A B S T R A C T

Introduction/Justification: 18F-FDG PET/CT imaging is widely used in oncology for staging and monitoring treatment response in multiple myeloma (MM). Studies have shown reduced 18F-FDG uptake in the brains of patients with disseminated malignancies, such as malignant lymphoma and other aggressive cancers. This phenomenon is likely associated with the Warburg effect and hyperlactatemia. **Objectives:** This study aimed to evaluate whether the brain-to-liver ratio (BLR) of 18F-FDG uptake in MM patients serves as a prognostic marker. **Materials and Methods:** A total of 82 MM patients diagnosed between March 2011 and May 2019 were included, with a median follow-up of 25 months (range: 0.1 −113). All patients underwent whole-body 18F-FDG PET/CT at diagnosis after fasting for at least six hours and with peripheral blood glucose levels below 180 mg/dL. A dose of 0.1 mCi/kg of 18F-FDG was intravenously administered 60 minutes before image acquisition. Brain and liver standardized uptake values (SUVmean) were determined using automated whole-brain segmentation and a spherical volume of interest (VOI) in the liver. The BLR was calculated by dividing the brain SUVmean by the liver SUVmean for each patient. Descriptive and bivariate analyses were performed. Overall survival (OS) and progression-free survival (PFS) were estimated using the Kaplan-Meier method and compared with the log-rank test (IBM-SPSS v.24). The follow-up data were updated in January 2025. **Results:** The cohort included 55% male patients, with a median age of 64 years (range: 39−87). At diagnosis, 67% had ISS stage III disease, 16% had an ECOG performance status ≥ 2, and 88% presented with bone lesions. Chemotherapy was administered to 94% of patients, with 27% receiving bortezomib. A complete response (CR), very good partial response (VGPR), or partial response (PR) was achieved by 71% of patients. Disease progression occurred in 47% of cases, and the overall mortality rate was 69%. The 60-month OS and PFS rates were 35% and 10%, respectively. The BLR was significantly correlated with sex (R= 32%, P= 0.006), overweight status (R = 32%, P =0.007), ISS stage (R = 23%, P = 0.04), and beta-2 microglobulin levels (R = 42%, P < 0.0001). Patients with a median BLR >2.7 had significantly better OS (50% vs. 13%, P= 0.006) and PFS (3% vs. 0%, P = 0.006). **Conclusion:** BLR derived from 18F-FDG-PET/CT at diagnosis appears to be a strong prognostic indicator of OS and PFS in MM patients, with a cut-off value of 2.7. BLR also correlates with beta-2 microglobulin, a well-established serum marker of tumor burden, and ISS stage III disease. The lower 18F-FDG uptake in more aggressive MM cases may be associated with neoplastic lactate production. Given that brain cells can utilize lactate as an alternative energy source when blood lactate levels rise, this may result in reduced brain FDG uptake. Consequently, BLR may serve as a marker of high glycolytic MM burden and provide an estimate of disease severity.

Keywords: 18F-FDG PET/CT, Brain-to-Liver Ratio (BLR), Multiple Myeloma, Prognostic Marker, Tumor Glycolysis.

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SYNTHESIS, CHARACTERIZATION, AND RADIOLABELING OF MODIFIED EGFR-TARGETING PEPTIDES: POTENTIAL THERANOSTIC AGENTS?

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A B S T R A C T

Introduction/Justification: Cancer remains one of the leading causes of mortality worldwide. Consequently, efforts to overcome the limitations of conventional therapies have increasingly focused on molecularly targeted treatments, with particular emphasis on peptides due to their anti-tumorigenic properties and high affinity for receptors overexpressed in tumors. Peptides designed to inhibit intracellular signaling pathways play a key role in molecularly targeted therapies, often focusing on receptors such as the Epidermal Growth Factor receptor (EGFr), which is overexpressed in many solid tumors. As targeting biomolecules, these peptides can also serve as carriers for radionuclides, enabling both molecular imaging and targeted radionuclide therapy. **Objectives:** This study aimed to develop modified peptides with high affinity for EGFr, thereby enabling their potential application as theranostic molecules. **Materials and Methods:** Anti-EGFr peptides were modified by incorporating two different spacers—hexa-aminocaproic acid (C6) or dodeca-aminocaproic acid (C12)—and by adding the chelating agent DOTA. These peptides were synthesized using the Fmoc/tBu strategy for peptide synthesis. Cleavage from the resin was performed using a reagent mixture with a high concentration of trifluoroacetic acid (reagent K). Subsequently, the peptides underwent characterization and purification through high-performance liquid chromatography (HPLC) and mass spectrometry. A preliminary radiolabeling assay of DOTA-C6-anti-EGFR was conducted using cyclotron-produced yttrium-86 (^{86}Y) in a NaOAc buffer (pH 5.5). The radiochemical reaction was carried out at 95°C for 30 min, followed by purification through a Sep-Pak C18 cartridge to determine the radiolabeling yield. **Results:** The peptides DOTA-C6-anti-EGFr and DOTA-C12-anti-EGFr were successfully synthesized, with yields of 33.8% and 3.3%. HPLC and mass spectrometry analyses confirmed the efficiency of the synthesis, cleavage, and purification processes, as evidenced by the molecular masses corresponding to the expected peptides. Preliminary radiolabeling data for DOTA-C6-anti-EGFr with ^{86}Y demonstrated a radiochemical yield of approximately 96.5%. **Conclusion:** The modified peptides targeting EGFr were successfully synthesized, characterized, and purified. The significantly lower yield obtained for the C12 spacer suggests that peptides incorporating the C6 spacer are more viable for further development. Moreover, the high radiochemical yield of DOTA-C6-anti-EGFR highlights its potential for future radiochemical and theranostic applications, warranting further investigation.

Keywords: Anti-EGFr peptides, Cancer, Radiolabeled peptides.

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COMPARATIVE STABILITY OF CT-BASED BONE VOLUME QUANTIFICATION USING 18F-FDG AND 68GA-PSMA PET/CT IN MULTIPLE MYELOMA

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A B S T R A C T

Introduction/Justification: Computed Tomography (CT) images obtained from hybrid nuclear medicine equipment have shown great potential for PET image segmentation. Previous studies in patients with Multiple Myeloma (MM) have demonstrated the feasibility of calculating bone volume (BV) from CT data in 18F-FDG PET/CT images. This segmentation technique allows for the extraction of variables such as mean Standardized Uptake Value (SUVmean), Percentage of Bone Involvement (PBI), and Intensity of Bone Involvement (IBI) across the entire skeleton. The aim of this study is to determine whether BV quantification based on CT Hounsfield units (HU) is stable across different radiotracers. **Objectives:** To compare BV calculations from PET/CT scans using 18F-FDG and 68Ga-PSMA in patients with MM. **Materials and Methods:** This study included 18F-FDG and 68Ga-PSMA PET/CT scans performed within a 1 to 8-day interval in 15 patients (53% male, mean age 66.7 ± 10.7 years) with biopsy- confirmed symptomatic MM. The study was approved by the local Ethics Committee (CAAE 91231918.0.0000.5404). BV was calculated using the Beth Israel plugin for PET image pre-segmentation, applying a threshold of HU > 100. The cropped PET images were converted to binary format using FIJI, followed by the application of a morphological closing image processing tool to include areas such as bone marrow within the binary contour. For 18F-FDG PET, the skull was excluded during pre-segmentation due to overlapping artifacts caused by cerebral uptake. Descriptive statistics were used to compare FDG and PSMA BV calculations for each patient, with individual percentage deviation assessed relative to the FDG-derived BV. The correlation between BV values was evaluated using Spearman's rank correlation coefficient (r_s), with a significance level of $p < 0.05$. **Results:** The average individual percentage deviation in BV between 18F-FDG PET/CT and 68Ga-PSMA PET/CT was 13 ± 3%, with a range of 7% to 20%. A strong positive correlation was observed between BV values ($p = 3 \times 10^{-10}$), with a very strong Spearman correlation coefficient ($r_s = 0.98$). **Conclusion:** Despite the exclusion of the skull in BV calculations for 18F-FDG, the results indicate a minimal decrease in BV compared to whole-skeleton BV derived from PSMA PET/CT. The very strong correlation between BV values for the two radiotracers suggests that the segmentation approach remains consistent across different PET tracers. Additionally, the proportional exclusion of the skull across patients supports the reliability of the method for BV quantification.

Keywords: 18F-FDG, 68Ga-PSMA, Bone Volume Quantification, Multiple Myeloma, PET/CT imaging.

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SERUM METABOLOMIC ANALYSES IN RECTAL CANCER PATIENTS: AN EXPLORATORY STUDY FROM A TIME-COURSE PERSPECTIVE

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A B S T R A C T

Introduction/Justification: Patients with colorectal cancer frequently develop cachexia, leading to severe depletion of skeletal muscle. Metabolomics, through the analysis of