Introduction

In 2012 approximately 14.7 million cancers were diagnosed (excluding non-melanoma skin cancers and other non-invasive cancers) and in 2010-11 nearly 7.98 million people died (Loranzo, 2012). Cancers as a group account for approximately 13% of all deaths each year with the most common being: lung cancer (1.4 million deaths), stomach cancer (740,000 deaths), liver cancer (700,000 deaths), colorectal cancer (610,000 deaths), and breast cancer (460,000 deaths). This makes invasive cancer the leading cause of death in the developed world and the second leading cause of death in the developing world (Jemal et al., 2011). Over half of cases occur in the developing world (Kaatsch et al., 2010).

Most of the deaths caused by cancers are due delayed screening and evaluation. Cancer screening can be done by many methods like blood test, urine tests, but medical imaging is vital (Wilson et al., 1968). With digital imaging techniques like Magnetic resonance induction (MRI), Computerized tomography (CT), Positron emission tomography (PET) and X-ray reports, a radiologist can detect the progression and metastasis. Modern diagnostic imaging has revolutionized medicine. In a matter of seconds, computed tomography (CT) machine can produce extremely detailed images of any part of the body (Higgins and Pomper, 2011). Medical diagnostic techniques are not only for screening and evaluation, but also useful in identifying metastasis (Gerber et al., 1977) and for pre-operative assessment of resectability (Tang et al., 2013). The evaluation of tumor by measuring lesion volume with the help of a radiologist and oncologist has become a standard procedure. The volumetric and morphometric analysis ensures the correct progress of the treatment. As a latest advancement in technology, an automated system for volume statistics has been developed. This method helps in reducing the time taken for evaluation of tumors.

Volumetric Measurement and Its Importance in Treating Cancer Patients

Volumetry is a process of quantification of the tumors by identification (pre-cancerous or target lesion) and evaluating the tumor by measuring the size. Volumetric image analysis is an accurate, precise, sensitive, and medically valuable biomarker of response in the assessment of tumors. Clinical endpoints or outcomes are used to determine whether the drug is effective and safe (Stephanie et al., 2003). In oncological trials, primary and surrogate endpoints that indicate therapeutic efficacy, such as overall survival (OS) and tumor response rates (TRR), respectively, necessitate an observation period of months to even years. In today’s standard clinical practice, TTR is regarded as the gold standard for evaluation of therapeutic effect and is widely used in oncological clinical trials (Therasse et al., 2000; Eisenhauer et al., 2009). TRR
Evaluation of TRR is based on the Response Evaluation Criteria in Solid Tumors (RECIST) criteria (Therasse et al., 2000; Eisenhauer et al. 2009). During the year 2000, an international committee published easily applicable criteria for measuring tumor response using X-ray, CT and MRI, which is known as Response Evaluation Criteria in Solid Tumors (RECIST), which involves formalized rules for measurement of tumor target lesions. The Response Evaluation Criteria in Solid Tumors (RECIST), updated in 2009, are currently considered as the ‘gold standard’ in most oncology settings (Therasse et al., 2000; Eisenhauer et al., 2009; Dudeck et al., 2011). They are based on uni-dimensional (1D) measurements (maximum diameter of target lesions) and their relative decrease or increase during therapy. RECIST is used in daily clinical practice and is considered appropriate to assess tumor response in solid tumors (Eisenhauer et al 2009). Therefore, RECIST has been adopted by academic institutes, cooperative groups, and industry for clinical trials with objective response or tumor progression as primary endpoints (Therasse et al., 2000).

TRRs are summarized in Table 1. Since TRR visualizes the direct effect of a drug on tumor size and regression of tumors in the absence of treatment is rare, TRR is attributable to treatment effect and for that reason a valid surrogate marker for efficacy of anti-cancer drugs (Dudeck et al., 2011). The best overall response is the best response recorded from the start of the treatment until disease progression/recurrence (taking as reference for progressive disease the smallest measurements recorded since the treatment started).

Table 1 explains the overall tumor response rate and the RECIST criteria. Ideally a drug trial will return results like CR or PR. Responses of SD or PD could be used to show that a drug is not an effective treatment for cancer. Although RECIST has its detractors, it continues to be an important set of evaluation rules in the medical and pharmaceutical communities.

Response to therapy in cancer patients can be monitored with several methods. Traditionally, tumor size measurement with CT via TRR is the standard body (Higgins and Pomper, 2011). Assessment of tumor size changes is crucial in clinical trials and patient care. The accuracy of the review and less amount of time helps in providing quick, correct results for treating cancer patients.

The goal of these measurements is to provide a quantitative assessment of whether the tumor is “changing” size. Size, in this case, is used as a surrogate for determining whether tumor necrosis (death) is occurring (Nishino et al., 2010). Increasing size is generally considered “growth” and decreasing size is correlated with tumor “death”.

The lesions are categorized as measurable and non-measurable. Measurable lesions must have a longest diameter of ≥10 mm on CT with a slice thickness of ≤5 mm (or a longest diameter of ≥20 mm on nonhelical CT with a slice thickness of >10 mm) or a longest diameter of ≥20 mm on chest radiography (Eisenhauer et al., 2009). Non-measurable lesions include other lesions that do not meet the criteria as measurable lesions, such as small lesions with a longest diameter of ≤10 mm, skeletal metastasis without a soft-tissue component, ascites, pleural effusion, the lymphangitic spread of tumor, leptomeningeal disease, inflammatory breast disease, cystic or necrotic lesions, lesions in an irradiated area, and an abdominal mass not confirmed by imaging.

**Dataset**

All the imaging datasets are collected from medical imaging laboratory of Parexel International, Hyderabad, India. The volumetric analysis is performed using the ALC® imaging software. For the analysis, we used CT images of liver anatomy with 5 mm slice thickness and slice interval without and gap (Marten et al., 2007). For a proper explanation of the volumetric measurements, we have collected some of the imaging datasets and simulated for the analysis purpose. It involves in viewing the images, identification of the tumors, creating a region of interest (ROI) and measuring the volumes.

**Methodology: Volumetric Data Analysis**

Firstly, in this analysis, we have considered taking Baseline and a follow up (after treatment) visit datasets. In the baseline visit, we have identified two target lesions (Figure 1) which were meeting the criteria of thickness (≥10 mm) and a proper shape with 17 mm and 11 mm thickness and also a non-target lesion (Figure 1a). The lesion identified in the liver lobe (lesion 3) is of improper, irregular in shape and size, so it has been taken as a non-target (Figure 1c). The Baseline visit is performed before the drug is administered to patients. This acts as the gold standard for evaluation of tumors. Similarly, in the follow up visit, all the three lesions are present and identified. Both the target lesions have increased in volumes, which showcases the actions of the drug on the tumors. The lesions have almost increased by one fold of the original sizes from 17 mm to 32 mm in target lesion 1, 11 mm to 25 mm in lesion 2 and an unequivocal progression of non-target lesion (#3) in the liver lobe (Figure 1c).

![Figure 1. Comparison of the Target and Non-Target Lesions](Image)
Figure 1 is a comparison of Baseline and follow up visit lesions in the CT scan image of Liver region. 1(a) is target lesion 1 from baseline and target lesion 1 from follow up which is grown from 17mm to 35mm. 1(b) is the comparison of target lesion 2 from baseline and follow up visits, which is increased from 11 mm to 25 mm. 1(c) is a non-target lesion of baseline and follow up visit of liver lobe, which is increased, however it is an unequivocal progression and cannot be measured (Le Cesne et al., 2009).

After collecting the data, the sum of the longest diameter (SLD) is calculated in order to identify the disease parameter. For the first visit dataset the total SLD is the sum of both the target lesions, which is 17 mm+11 mm equals to 28 mm. In the second visit dataset, total SLD is a sum of target lesions, 32 mm+25 mm equals to 57 mm of thickness. And for non-target lesion calculating the SLD is not possible due to its unequivocal increase (Lavin et al., 1980; Spratt et al., 1996). The actual SLD is difference of volumes between two lesion and percentage change (Lavin and Flowerdew, 1980).

Taking the RECIST into consideration, the disease parameter for the tumor is a Progression disease (PD). Due its unequivocal increase from baseline to follow up visit, the non-target lesion is also placed under the PD (Nishino et al., 2010).

The overall evaluation of the target tumors reflects the volumetric statistics (Table 2) with regards to progression by size (James et al., 1999). As per RECIST criteria, in the datasets collected for the lesion evaluation, there is an increase in the size of the lesion (Therasse et al., 2000). The percentage increase of the lesion helps in placing it in the appropriate category.

**Discussion**

This analysis offers in depth insights on how to measure the tumor volume, along with it, metastasis can also be identified. The high incidence of skeletal metastasis in cancer patients warrants careful detection with imaging and follow-up (Gerber et al., 1977; Tarin et al., 1984).

Volumetric measurements of solid tumors can be accurate in the proper setting. The accuracy and precision of measurement is continuously improving, and usually higher than for corresponding measurements of longest diameter (Marten et al., 2007). The sensitivity of volumetrics for distinguishing between measurement error and medically meaningful changes in tumor biology is dependent on context.

With Volumetry the actual actions of the drug to the patients is revealed and calculated. All the clinical therapies are performed purely based on risk and benefit ratio (Miller et al., 1989). The drug should always be higher on the benefit than risk. So with the help of radiological techniques from the radiologist and a clinical oncologist the huge amounts of money, large time frame involving numerous subjects can be limited to a certain extent (Stephanie et al., 2003).

It seems likely that volumetrics will also succeed in screening of cancers. It is clearly evident to claim that volumetric image analysis is qualified as a biomarker of response in patients with solid tumors, quantifying changes in tumor volume could constitute a major paradigm shift in clinical practice. And evidence is mounting that volumetric measurements will enhance assessments of response in many cases, and aid in cancer evaluation.

In conclusion, by presenting and standardizing the CT stage reports in cancer treatment, job of the radiology clinicians assessing the tumors will be made easy. The weight of the evidence suggests there are many circumstances in which volumetric image analysis adds value to screen and assess tumors well. And also, the diagnostic techniques are useful in identifying the cancer metastasis.

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