J of Nuclear Medicine Technology, first published online November 9, 2022 as doi:10.2967/jnmt.122.264714

Technologist Based Implementation of Total Metabolic Tumor Volume into Clinical Practice

Original Research

Erina Quinn DO[1], Claire Olson CNMT[2], Manoj K Jain MD[2], Jaiden Sullivan CNMT[3], Matthew P Thorpe MD[3], Geoffrey B Johnson MD[3,4], Jason R Young MD[2]

Mayo Clinic, 4500 San Pablo Rd S, Jacksonville, FL 32224

Lake Erie College of Osteopathic Medicine – Bradenton,[1] Mayo Clinic Jacksonville Department of Radiology[2], Mayo Clinic Department of Radiology[3], Mayo Clinic Rochester Department of Immunology[4]

WORD COUNT: 1871

Short running title: Implementation of MTV into Clinical Practice

Abstract

Metabolic tumor volume is a volume defined as the total metabolically active tumor volume of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) exams. Calculating the metabolic tumor volume (MTV) is often time consuming requiring a high degree of manual input. A comparison of MTV calculations obtained by a board-certified Nuclear Radiologist and two Nuclear Medicine Technologist Students (NMTS) was performed in this study. A 30-minute training session with a Nuclear Radiologist was performed with the NMTS after their classroom time as part of their educational program. The NMTS calculated MTV within 7.5% of the Radiologist in a set of diffuse large B-cell lymphoma (DLBCL) patients undergoing initial staging 18F-FDG PET/CT. These findings suggest NM Technologists may help accelerate implementation of MTV into clinical practice with favorable accuracy, possibly as an initial step followed by interpreting physician validation. The aim of this study is to explore improved efficiency of calculating total MTV by integrating Nuclear Medicine (NM) Technologists with a semi-automated workflow.

Introduction

Many methods are used to measure metabolic tumor volume (MTV) from ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT), which may help predict patient outcomes, especially for those with diffuse large B-cell lymphoma (DLBCL). (*1-5*) MTV is a volume defined either by quantitative or manually selected segments representing the metabolically active tumor on 18F-FDG PET/CT.(1) Total MTV (TMTV) is calculated by adding the MTV of all malignant lesions and is a method for measuring total tumor burden. TMTV has shown promise in the initial staging and treatment response of DLBCL. (*2,4,6-7*) However, tumor segmentation of 18F-FDG avid lesions on PET/CT is often time-consuming. Advancements in threshold-based segmentation methods for filtering out background activity and/or signal-to-background ratios have been proposed to increase the efficacy of results. (*3*) Therefore, the optimal tumor segmentation method varies based on the purpose of the study.

Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma. (*8*) The current standard for staging DLBCL is the Lugano classification which includes a five-point Deauville score when staging with ^{18}F-fluorodeoxyglucose positron emission tomography / computed tomography (18F-FDG PET/CT). (*9*) Yet, many studies support the significant prognostic value of TMTV in DLBCL. (*2-7,9*) This study explores the utilization of Nuclear Medicine Technologist students for the clinical implementation of TMTV.

Methods

An exploratory project design was implemented. Two Nuclear Medicine Technologist Students (NMTS) at Mayo Clinic Rochester received a 30-minute training session on distinguishing physiologic from pathologic lymphomatous 18F-FDG uptake from a board-certified Nuclear Radiologist. The NMTS previously experienced four months of Technologist classroom time and 8-12 hours of experience observing the technologist-side of clinical PET practice (~85 exams per day). The NMTS had no other PET education or image interpretation experience. The patient cohort was composed of 10 random patients with DLBCL who were treated at a large tertiary referral center between June 22, 2016, and September 24, 2018. The NMTS independently evaluated the exams from these patients before (pre) and after (post) systemic therapy. The images were reviewed by the NMTS and Radiologist separately using the MIM Inc. "LesionID" workflow (MIM Inc. Cleveland, OH, USA). The workflow automatically segments PET lesions based on an absolute SUVmax threshold. The threshold was set using the SUVmax within a 3 cm spherical region of interest within normal liver. The workflow then segmented everything with an SUVmax greater than the liver threshold. The NMTS and Radiologist separately evaluated each segmentation to distinguish lymphoma from non-lymphoma / physiologic segmentation. The non-lymphomatous segments were deleted after noting anatomic location and the total MTV was then calculated. If the NMTS was uncertain if a segment included lymphoma, it was included in the MTV calculation.

Results

The mean Radiologist-derived MTV values from the 10 patients were 446.0 mL (± 555.6) and 38.5 mL (± 77.6) for Pre and Post therapy exams, respectively. The mean MTV of NMTS was 414.8 mL (±597.6) and 27.7 mL (±57.3) for Pre and Post therapy exams, respectively (Figure 1). The mean Radiologist MTV values were 7.5% and 28.0% higher than the NMTS values for the Pre and Post therapy exams, respectively. There were 2/10 patients with critical missed segments by the NMTS. These critical segments include a mediastinal mass that was perceived as physiologic heart uptake and a scalp lesion mistaken for physiologic brain activity. The mean Radiologist number of non-lymphomatous segments removed was 20.6 (range 8-28) and 18.3 (range 9-41) for the Pre and Post therapy exams, respectively. The mean NMTS number of non-lymphomatous segments removed was 19.2 (range 7-33) and 17.8 (range 7-49) for the Pre and Post therapy exams, respectively. The common sites of removed physiologic segmentation included urinary bladder (5%), brain (5%), lung (7%), mouth (8%), bowel (8%), kidney (22%) and musculoskeletal (25%). Statistical analysis revealed no significant difference between total MTV and number of lesions between NMTS and radiologists.(Table 1).

Discussion

Our study demonstrates a potential role Nuclear Medicine Technologist students may have in calculating total MTV for patients with DLBCL. We developed an effective two-part MTV calculation workflow: 1) Technologists set a threshold, remove obvious erroneous segments, and flag uncertain segments then 2) Radiologist reviews and finalizes the segmentation for MTV

calculation. Once final, the Technologist could then review the final segmentation for continuous feedback and quality improvement, especially around areas with high physiologic uptake which were the regions of discordant reporting between the NMTS and the Radiologist. There was minor difference in calculations of the total MTV when comparing the NMTS to the Radiologists with the caveat of missing two major lymphomatous lesions.

Our results demonstrate how NMTS with minimal training can aid Radiologists in tumor segmentation using a fixed threshold of normal liver SUVmax. This fixed absolute threshold method has been shown favorable in calculating MTV to aid in predicting prognosis and patient outcomes. (*1,10-12*)

Segmenting tumors on 18F-FDG PET remains a challenging task due to relative low resolution of PET images, partial volume effect, high variability of biodistribution, and high intensity of physiologic uptake.(*12*) An alternative to utilization of Nuclear Medicine Technologist students for increasing efficiency of tumor segmentation is the use of artificial intelligence (A.I.) and machine learning. (*13-15*) Early studies have shown promise in using a deep learning method to generate TMTV values prognostic of outcome in a large group of patients with DLBCL. (*16*)

Conclusion

Our results suggest favorable accuracy in utilization of Nuclear Medicine Technologist students for TMTV calculation as a preliminary step within a group of patients with DLBCL. However, more data is needed to support this approach.

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Patient #	Pre/Post Therapy	NMTS MTV	Radiologist MTV	NMTS and Radiologist absolute Difference in MTV	NMTS Total Number of Lesions	Radiologist Total Number of Lesions
1	post	0	0	0	10	15
1	pre	60	428	368	31	27
2	post	0	0	0	7	12
2	pre	4	11	7	9	20
3	post	0	0	0	14	14
3	pre	102	102	0	10	10
4	post	106	214	108	27	41
4	pre	1059	1041	18	28	28
5	post	0	0	0	12	12
5	pre	48	47	1	33	27
6	post	171	171	0	24	15
6	pre	1573	1581	8	17	23
7	post	0	0	0	49	39
7	pre	4	4	0	22	22
8	post	0	0	0	11	11
8	pre	1296	1130	166	11	17
9	post	0	0	0	10	9
9	pre	0	0	0	24	24
10	post	0	0	0	14	15
10	pre	2	102	100	7	8

Table 1. Comparison of nuclear medicine technologist students (NMTS) and radiologists' pre and post test values for MTV ($p = 0.893$) and number of lesions ($p=0.771$).

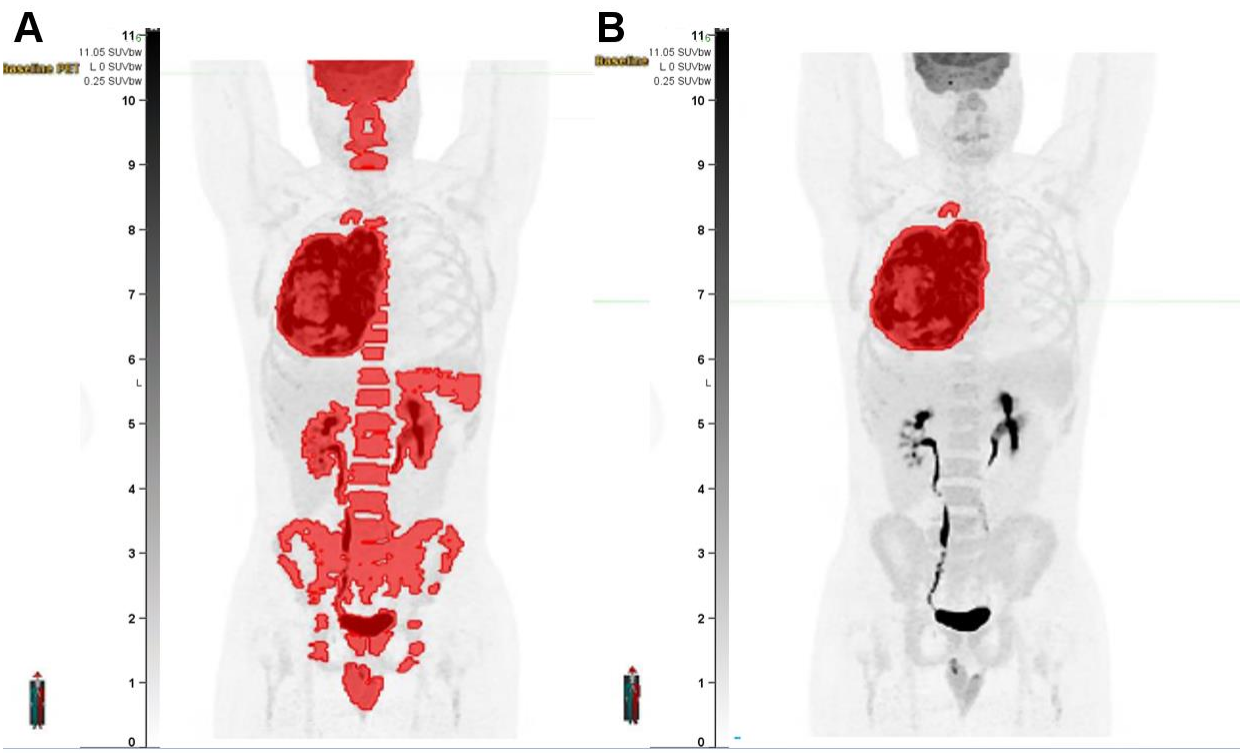
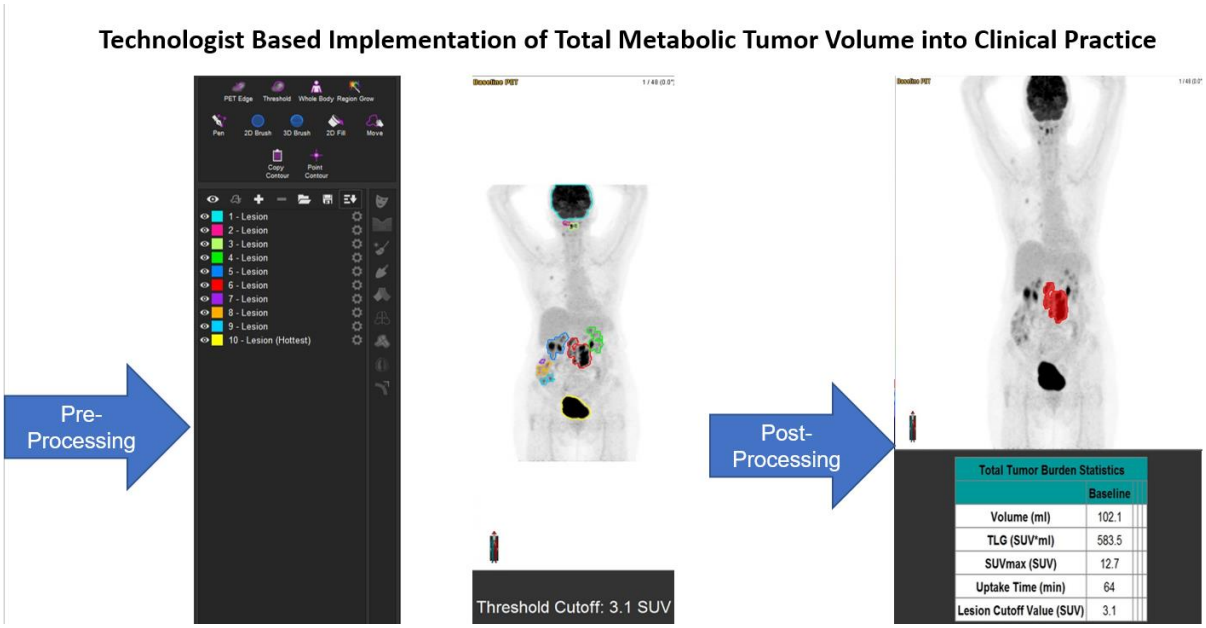


Figure 1. Maximum intensity projection from an ^{18}F-fluorodeoxyglucose positron emission tomography in a patient with diffuse large B-cell lymphoma demonstrating automated segmentation using normal liver standard uptake value as a threshold with volumetric regions of interest produced throughout the body (A). After manual input from a Nuclear Medicine Technologist student, the segments around physiologic uptake are removed and only the lymphomatous lesions are segmented (B).



Graphical Abstract