

Energy Agency (IAEA) technical cooperation projects for development of Latin American Countries (IAEA/TCLAC: EX-BRA6033-2401375).

Keywords: Head and neck cancer, PET/CT scan, PSMA PET/CT scan;.

<https://doi.org/10.1016/j.htct.2024.04.084>

TNFRSF1B GENE VARIANTS IN RISK AND CLINICOPATHOLOGICAL ASPECTS OF PATIENTS WITH CUTANEOUS MELANOMA

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Introduction/Justification: Cutaneous melanoma (CM) is a low incidence tumor worldwide but is associated with high mortality. Skin exposure to ultraviolet radiation from sunlight and genetic factors are related to carcinogenesis of CM. CM is also one of the most immunogenic types of solid tumors, eliciting an active antitumor response. Regulatory T lymphocytes (Tregs) modulate the destruction of abnormal cells by binding tumor necrosis factor (TNF) to /tumor necrosis factor receptor 2 (TNFR2) on their surfaces. Treg depletion reduced the number of metastases in TNFR2-deficient animals. Basal levels of TNFR2 altered relapse-free survival in CM patients, and antibodies targeting TNFR2 on Tregs are seen as promising agents to promote tumor immune-mediated control. TNFR2 is encoded by the polymorphic gene TNFRSF1B. Therefore, the ability to destroy abnormal cells varies among individuals, and may lead to distinct risk for melanoma and distinct clinicopathological aspects in CM patients. **Objectives:** This study aimed to analyze the roles of TNFRSF1B c.587T>G, c.*188A>G, c.*215C>T, and c.*922C>T single nucleotide variants (SNVs) in risk of CM and in clinicopathological aspects of CM patients. **Materials and Methods:** All consecutive patients with CM diagnosed at the General Hospital of the University of Campinas and the Cancer Hospital of Barretos from November 2018 to July 2000 were enrolled in study. Blood donors from the Hematology and Hemotherapy Center served as controls of the study. Clinicopathological characteristics of patients and controls were obtained from the medical records. Genotyping was performed by real-time polymerase chain reaction (RT-PCR) in DNA extracted from peripheral blood leukocytes of

patients and controls. Differences between groups of patients were analyzed using Fisher's or chi-square test, and multiple comparisons were adjusted by the Bonferroni method. **Results:** A total of 433 patients and 502 controls were enrolled in the study. The TNFRSF1B c.587TT genotype was more common in patients than in controls (63.5 versus 61.6%, $p=0.04$); individuals with c.587TT genotype were under 1.41 (CI95%: 1.01-1.98)-fold increased risk for CM than those with the remaining genotypes. An excess of the c.587TT genotype was seen in patients aged ≤ 54 years compared to older patients (69.5 versus 57.0%, $p=0.007$). No associations of genotypes with pathological aspects of tumors were found in the study. **Conclusion:** Our findings show, for the first time, that TNFRSF1B c.587T>G can affect the risk and age of onset of CM. **Acknowledgements:** The study was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES #88887.337514/2019-00), Fundação de Apoio ao Ensino e à Pesquisa do Estado de São Paulo (FAPESP #2019/09168-8).

Keywords: Clinicopathological aspects, Melanoma, Risk.

<https://doi.org/10.1016/j.htct.2024.04.085>

COMPARISON BETWEEN PET/CT WITH 18F-PSMA-1007 AND WITH 18F-FDG IN MUSCLE-INVASIVE BLADDER UROTHELIAL CARCINOMA

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Introduction/Justification: Muscle-invasive bladder cancer (MIBC) presents high rates of metastasis and recurrence, making its monitoring challenging. PET/CT with 18F-FDG is relevant in evaluating this disease, although its urinary excretion makes the analysis of some cases difficult, even when diuretics are used. Prostate-specific membrane antigen (PSMA) is also expressed in neoangiogenesis of MIBC, making it a potential disease marker. In particular, the radiotracer 18F-PSMA-1007, unlike other analogs of this molecule, is predominantly excreted through the biliary tract, thereby facilitating the evaluation of the urinary tract. **Objectives:** The aim of this study was to compare PET/CT with 18F-FDG and with 18F-PSMA-1007 in evaluating MIBC. **Materials and Methods:** Four male patients (ages 57-73 years) were prospectively studied, undergoing PET/CT 60 minutes after intravenous administration of 0.11 mCi/kg 18F-FDG and 5 and 90 minutes after intravenous injection of 18F-PSMA-1007. Additional late (2h) pelvic images were obtained with both tracers after intravenous furosemide injection. Images were analyzed by 2 experienced nuclear physicians and 1 radiologist. The maximum standardized uptake value (SUVmax) of each lesion was measured

for both radiotracers. **Results:** 18F-PSMA-1007 uptake in bladder lesions and regional lymph nodes progressively increased between 5, 90 minutes and 2 hours. A total of 11 lesions were identified in the 4 patients using 18F-PSMA-1007 and 9 using 18F-FDG. Two patients had undergone transurethral resection and had no active macroscopic lesions in the bladder. 18F-PSMA-1007 detected bladder lesions in the other 2 patients (SUV_{max} = 9.8 and 23.4), while FDG detected only 1 (SUV_{max} = 30.0), with the other lesion indistinguishable from radioactive urine, even after diuretic administration. Both tracers detected lymph node metastases in 3 patients (SUV_{max} = 4.1 to 15.8, and 9.5 to 18.3, respectively, for 18F-PSMA-1007 and 18F-FDG), and bone metastasis in 1 patient (SUV_{max} = 11.1 and 10.1 for 18F-PSMA-1007 and 18F-FDG, respectively). Two patients had pulmonary inflammatory/infectious processes that were FDG-avid but not 18F-PSMA-1007-avid. **Conclusion:** PET/CTs with 18F-FDG and 18F-PSMA-1007 appear to have similar sensitivities for MIBC lesions. Due to lower uptake in inflammatory processes, 18F-PSMA-1007 appears to have higher specificity and, due to significantly lower urinary excretion than 18F-FDG, may be more favorable for evaluating the primary bladder lesion. The significant uptake of 18F-PSMA-1007 in MIBC lesions raises the possibility of theranostic approach in selected patients.

Keywords: 18F-FDG PET/CT, bladder cancer, PSMA PET;

<https://doi.org/10.1016/j.htct.2024.04.086>

COMPARISON OF IBI AND PBI CALCULATED FOR 68GA-PSMA AND 18F-FDG IN MULTIPLE MYELOMA PATIENTS

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Introduction/Justification: The benefits of using 18F-FDG PET/CT for staging and managing treatment in patients with multiple myeloma (MM) are extensively documented. Recent studies indicate that 68Ga-PSMA PET/CT is also an excellent marker for MM lesions and may complement 18F-FDG due to the significant genetic heterogeneity observed in these patients' lesions. The involvement of bone tissue stands out as one of the most critical aspects of MM. To quantify this

involvement, two quantitative parameters have recently been proposed: Percentage of Bone Involvement (PBI) and Intensity of Bone Involvement (IBI). **Objectives:** This study aims to compare PBI and IBI in 68Ga-PSMA and 18F-FDG PET/CT images for multiple myeloma patients. **Materials and Methods:** Fifteen patients were included in the study, 8 men (53.3%), with a mean age of 66.7 ± 10.7 years. The patients underwent 68Ga-PSMA and 18F-FDG PET/CT scans with a maximum interval of 8 days between images (median 4 days). The bone tissue was segmented in the images based on the Hounsfield scale of the CT image, followed by processing for closing of the volume of interest (VOI). Both PBI and IBI were calculated for the two radiotracers, with the liver SUV used as a reference for 18F-FDG and the left atrium as a reference for 68Ga-PSMA. Spearman's rank-order correlation assessed the relationship between PBI and IBI data. **Results:** On average, PBI values were higher for 68Ga-PSMA than for FDG, at $3.07\% \pm 2.5\%$ and $1.96\% \pm 3.8\%$, respectively. The mean IBI values were similar for both radiotracers: 0.08 ± 0.13 for 18F-FDG and 0.08 ± 0.09 for 68Ga-PSMA. The median IBI calculated for 68Ga-PSMA was 0.05, higher than the 0.01 found for 18F-FDG. Despite the similarity in average values between 68Ga-PSMA and 18F-FDG, the maximum PBI and IBI values were found in different patients for both radiotracers. Additionally, the Spearman test did not indicate correlation between the variables: ($r = 0.39$; $p = 0.16$) for PBI and ($r = 0.41$; $p = 0.13$) for IBI. **Conclusion:** The average and maximum values of PBI and IBI for 68Ga-PSMA and 18F-FDG are close. However, no correlation was found between them, highlighting that the heterogeneous genetic profile of the disease results in different uptake patterns for both radiotracers.

Keywords: FDG, IBI, multiple myeloma, PSMA.

<https://doi.org/10.1016/j.htct.2024.04.087>

18F-FLUORIDE PET/CT vs 18F-PSMA-1007 TO DETECT BONE METASTASES IN PROSTATE CANCER – A HEAD-TO-HEAD PROSPECTIVE COMPARISON

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