or the maximum intensity projection (MIP).

5. Compared with 3D-CT, 4D-CT improves target localization and minimizes motion artifacts.

As a result, during therapy, there is less radiation exposure to healthy tissue and improved tumor coverage.

A dosimetric study by Huang et al. assessed the accuracy of current stereotactic body radiation therapy (SBRT) lung treatment planning methodologies for irregular breathing patterns via MIP and AIP images generated from four-dimensional computed tomography (4DCT). The study concluded that the inaccuracy inherent in 4DCT MIP and AVG images could be mitigated by reducing respiratory motion via volumetric image guidance (CBCT) or with abdominal compressions. Average intensity projection (AIP)

underestimates the ITV; therefore, MIP is utilized for estimating size (10).

4DCT Disadvantages

1. Only a brief picture of the patient's breathing is taken; the entire breathing pattern is not taken into consideration during treatment, particularly for patients who have respiratory issues.

2. In SBRT, 4DCT image artifacts are associated with poorer local control. With erratic breathing and a comparatively short 4DCT acquisition period, it is challenging to obtain enough data for artifact-free 4DCT reconstruction (11).

The suggested method for overcoming the aforementioned drawbacks is the employment of both 4D MRI and 5D CT, which allows for much longer acquisition periods and mitigation strategies to reduce the severity of breathing disorders (12).

Second, the efficacy of the system could be assessed by comprehensive 4DCT quality assurance (QA).

Our patient underwent Comprehensive QA prior delivery.

Advancements

The CyberKnife System, a real-time robotic beam system, is the only radiotherapy system that can maintain submillimeter precision during treatment delivery. It has an integrated image guidance, automatic motion tracking, and retargeting system to account for motion. It employs an orthogonal imaging system to monitor movements during delivery with an optical camera placed above the couch. In addition, diagnostic kV sources are fixed to the ceiling and floor panel detectors, which further enhance its accuracy.

With the advancement of technology, magnetic resonance imaging-guided radiotherapy (MRIgRT) has become possible. It offers higher geometric accuracy and treatment efficacy through online adaptation. The emphasis is now on the increased use of artificial intelligence. With the development of wide field of view CT, 4DCT is mostly used in the context of radiation therapy planning; nevertheless, it has now opened up significant opportunities in the diagnostic sector.

Conclusion

Tumor movement is complex, with some showing superior to inferior motion and others showing anterior to posterior motion. Tumor displacement is dependent on the tumor site and location. The management of respiratory motion is absolutely necessary. Our Study demonstrated superiority of 4DCT over conventional techniques. Use of generic motion margins than custom margins, help reduce normal tissue irradiation. For targets moving with respiration and digestion, we suggest using 4DCT gated planning, as it is promising due to its advantages and superior outcomes. The same was demonstrated in our patient, with excellent results in surveillance image and resultant less tissue toxicity.

Author contribution

SA and KG wrote the main script, revised the script, conceptualized it, and prepared figures. **SA** gathered resources.

Conflict of interest

There is no Conflicts of interest.

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