



# Prognostic significance of pretreatment $^{18}\text{F}$ -FDG positron emission tomography/computed tomography in pediatric neuroblastoma

Andrew J. Sung<sup>1</sup> · Brian D. Weiss<sup>2,3</sup> · Susan E. Sharp<sup>1,4</sup> · Bin Zhang<sup>3,5</sup> · Andrew T. Trout<sup>1,3,4</sup> 

Received: 25 August 2020 / Revised: 28 December 2020 / Accepted: 8 February 2021 / Published online: 25 February 2021  
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## Abstract

**Background**  $^{18}\text{F}$ -2-fluoro-2-deoxyglucose (FDG) positron emission tomography (PET) shows tumor activity in most neuroblastomas, but the role of  $^{18}\text{F}$ -FDG PET/CT in neuroblastoma remains to be defined.

**Objective** This study explored the prognostic significance of  $^{18}\text{F}$ -FDG PET in newly diagnosed neuroblastic tumors.

**Materials and methods** This retrospective study reviewed all  $^{18}\text{F}$ -FDG PET/CT examinations performed for a new diagnosis of suspected neuroblastoma. *MYCN* amplification status, tumor recurrence and survival were abstracted from the medical record. Primary tumors were manually segmented to measure maximum standardized uptake value ( $\text{SUV}_{\text{max}}$ ), mean standardized uptake value ( $\text{SUV}_{\text{mean}}$ ), tumor volume and total lesion glycolysis. Univariate and multivariable analyses using Cox proportional hazards regression testing assessed the predictive performance of PET indices for event-free survival and overall survival with thresholds determined using receiver operating characteristic curve analysis.

**Results** Fifty-five children were included, with a median age of 2.9 years (interquartile range [IQR] 1.8–3.0 years).  $\text{SUV}_{\text{max}}$ , tumor volume and total lesion glycolysis were higher in *MYCN*-amplified tumors ( $P=0.012$ ,  $P<0.0001$ ,  $P<0.0001$ , respectively) and in higher International Neuroblastoma Risk Group (INRG) stages ( $P=0.0008$ ,  $P=0.0017$ ,  $P=0.0017$ , respectively). After adjusting for age, tumor  $\text{SUV}_{\text{max}}$  ( $P=0.028$ ) and  $\text{SUV}_{\text{mean}}$  ( $P=0.045$ ) were associated with overall survival. An  $\text{SUV}_{\text{max}}$  threshold of 4.77 ( $P=0.028$ ) best predicted overall survival, with median overall survival of 2,604 days ( $\text{SUV}_{\text{max}}>4.77$ ) vs. >2,957 days ( $\text{SUV}_{\text{max}}\leq 4.77$ ). No PET parameters were independently significantly associated with overall survival or event-free survival after controlling for *MYCN* status, stage or treatment risk stratification.

**Conclusion** Tumor metabolic activity is higher in higher-stage *MYCN*-amplified neuroblastic tumors. Higher  $\text{SUV}_{\text{max}}$  and  $\text{SUV}_{\text{mean}}$  were associated with worse overall survival but were not independent of other prognostic markers.

**Keywords** Cancer · Children · Computed tomography ·  $^{18}\text{F}$ -2-fluoro-2-deoxyglucose · Neuroblastoma · Positron emission tomography · Prognosis · Tumor

✉ Andrew T. Trout  
andrew.trout@cchmc.org

<sup>1</sup> Department of Radiology,  
Cincinnati Children's Hospital Medical Center,  
3333 Burnet Ave., MLC 5031, Cincinnati, OH 45229, USA

<sup>2</sup> Cancer and Blood Diseases Institute,  
Cincinnati Children's Hospital Medical Center,  
Cincinnati, OH, USA

<sup>3</sup> Department of Pediatrics,  
University of Cincinnati College of Medicine,  
Cincinnati, OH, USA

<sup>4</sup> Department of Radiology,  
University of Cincinnati College of Medicine,  
Cincinnati, OH, USA

<sup>5</sup> Division of Biostatistics and Epidemiology,  
Cincinnati Children's Hospital Medical Center,  
Cincinnati, OH, USA

## Introduction

Neuroblastoma is the most common extracranial solid tumor of childhood, accounting for 8–10% of all childhood malignancies and 15% of pediatric cancer-related deaths [1]. Despite advances in multi-modal therapy including dose-intensive and myeloablative therapy with hematopoietic stem cell support, radiation therapy and immunotherapy, the survival for children presenting with metastatic neuroblastoma (International Neuroblastoma Risk Group Staging System [INRGSS] Stage M) remains poor, with a 3-year event-free survival of 60% [2].

While  $^{123}\text{I}$ -metaiodobenzylguanidine (MIBG) scintigraphy remains the dominant disease-specific imaging modality for neuroblastoma,  $^{18}\text{F}$ -2-fluoro-2-deoxyglucose (FDG) positron emission tomography (PET) shows tumor activity in the majority of cases [3]. Despite showing tumor activity, the

contribution of  $^{18}\text{F}$ -FDG to the management of children with neuroblastoma remains incompletely defined. Currently,  $^{18}\text{F}$ -FDG PET/CT is selectively used at some sites because of MIBG availability [4] and is used for non-MIBG-avid tumors but is otherwise not widely applied in children with neuroblastoma.

$^{18}\text{F}$ -FDG has the potential to contribute to the management of children with neuroblastoma. Studies have shown that  $^{18}\text{F}$ -FDG might have higher sensitivity than MIBG for detecting soft-tissue lesions [5] and stage 1 or stage 2 disease [6]. Other studies have suggested that pretreatment  $^{18}\text{F}$ -FDG PET/CT might have prognostic significance in newly diagnosed neuroblastoma, with a few studies showing that maximum standardized uptake value ( $\text{SUV}_{\text{max}}$ ) is correlated with longer event-free survival and overall survival [5, 7, 8]. However, findings are not consistent across studies, and the role of  $^{18}\text{F}$ -FDG PET/CT remains to be elucidated. The purpose of this study was to explore the prognostic significance of  $^{18}\text{F}$ -FDG PET in children with newly diagnosed neuroblastic tumors by reviewing our clinical experience.

## Materials and methods

### Patients

The institutional review board at Cincinnati Children's Hospital Medical Center approved this retrospective study and waived the requirement for written informed consent. We reviewed the electronic medical record (Epic; Epic Systems Corp., Verona, WI) and imaging record for all children who had undergone clinically indicated  $^{18}\text{F}$ -FDG PET/CT imaging for a new diagnosis of suspected neuroblastoma at our institution between July 2006 and July 2019. Children were excluded if they had undergone prior treatment for neuroblastoma, including surgery or chemotherapy, or if a primary tumor other than a neuroblastic tumor was subsequently identified. When available, additional data were collected from the electronic medical record including age, gender, height, weight, tumor histology characteristics, *MYCN* amplification status, lactate dehydrogenase (LDH) levels and treatment risk stratification.

### Imaging

$^{18}\text{F}$ -FDG PET/CT examinations were performed according to our standard clinical protocol. After fasting for at least 4 h, 3.7–5.2 MBq/kg of  $^{18}\text{F}$ -FDG was administered intravenously and imaging was performed approximately 1 h after radiopharmaceutical administration. A low-dose non-contrast CT scan was obtained during shallow breathing from the skull vertex to toes for the purposes of localization and attenuation correction. Attenuation-corrected PET images were reconstructed with a  $144 \times 144$  matrix.

### Data analysis

For the purpose of this study, we reviewed attenuation-corrected PET images and reconstructed localization CT images using a commercially available viewing platform (MIM Software, Cleveland, OH). Using the PET-edge tool, a single observer (A.J.S., pediatric radiology fellow) drew regions of interest around the primary tumor to measure  $\text{SUV}_{\text{max}}$ , mean standardized uptake value ( $\text{SUV}_{\text{mean}}$ ), tumor volume and total lesion glycolysis (defined as:  $\text{SUV}_{\text{mean}} \times \text{tumor volume}$ ) (Fig. 1). The primary tumor was defined as the dominant soft-tissue mass and all immediately adjacent, inseparable tumor-involved lymph nodes. Mean liver standardized uptake value ( $\text{SUV}_{\text{liver}}$ ) was measured from a spherical volume of interest placed in the right hepatic lobe. This volume of interest was positioned to avoid large vessels and tumor-involved liver parenchyma. All measurements were reviewed and adjusted as needed by a board-certified nuclear radiologist with 6 years of post-fellowship experience (A.T.T.).

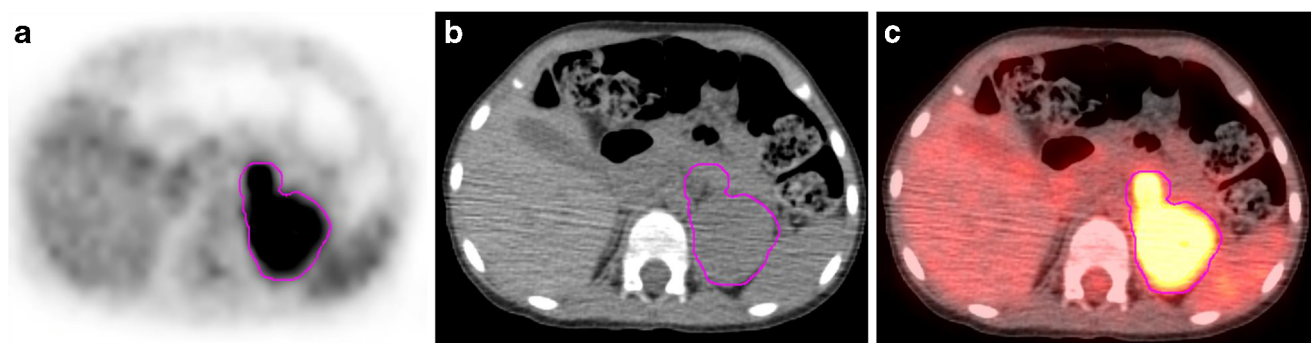
### Statistical analysis

Continuous variables were summarized with means  $\pm$  standard deviations and medians with interquartile ranges (IQR) as appropriate, and categorical variables were summarized with counts and percentages. Event-free survival was defined as the time from diagnosis to tumor progression, recurrence or death. Overall survival was defined as the time from diagnosis to death or last follow-up. We employed univariate and multivariable (including age, *MYCN* amplification, stage and treatment risk stratification) analyses using Cox proportional hazards regression models to assess the predictive performance of PET indices for event-free survival and overall survival. Optimal thresholds for the PET indices were determined using receiver operating characteristic (ROC) curve analysis, and the survival significance of these thresholds was determined using a log-rank test. We used Kaplan–Meier estimator to illustrate the difference in overall survival between two groups based on the threshold. Student's *t*-test was used for comparison of means. A *P*-value of less than 0.05 was considered statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

## Results

### Study population

During the study period, 130 children had undergone FDG PET/CT for suspected neuroblastoma. Of these, 55 children were ultimately confirmed to have a neuroblastic tumor: ganglioneuroma ( $n=2$ ), ganglioneuroblastoma ( $n=6$ ), neuroblastoma ( $n=47$ ). The remaining 75 children were excluded for the



**Fig. 1** Sample tumor segmentation on axial  $^{18}\text{F}$ -FDG positron emission tomography (PET) (a), axial localization CT (b) and fused axial PET/CT (c) images in a 3.5-year-old boy with left suprarenal neuroblastoma.

Maximum standardized uptake value was 6.5, mean standardized uptake value was 2.6, tumor volume was 65 mL and total lesion glycolysis was 170

following reasons: 59 had prior treatment at the time of the PET/CT scan, 5 had no primary tumor or mass identified and 11 had processes other than neuroblastoma (1 renal cell carcinoma, 1 Ewing sarcoma, 1 low-grade fibromyxosarcoma, 1 infantile fibrosarcoma, 1 rhabdomyosarcoma, 1 pheochromocytoma, 1 sclerosing mediastinitis, 1 fibroid, 1 lymphatic malformation, 1 inflammatory tissue, 1 periportal fibrosis).

The demographics and clinical characteristics of the 55 included children are summarized in Table 1. The median age at the time of PET/CT was 2.9 years (IQR 1.8–3.0 years) and 29 (53%) patients were boys.

### $^{18}\text{F}$ -FDG positron emission tomography findings

The metabolic indices for the primary tumor were as follows (mean  $\pm$  standard deviation [range]):  $\text{SUV}_{\text{max}}$   $4.4 \pm 2.2$  (1.1–11.2);  $\text{SUV}_{\text{max}}/\text{SUV}_{\text{liver}}$   $5.2 \pm 2.6$  (1.5–13.0);  $\text{SUV}_{\text{mean}}$   $2.0 \pm 0.8$  (0.8–4.7); tumor volume  $178 \pm 232$  mL (0.80–1,039 mL); total lesion glycolysis  $418 \pm 601$  (0.8–2,681).

### Outcomes

Median follow-up for the included population was 1,508 days (range 27–4,433 days). During the study period, 14 children (25% of 55) experienced an event and 11 children (20% of 55) died. In comparing children with events and those without events, there were statistically significant differences in the primary tumor site, bone marrow involvement,  $\text{SUV}_{\text{max}}/\text{SUV}_{\text{liver}}$ ,  $\text{SUV}_{\text{mean}}$  and total lesion glycolysis (Table 1). All PET/CT measures were significantly higher in higher INRG stages (Table 2).

### Prognostic performance of $^{18}\text{F}$ -FDG positron emission tomography

Univariate analysis revealed tumor  $\text{SUV}_{\text{max}}$  ( $P=0.025$ ) to be significantly associated with overall survival, with a hazard ratio of 1.29 (95% confidence interval [CI] 1.03–1.62). After adjusting for age,  $\text{SUV}_{\text{max}}$  ( $P=0.028$ ) and  $\text{SUV}_{\text{mean}}$  ( $P=0.045$ )

were statistically significantly associated with overall survival, with age-adjusted hazard ratios of 1.30 (95% CI 1.03–1.63) and 2.04 (95% CI 1.02–4.08), respectively. An  $\text{SUV}_{\text{max}}$  threshold of 4.77 ( $P=0.028$ ) best predicted overall survival with a median overall survival of 2,604 days for children with  $\text{SUV}_{\text{max}}$  above this threshold versus >2,957 days (median not reached during the study period) for children with  $\text{SUV}_{\text{max}}$  below this threshold (Fig. 2). Tumor volume and total lesion glycolysis were not significantly associated with overall survival, and no parameters were significantly associated with event-free survival. No parameters were significantly associated with overall survival or event-free survival after adjustment for *MYCN* amplification, tumor stage and risk classification. Among children with stage M disease, no parameters were significantly associated with either overall survival or event-free survival.

### Imaging parameters and *MYCN* status

Forty-nine children (89% of 55) had *MYCN* fluorescence in situ hybridization (FISH) analysis performed; 14 of these 49 (29%) had *MYCN*-amplified tumors. Children with *MYCN*-amplified tumors were older than those without ( $3.6 \pm 2.2$  years vs.  $2.3 \pm 1.6$  years,  $P=0.04$ ). Additionally, mean  $\text{SUV}_{\text{max}}$  ( $5.9 \pm 2.3$  vs.  $4.1 \pm 2.1$ ,  $P=0.012$ ),  $\text{SUV}_{\text{max}}/\text{SUV}_{\text{liver}}$  ( $7.2 \pm 2.6$  vs.  $4.8 \pm 2.3$ ,  $P=0.002$ ), tumor volume ( $409 \pm 339$  mL vs.  $106 \pm 104$  mL,  $P<0.0001$ ) and total lesion glycolysis ( $987 \pm 852$  vs.  $243 \pm 335$ ,  $P<0.0001$ ) were higher in *MYCN*-amplified tumors versus non amplified tumors (Fig. 3).

### Discussion

In this study, we report the metabolic indices from pretreatment  $^{18}\text{F}$ -FDG PET/CT in children with newly diagnosed neuroblastic tumors, and their associations with other indicators of disease severity and survival status. Tumor metabolic activity measured on  $^{18}\text{F}$ -FDG PET was significantly greater in children with *MYCN* amplification and children with higher-

**Table 1** Patient characteristics based on event (progression, recurrence or death)

Characteristics	Total	Event	No event	<i>P</i> -value
Total	55	14 (25%)	41 (75%)	
Alive	44	3	41	
Deceased	11	11	0	
Median age in years [IQR]	2.9 [1.8–3.0]	3.7 [0.9–6.5]	2.3 [1.4–3.2]	0.077 <sup>a</sup>
Gender				1 <sup>b</sup>
Male	29	6	23	
Female	26	5	21	
Primary site				<b>0.029<sup>b</sup></b>
Adrenal	33	12	21	
Extra-adrenal	22	2	20	
Histopathology				0.16 <sup>a</sup>
Ganglioneuroma	2	0	2	
Ganglioneuroblastoma	6	0	6	
Neuroblastoma, differentiating	6	0	6	
Neuroblastoma, poorly differentiated	27	8	19	
Neuroblastoma, unknown	14	6	8	
INRG stage				0.38 <sup>a</sup>
L1	10 (18%)	0	10	
L2	16 (29%)	1	15	
M	28 (51%)	12	16	
MS	1 (2%)	1	0	
Risk stratification				0.18 <sup>a</sup>
Low	20 (36%)	1	19	
Intermediate	5 (9%)	1	4	
High	30 (54%)	12	18	
Bone marrow involvement				<b>0.0018<sup>b</sup></b>
Yes	23	11	12	
No	32	3	29	
MYCN status				0.27 <sup>a</sup>
Amplified	14	5	9	
Not amplified	35	8	27	
Unknown	6	1	5	
Serum LDH (IU/L)	1,702±3,447	1,287±1,034	1,901±4,148	0.33 <sup>a</sup>
Primary tumor size (mL)	178±232	198±153	172±254	0.077 <sup>a</sup>
SUV <sub>max</sub>	4.4±2.2	5.4±2.5	4.0±2.0	0.062 <sup>a</sup>
SUV <sub>max</sub> /SUV <sub>liver</sub>	5.2±2.6	6.6±2.4	4.7±2.6	<b>0.034<sup>a</sup></b>
SUV <sub>mean</sub>	2.0±0.8	2.4±0.8	1.9±0.8	<b>0.027<sup>a</sup></b>
Total lesion glycolysis (SUV <sub>mean</sub> *mL)	418±601	535±488	378±635	<b>0.022<sup>a</sup></b>

<sup>a</sup> Mann–Whitney *U* test; *P*<0.05 is significant (bold)

<sup>b</sup> Fisher exact test; *P*<0.05 is significant (bold)

INRG International Neuroblastoma Risk Group, IQR interquartile range, LDH lactate dehydrogenase, SUV standardized uptake value

stage disease. Further, in our population of 55 children, SUV<sub>max</sub> and SUV<sub>mean</sub> were significantly negatively associated with overall survival after adjustment for age. Specifically, tumors with greater metabolic activity had lower overall survival.

Based on receiver operating characteristic (ROC) curve analysis, we identified a threshold SUV<sub>max</sub> of 4.77 to

optimally stratify our patient population based on overall survival. In children with a primary tumor SUV<sub>max</sub> of 4.77 or less, median overall survival was not reached for the study population during the study period. However, for children with a primary tumor with SUV<sub>max</sub> of greater than 4.77, median overall survival was 2,604 days. Prior studies have

**Table 2** Positron emission tomography/computed tomography (PET/CT) indices based on International Neuroblastoma Risk Group (INRG) stage

		SUV <sub>max</sub>	SUV <sub>max</sub> /SUV <sub>Liver</sub>	SUV <sub>mean</sub>	Tumor volume	TLG
Stage	L1	3.2±1.8	3.1±1.6	1.9±1.0	54.9±68.3	96.0±120.5
	L2	3.4±1.8	4.2±2.2	1.6±0.7	132.9±229.8	188.5±278.9
	M	5.5±2.1	6.5±2.5	2.4±0.7	255.1±250	678.0±727.3
	MS <sup>a</sup>	2.2	N/A <sup>b</sup>	1.7	16.0	27.5
<i>P</i> -value <sup>c</sup>		<b>0.0008</b>	<b>0.00019</b>	<b>0.012</b>	<b>0.0017</b>	<b>0.0017</b>

N/A not applicable, SUV standardized uptake value, TLG total lesion glycolysis

<sup>a</sup> Only one patient

<sup>b</sup> Diffuse liver metastases precluded measurement of normal liver

<sup>c</sup> One-way analysis of variance; *P*<0.05 is significant (bold)

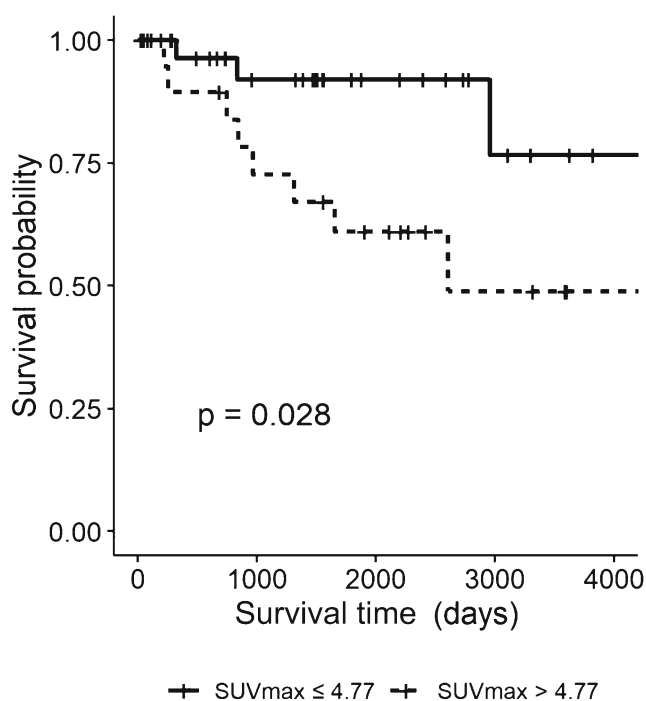
similarly shown <sup>18</sup>F-FDG PET metabolic indices to predict survival of children with neuroblastoma. In a cohort of 50 children, Lee et al. [7] showed primary tumor SUV<sub>max</sub> to predict event-free survival but not overall survival. In that study, a threshold value of 4.0 showed a 2-year event-free survival of more than 80% with low-FDG-uptake tumors and less than 30% with high-FDG-uptake tumors. Papathanasiou et al. [9], in a cohort of 28 children, all with International Neuroblastoma Staging System (INSS) stage 4 neuroblastoma, showed SUV<sub>max</sub> to be significantly associated with both progression-free survival and overall survival at an SUV<sub>max</sub> threshold of 5.3. Finally, Kang et al. [8], in a series of 20 children, reported SUV<sub>max</sub> to be significantly associated with both progression-free survival and overall survival, but

at a higher threshold of 7.78. Taken together, the results of our study and these prior studies clearly demonstrate a relationship between metabolic activity of primary neuroblastic tumors and patient survival. The specific SUV<sub>max</sub> threshold identified in each of these studies to optimally stratify survival varies, likely based on population and technical differences.

Our study also identified differences between *MYCN*-amplified and non-amplified primary tumors. Specifically, *MYCN*-amplified tumors were, on average, larger in volume with higher SUV<sub>max</sub> and total lesion glycolysis than non-amplified tumors. These findings are concordant with those from Liu et al. [10], who demonstrated higher SUV<sub>max</sub>, metabolic tumor volume and total lesion glycolysis in *MYCN*-amplified tumors. These authors also showed SUV<sub>max</sub>, metabolic tumor volume and total lesion glycolysis to be significant predictors of overall survival. While these findings are similar to those in our study, there is an important methodological difference: Liu et al. [10] used a 40% SUV<sub>max</sub> cut-off threshold to calculate metabolic tumor volume and total lesion glycolysis, which might have enriched their study data with higher-grade (more metabolically active) tumor components.

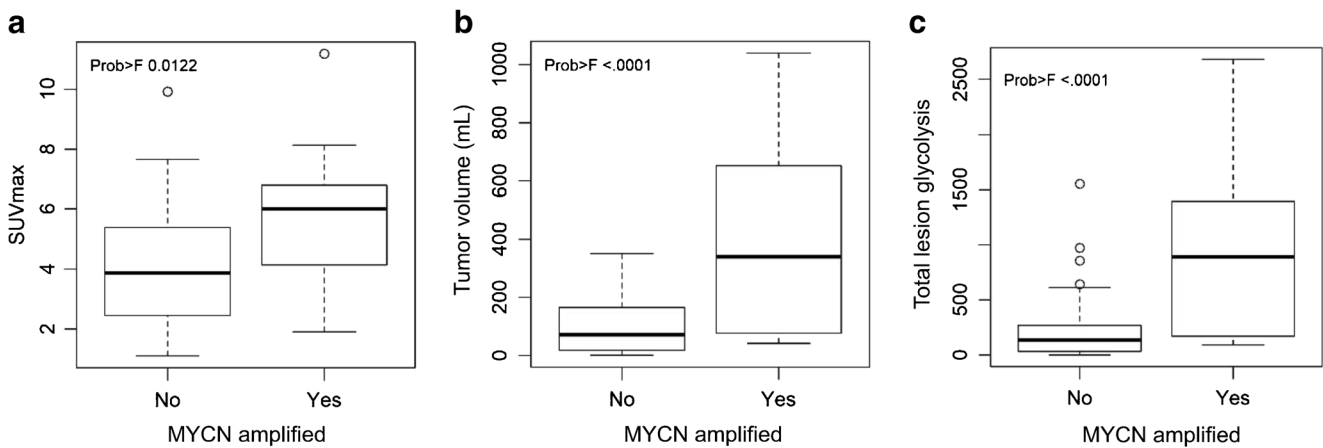
Interestingly, when multivariate Cox proportional hazard regression models controlled for *MYCN* status, stage and treatment risk stratification, none of the PET parameters was independently significantly associated with overall survival or event-free survival in our cohort. This result is similar to findings by Lee et al. [7], although a single parameter, T<sub>max</sub>/L<sub>mean</sub> (total tumor SUV<sub>max</sub>/mean liver SUV), did remain associated with overall survival in their analysis (hazard ratio 3.2, 95% CI 1.2–8.9, *P*=0.02). In conjunction with our findings of higher SUV in higher-stage or *MYCN*-amplified tumors, this suggests an interplay among tumor metabolic activity, tumor stage and *MYCN* amplification status.

There are several limitations to our study. First, as a retrospective study, our results are inherently subject to selection bias. Although <sup>18</sup>F-FDG PET/CT is now performed in most newly diagnosed neuroblastoma cases in our practice, historically it was only performed for MIBG-negative tumors and when MIBG scans were not initially readily available.



**Fig. 2** Overall survival curve based on a threshold maximum standardized uptake value (SUV<sub>max</sub>) of 4.77. Vertical marks along the survival curves reflect censoring





**Fig. 3** Box and whisker plots of positron emission tomography/computed tomography (PET/CT) metabolic indices for *MYCN*-

amplified vs. non-*MYCN*-amplified tumors. **a** Maximum standardized uptake value (SUV<sub>max</sub>). **b** Tumor volume. **c** Total lesion glycolysis

Second, we did not account for the various treatment regimens to which our study population might have been exposed. While treatment paradigms for low- and intermediate-risk tumors — accounting for 45% of our cohort — did not change substantially over the period of the study, the treatment paradigms for high-risk tumors have changed significantly over the last 15 years (e.g., tandem stem cell transplants and dinutuximab immunotherapy have become standard of care). These changes might have impacted outcomes, but cohorts treated under each paradigm are too small to make statistically meaningful conclusions. Third, because this study was focused on <sup>18</sup>F-FDG PET/CT, we did not explore or incorporate findings from <sup>123</sup>I-MIBG imaging performed in the included patients. Last, though ours is the largest cohort described to date, our sample size of 55 is still relatively small. With several studies now published on pretreatment FDG PET/CT in neuroblastoma, a meta-analysis would provide greater statistical power and might provide further insight into the relevance of metabolic features.

### Conclusion

Tumor metabolic activity is higher in newly diagnosed higher-stage, *MYCN*-amplified neuroblastic tumors. Higher SUV<sub>max</sub> and SUV<sub>mean</sub> were associated with worse overall survival but were not independent of other prognostic markers.

### Declarations

**Conflicts of interest** None

### References

1. Maris JM, Hogarty MD, Bagatell R et al (2007) Neuroblastoma. *Lancet* 369:2106–2120
2. Park JR, Kreissman SG, London WB et al (2019) Effect of tandem autologous stem cell transplant vs. single transplant on event-free survival in patients with high-risk neuroblastoma: a randomized clinical trial. *JAMA* 322:746–755
3. Monclair T, Brodeur GM, Ambros PF et al (2009) The international neuroblastoma risk group (INRG) staging system: an INRG task force report. *J Clin Oncol* 27:298–303
4. Liu Y-L, Lu M-Y, Chang H-H et al (2016) Diagnostic FDG and FDOPA position emission tomography scans distinguish the genomic type and treatment outcome of neuroblastoma. *Oncotarget* 7: 18774–18786
5. Kushner BH, Yeung HW, Larson SM et al (2001) Extending positron emission tomography scan utility to high-risk neuroblastoma: fluorine-18 fluorodeoxyglucose positron emission tomography as sole imaging modality in follow-up of patients. *J Clin Oncol* 19: 3397–3405
6. Sharp SE, Shulkin BL, Gelfand MJ et al (2009) <sup>123</sup>I-MIBG scintigraphy and <sup>18</sup>F-FDG PET in neuroblastoma. *J Nucl Med* 50:1237–1243
7. Lee JW, Cho A, Yun M et al (2015) Prognostic value of pretreatment FDG PET in pediatric neuroblastoma. *Eur J Radiol* 84:2633–2639
8. Kang SY, Rahim MK, Kim Y-I et al (2016) Clinical significance of pretreatment FDG PET/CT in MIBG-avid pediatric neuroblastoma. *Nucl Med Mol Imaging* 51:154–160
9. Papathanasiou ND, Gaze MN, Sullivan K et al (2011) <sup>18</sup>F-FDG PET/CT and <sup>123</sup>I-metaiodobenzylguanidine imaging in high-risk neuroblastoma: diagnostic comparison and survival analysis. *J Nucl Med* 52:519–525
10. Liu C-J, Lu M-Y, Liu Y-L et al (2017) Risk stratification of pediatric patients with neuroblastoma using volumetric parameters of <sup>18</sup>F-FDG and <sup>18</sup>F-DOPA PET/CT. *Clin Nucl Med* 42:e142–e148

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