Published in final edited form as:

Pediatr Blood Cancer. 2018 December ; 65(12): e27412. doi:10.1002/pbc.27412.

The Role of Routine Imaging in Pediatric Cutaneous Melanoma

Hadeel Halalsheh, MD¹, Sue C. Kaste, DO^{1,2,7}, Fariba Navid, MD^{3,8}, Armita Bahrami, MD⁴, Barry L. Shulkin, MD^{2,7}, Bhaskar Rao, MD⁵, Michelle Kunkel, CRA⁶, Nathan Artz, PhD², and Alberto Pappo, MD¹

¹Department of Oncology, St Jude Children's Research Hospital, Memphis, Tennessee

²Department of Diagnostic Imaging, St Jude Children's Research Hospital, Memphis, Tennessee

³Division of Hematology, Oncology and Bone Marrow Transplant, Children's Hospital Los Angeles, California

⁴Department of Pathology, St Jude Children's Research Hospital, Memphis, Tennessee

⁵Department of Surgery, St Jude Children's Research Hospital, Memphis, Tennessee

⁶Cancer Center Administration, St Jude Children's Research Hospital, Memphis, Tennessee

⁷Department of Radiology, University of Tennessee school of Health science, Tennessee

⁸Keck School of Medicine, University of Southern California, Los Angeles, CA.

Abstract

Background: Optimal imaging for children with pediatric melanoma (MM) is unknown.

Methods: We reviewed clinical and imaging findings of patients with AJCC stage IIC-IV MM treated on our institutional MEL06 trial. All patients had baseline brain MRI/CT, PET/CT, CT chest, abdomen, and pelvis (CTCAP). Patients on stratum A (PEG-interferon; AJCC IIC, IIIA, IIIB) (n=16) had imaging every 6 months; stratum B1 (PEG-interferon and temozolomide; unresectable measurable disease, metastatic, or recurrent, n=2) had PET-CT scans every 2 months and brain imaging studies every 4 months; stratum B2 patients (PEG-interferon and temozolomide; unresectable non-measurable, metastatic, or recurrent, n=3) had imaging every 4 months. Off therapy imaging was done every 6 months for 3 years

Results: There were 21 patients (11 female, 11 spitzoid, median age 14 years, head/neck (6), trunk (7), extremities (8)). Patients with spitzoid melanoma underwent 236 imaging studies in total (86 PET/CT, 81 CTCAP, 11 CT chest, 10 CT brain, 48 MRI brain) at a median cost per patient of \$32,718. Thirteen studies (5.8%) had findings that led to 2 biopsies (one positive). For conventional MM, 162 studies (61 PET/CT, 57 CTCAP, 8 CT chest, 7 CT brain, and 29 MRI

Corresponding: Alberto S. Pappo; St Jude Children's Research Hospital, 262 Danny Thomas Pl, Memphis, TN 38105; Phone: (901) 595-2322; Fax: (901) 521-9005; alberto.pappo@stjude.org.

CONFLICT OF INTEREST

No conflict of interest

This work was presented previously at ASPHO (American Society of Pediatric Oncology) meeting 2018 as a poster and SPR (Society of Pediatric Radiology) meeting 2018 as an oral presentation.

brain) were performed with a median cost per patient of \$23,420. Twenty (14%) had findings leading to six biopsies (4 positive). At 6.3 years (range 0.4–9.2) 17 patients remain disease free.

Conclusion: Children with spitzoid melanoma require minimal imaging at diagnosis and follow-up. Patients with conventional MM should be imaged according to adult guidelines.

Keywords

melanoma; imaging; spitzoid; children

INTRODUCTION

Cutaneous melanoma (MM) in children and adolescent is rare with most cases affecting patients between 15 and 19 years of age. [1] Genomic and pathologic analysis have identified three distinct subgroups of lesions that are associated with markedly different risks for treatment failure: *de novo* conventional melanoma, melanoma arising in a congenital melanocytic nevus, and spitzoid melanoma. [2]

The optimal imaging approach to diagnose and follow pediatric patients with MM have not been well established, therefore, guidelines for adults are usually followed regardless of the histologic or genomic subtype. The use of imaging modalities such as computed tomography (CT) modalities is costly and associated with risks such as radiation exposure, and complications related to anesthesia.

To better define the role of imaging in children and adolescents with MM, we reviewed our experience at St. Jude Children's Research Hospital in children who were uniformly treated on an institutional melanoma trial.

PATIENTS AND METHODS

We retrospectively reviewed the medical records of patients aged 0–21 years with AJCC stage IIC-IV cutaneous MM treated on our institutional MEL06 protocol. [3] Patients were referred for protocol enrollment after diagnosis of MM and were followed-up through December 2017. We analyzed patient characteristics, imaging modalities, imaging findings, clinical data, histopathology findings, treatment, and outcome.

Imaging modalities and treatment in this protocol included brain magnetic resonance imaging (MRI) or CT, positron emission tomography/computed tomography (PET/CT), CT chest, abdomen, and pelvis (CTCAP) and interferon and temozolomide, respectively. The treatments according to stage as well as the scheduled imaging procedures are depicted in Fig. 1.

The diagnosis of melanoma in all cases was centrally reviewed and additional genomic tests such as fluorescence in situ hybridization (FISH), comparative genomic hybridization (CGH), and mutational analysis were performed to define the subtype of melanoma. The specific criteria for the diagnosis of spitzoid melanoma have been summarized previously. [4] Telomerase Reverse Transcriptase (*TERT*) promoter mutational analysis was performed retrospectively in all patients with spitzoid melanoma.

Imaging findings were considered suspicious for disease if the interpreting physician reported persistent abnormal findings through more than one imaging modality leading to further clinical/radiological follow-up, tissue biopsy and/or evaluation by another imaging modality. Imaging findings and number were collected until the time of first event, defined as disease recurrence, progression or death. Cost of each scan includes the technical charge and the professional fee; the cost of anesthesia was excluded.

Effective doses for common radiation-based imaging exams at our institution were recently published for five age groups. [5] Dose estimates were derived using updated age-averaged and gender-averaged tissue-weighting factors provided in Report 103 by the International Committee on Radiological Protection and are currently used by our Institutional Review Board as a reference for reviewing research protocols. To provide a general estimate of radiation dose burden for each patient in this study, effective dose from a particular imaging examination type (eg. Head CT, Chest CT, FDG-PET, etc.) was assigned using this reference and the age of the subject at time of enrollment. Cumulative effective dose was then approximated for each patient by summing dose values for protocol-related imaging as well as additional imaging performed due to abnormal findings.

The decision to obtain tissue for histologic analysis was left to the discretion of the treating physician.

RESULTS

Patient Characteristics

From June 2007 through September 2012 we identified 21 patients (11 females) meeting eligibility criteria. The median age was 14 years (range, 3.2–22.1). Ten patients had conventional melanoma (CM) and 11 patients had spitzoid melanoma (Table 1). Primary sites were head and neck (n=6), trunk (n=7), and extremities (n=8). Sixteen patients were treated on stratum A, two on stratum B1, and three on stratum B2. A total of 398 imaging studies (147 PET/CT, 138 CTCAP, 19 CT chest, 17 CT brain, and 77 MRI brain) were performed with a median of 8, 7, 0, 1 and 3 studies per patient, over an average of 35 months of follow-up; respectively. The total cost for all the imaging studies performed in these patients is estimated to be \$577,952.00. The average and median cumulative effective doses of imaging-based radiation across patients were 108.8 mSv (range 32.5 – 198.5 mSv) and 107 mSv, respectively.

Analysis by Subtype of Melanoma

Spitzoid Melanoma—The median age was 8.4 years (range, 3.5–14.6 years). All but one of the 11 patients were treated on stratum A. A total of 236 scans were performed (86 PET/CT, 81 CTCAP, 11 CT chest, 10 CT brain, and 48 MRI brain) with a median of 8, 7, 0, 4 and 0 studies per patient respectively (Table 2). The median cost was \$32,718.00 per patient (range \$12,479.00 - \$41,634.00). The average and the median cumulative doses of imaging-based radiation were 101 mSv (range 65 – 130.4 mSv) and 102 mSv per patient, respectively. Of the 236 scans, 13 (5.8%) were suspicious for metastasis/progression/recurrence which led to an additional 28 studies and two biopsies. One of the two lung

biopsies in two patients was positive for disease and the other showed granuloma. The remaining abnormalities (n=11) either remained stable (n=4), regressed (n=4) or were thought to be due to benign based on radiographic appearance and therefore no biopsy was obtained (n=3, intussusception, thyroid cyst, non-ossifying fibroma). Of the 13 suspicious scans performed on 10 patients, only one had an abnormality that was attributed to disease; this was detected 12 months after diagnosis. This patient died of disease 18 months after diagnosis, whereas the remaining patients were in first remission 4.9–9.2 years after diagnosis. In retrospect only one had a documented *TERT* promoter mutation.

Characteristics of Suspicious Scans and Outcomes

At Diagnosis: Four CT scans of the chest were positive: one patient had a lung nodule measuring 0.9×1.1 cm that slightly increased and became more dense over 2 weeks; confirmed by biopsy to be a granuloma. CT scans in two other patients showed nodules that initially measured <5 mm and repeat scan 2 weeks later were interpreted to be suspicious for infection in one and stable in the other. Scan in the fourth patient showed a 3-mm nodule which regressed in a follow-up scan one week later.

During Therapy: Five scans were suspicious for disease: one showed multiple pulmonary nodules (largest 6 mm in diameter), that progressed on follow-up scans, and confirmed on biopsy to be metastatic disease. One PET/CT scan in another patient showed a metabolically avid lesion in the femoral head 9 months after diagnosis, which on X-ray and MRI of the femur was typical of a non-ossifying fibroma (Fig. 2). In a third case, PET/CT and CT of the abdomen showed enlargement of an abdominal lymph node (largest 2.3×0.9 cm) with moderately elevated uptake, which remained stable in follow-up scans. In the fourth patient, a sphenoid lucency on CT of the brain was negative on PET/CT and regressed on a follow-up scan. The last scan was an MRI brain which showed leptomeningeal enhancement suspicious for metastasis which remained stable on multiple subsequent scans and in retrospect was a vascular anomaly.

Off Therapy Follow-Up: Four scans had findings suspicious for disease: one CT chest showed new small lung nodules that remained stable on a follow-up scan after 3 months. In one patient, a PET/CT scan showed avidity in the thyroid gland which was found on follow-up thyroid US to be a benign thyroid cyst. CT and PET/CT in another patient showed an abdominal mass detected by CT and PET/CT which proved by US to be an intussusception. PET/CT scan in the fourth patient showed a metabolically active enlarged cervical lymph node larger than 1 cm, clinically palpable and tender. It regressed on a follow-up scan 4 weeks later.

Conventional Melanoma—The median age was 17.1 years (range, 3.9–22.1 years). Six patients were treated on stratum A, two on stratum B1, and two on stratum B2. A total of 161 scans were performed (61 PET/CT, 57 CTAP, 8 CT chest, 7 CT brain, and 27 MRI brain) with a median of 7, 6.5, 0, 1, 3 studies per patient respectively (Table 2). The median cost per patient was \$23,420 (range \$7,870 - \$41,756). The average and the median cumulative doses of imaging-based radiation were 117.4 mSv (range 32.5 – 198.5 mSv) and 119.9 mSv per patient, respectively. Twenty scans (14%) demonstrated suspicious lesions in

nine different patients which led to 19 additional scans and prompted six diagnostic biopsies in five patients (one patient had a lung lesion at diagnosis with pathology of intra-parenchymal lymph node, nine months after diagnosis developed locoregional recurrence proved by a biopsy). Four of the six biopsies identified disease in four patients: two were performed at the time of enrollment to confirm presumed recurrence at time of referral from other institutions for study enrollment; and two were done for loco-regional recurrence while patients were on active therapy. For the locoregional recurrences, one patient detected a mass on his occiput at the site of primary tumor before the follow-up scan. In the second patient recurrence was detected by the patient shortly after a suspicious scan. The remaining scans where no biopsies were done (n= 14) either remained stable (n=7), regressed (n=3), markedly progressed (n=3) or was of benign etiology (n=1, benign ovarian cyst). In total, seven of the 20 scans showed true disease; of which five scans were from three patients who died of disease. The other two scans were from two patients who are alive and in second complete remission both at 6.3 years of follow-up. The rest of patients were in first complete remission 6.1–7.6 years after diagnosis.

Characteristics of Suspicious Scans and Outcomes

At Diagnosis: Seven scans had abnormal findings: Chest CT showed lung nodules/hilar abnormalities in three patients: One showed multiple lung nodules (largest 0.5 cm) and biopsy showed intra-parenchymal lymph node. This patient developed loco-regional recurrence 9 months after diagnosis but was disease free at last follow-up 6.3 years after diagnosis. The other two scans showed a 0.3 cm lung nodule and a 0.9 cm hilar lymph node (slightly avid by PET/CT), respectively. Both remained stable over follow-up scans. A benign ovarian cyst was seen in one patient. In two other scans recurrence was presumed at presentation for study enrollment, both had confirmatory biopsies. The last scan showed multiple metastatic sites that progressed later.

During Therapy: Seven scans showed abnormalities: mediastinal lymph node enlargement in one patient that remained stable in two follow-up scans 4 then 6 weeks later. In the second case PET/CT and MRI brain showed enhancement in the superficial tissues overlying the superior frontoparietal region. Clinical examination revealed a skin pustule that regressed on a follow-up scan. Loco-regional enhancement was detected on three scans: in one, the patient felt a mass at the site of the primary tumor in the scalp. PET/CT and CT scans showed a 7-mm enhancing nodule that was confirmed to be recurrent disease by tissue biopsy. The second scan was a PET/CT scan which showed a 1.8 cm cervical lymph node with mild avidity. He was scheduled to undergo a follow-up scan in 4 weeks after completing a course of antibiotics but presented with clinically enlarging lymph node before that time. Biopsy confirmed disease recurrence. The last scan was a brain MRI that showed mild enhancement in the cervical area with no discrete mass. The patient had a soft tissue swelling that was improving at the same time. Follow-up 6 weeks later showed stable scan. The last two scans showed marked progression of metastatic disease in two patients, each of whom had a wide spread metastatic disease at diagnosis.

Off Therapy Follow-Up: Six scans showed abnormalities concerning for disease recurrence: a CT chest showed a 0.15 cm lung nodule that remained stable in the follow-up

scan. Loco-regional enhancement was seen by PET/CT in two patients. In the first case, the size of the lymph node was normal. Though it remained of normal size, metabolic avidity shown by PET/CT increased at follow-up. Biopsy showed benign lymphoid hyperplasia. In the other patient, the lymph node size was also normal and remained stable on a short follow-up scan. In a fourth case, metabolic activity shown on PET/CT scan increased activity in the high left parietal bone. The activity was attributed to normal brain activity and regressed on a follow-up PET/CT scan 3 months later. CT scan showed enlarged mesenteric lymph nodes (largest 1.7 cm) in a fifth case which remained stable 3 months later. The last scan was a PET/CT scan that showed increased metabolic activity in the subcarinal soft tissue without definitive CT demonstrable abnormality. This finding was thought to be brown fat. A repeat study performed 3 months later with diazepam pretreatment showed no metabolic activity.

Events and Outcome—After a median follow-up of 3 years (range 0.4–9.2 years), 17 patients are alive and disease free. Four patients died of disease: one with stage IIIB spitzoid melanoma with a *TERT* promoter mutation, treated on stratum A. The remaining three patients had recurrent/metastatic CM at time of presentation and progressed early on therapy (clinical progression confirmed by imaging) and died of disease 4, 6, and 7 months after enrollment.

Two other patients developed loco-regional disease recurrences 9 and 11 months after diagnosis, and both had a mass detected clinically by the patient prior to or shortly after a suspicious finding was seen on imaging, respectively. The first patient underwent resection of the recurrent disease followed by local radiation of 30 Gy and is alive and disease free 6.3 years after diagnosis (Fig. 3). The other patient underwent resection of the recurrent melanoma and was treated with vemurafenib and ipilimumab and local radiation therapy at 30 Gy and is alive and disease free 63 and 76 months after recurrence and initial diagnosis respectively.

DISCUSSION

Malignant melanoma is uncommon in children and adolescents. Due to its rarity, imaging and treatment guidelines are not well established. Current practices are guided by data derived from adult patients although no clear guidelines exist in adults. In the National Cancer Comprehensive Network (NCCN) guidelines version 2.2018, CTAP scan or whole body FDG PET/CT scan with brain MRI is recommended in stage IIIC and higher. Neck CT is performed if clinically indicated at baseline and imaging of other sites is dependent on signs or symptoms suggestive of metastatic disease. For assessing response to therapy, imaging is recommended “at clinically appropriate intervals”. For surveillance for recurrence in patients with no evidence of disease, imaging is recommended at “3–12 months interval”. There is debate as to whether close follow-up in adult patients with melanoma is necessary. [6–9]

In a previous study at our center, imaging identified clinically undetectable metastases in 25% of patients with malignant melanoma (8 out of 33 patients), all had thick lesions (Clark’s level IV or V) or unknown primary sites. Based upon those findings, we

recommended CT of the chest, abdomen, and local-regional nodal basins at diagnosis to determine disease extent on all patients. [10] Our findings contrasted with those reported by Buzaid et al on CT scans performed on 151 adult patients with primary melanoma; of the 29 suspicious scans 24 subsequently proved to have benign processes by biopsy or follow-up studies, three had second primary tumors, and only two were found to have metastatic melanoma. The authors concluded that body CT is not a useful imaging study in the detection of occult metastases in patients with primary melanoma.[11] In a study of adult melanoma Gold et al showed that the yield of radiological studies in patients with positive sentinel lymph node (SLN) biopsy at initial diagnosis in detecting distant metastases was only 3.7% (four positive scans out of 107 after the result of positive SLN), with body CT scans and PET scans having the highest yield, and recommended restricting work-up to patients with thick melanoma (≥ 4 mm Breslow thickness) and macrometastasis on SLN biopsy. [12] Two recent abstracts suggest that the yield of chest radiographs for surveillance after therapy for melanoma is low and that PET may more accurately assess the long term benefits of immunotherapy in these patients. [13,14]

Ultrasound (US) is highly sensitive and specific in evaluating regional lymph nodes in melanoma at diagnosis when compared to CT scan, PET scan, and combined PET/CT; while for distant metastases, PET/CT had the highest sensitivity and specificity. [15–17] In a prospective study of 211 adults with melanoma Francken et al found that 73% of first melanoma recurrences were detected by the patient or their partner. [6] This was also seen in other studies. [9,18–21] In our cohort, two out of three recurrences were detected clinically by the patient before or shortly after an abnormal scan, both were loco-regional. Based on these findings self-examination and US may replace CT scan for disease follow-up; both of which are associated with less cost, no radiation exposure, and a high detection rate.

Spitzoid melanoma presents at a younger age, and despite a high incidence of nodal metastasis, survival approaches 100%. [22–24] In our cohort the median age of diagnosis in patients with spitzoid melanoma was 8.4 years compared to 17.1 year in patients with CM, similar to other reports. [25] Studies at our institution have identified alterations in the *TERT* promoter that are linked to an aggressive behavior in spitzoid melanoma. [4] In our current series the only patient with spitzoid melanoma with metastasis tested positive for a *TERT* promoter mutation.

The average 5-year survival rate for patients with metastatic conventional melanoma is less than 10%. [26,27] Several new targeted and immune therapies have shown antitumor activity with acceptable side effects in patients with advanced melanoma. [28–30] Number and site of metastasis are among several factors that influence survival in patients with metastatic melanoma [27] suggesting that close follow-up imaging of patients with CM to detect low disease burden and at an early stage, coupled with new immune therapies may prolong survival for patients with high risk disease.

Baseline and follow-up imaging expose patients to ionizing radiation, and can result in high cumulative effective doses of radiation. [31] A number of reports have shown that CT scans during childhood and adolescence may be associated with an increase in future cancer risk. [32–34] In this study, patients received an average of 108.8 mSv across imaging exams over

an average period of 35 months. This represents an average effective dose per year of 37.3 mSv. For reference, annual dose due to background radiation is ~3.1 mSv in the United States, [<https://www.nrc.gov/about-nrc/radiation/around-us/doses-daily-lives.html>] and the occupational limit established by the U.S. Nuclear Regulatory Commission for radiation workers is 50 mSv per year. [<https://www.nrc.gov/reading-rm/doc-collections/cfr/part020/part020-1201.html>] Effective dose is inherently a population-based metric that does not account for individual characteristics such as age or gender. It is useful for comparison purposes but is not intended for stochastic assessment of epidemiological risk from radiation-based medical imaging exams. [35,36] Sedations for MRI in children have also been associated with reduced cerebral blood flow and increased cerebral blood volume, [37] and repeated procedural sedation with general anesthesia may decrease neurocognitive outcomes in selected pediatric patients. [38] Another drawback of routine imaging is the detection of incidental findings that lead to unnecessary evaluations. [39] Finally cost is an important factor to consider given the high cost of health care, [39] therefore the potential benefits of surveillance must be balanced with the cost and risks of routine surveillance imaging. Mooney et al. reported that screening for asymptomatic pulmonary metastasis in patients with melanoma accounted for approximately 80% of the program costs. [40] Similarly, Meyers et al. reported that more than \$100,000 was spent on 20 patients to find only one recurrence that could not be detected or suspected by other means. [18] In our cohort, more than \$500,000 were spent on scans to detect recurrent or progressive disease in six patients. Of these six patients, we identified one patient (spitzoid melanoma) with asymptomatic disease in whom imaging detected metastatic disease; the remaining five patients had CM who either had clinically detected mass at time of recurrence (n=2) or wide spread disease at diagnosis (n=3).

Although our study has a unified imaging protocol for all patients, it has some limitations; the small sample size and the retrospective analysis. These finding should be investigated in a larger cohort of patients.

In conclusion, we report herein a comparison between imaging findings for spitzoid melanoma and CM in pediatric patients. Our results suggest that children and adolescents with spitzoid melanoma lacking *TERT* promoter alterations require minimal imaging at diagnosis and follow-up given their low-risk of recurrence and the high cost and potential risks associated with advanced imaging studies. Patients with CM and spitzoid with *TERT* promoter alteration should be imaged according to the adult guidelines.

ACKNOWLEDGEMENTS

This study was supported in part by Cancer Center Support CORE Grant P30 CA 21765 from the National Cancer Institute, and the American Lebanese Syrian Associated Charities (ALSAC).

Abbreviations:

MM	Malignant Melanoma
CT	Computed Tomography
PET/CT	Positron Emission Tomography/Computed Tomography

CTCAP	CT chest, abdomen, and pelvis
MRI	Magnetic Resonance Imaging
CM	Conventional Melanoma
TERT	Telomerase Reverse Transcriptase
NCCN	National Cancer Comprehensive Network
SLN	Sentinel Lymph Node
CGH	Comparative Genomic Hybridization
FISH	fluorescence in situ hybridization

REFERENCES

1. Campbell LB, Kreicher KL, Gittleman HR, et al. Melanoma Incidence in Children and Adolescents: Decreasing Trends in the United States. *J Pediatr* 2015;166(6):1505–1513. [PubMed: 25866386]
2. Lu C, Zhang J, Nagahawatte P, et al. The genomic landscape of childhood and adolescent melanoma. *J Invest Dermatol* 2015;135(3):816–823. [PubMed: 25268584]
3. Navid F, Herzog CE, Sandoval J, et al. Feasibility of Pegylated Interferon in Children and Young Adults With Resected High-Risk Melanoma. *Pediatr Blood Cancer* 2016;63(7):1207–1213. [PubMed: 27038395]
4. Lee S, Barnhill RL, Dummer R, et al. TERT Promoter Mutations Are Predictive of Aggressive Clinical Behavior in Patients with Spitzoid Melanocytic Neoplasms. *Scientific reports* 2015;5:11200. [PubMed: 26061100]
5. Brady SL, Mohaupt TH, Kaufman RA. A Comprehensive Risk Assessment Method for Pediatric Patients Undergoing Research Examinations Using Ionizing Radiation: How We Answered the Institutional Review Board. *AJR Am J Roentgenol* 2015;204(5):W510–518. [PubMed: 25905957]
6. Francken AB, Shaw HM, Accortt NA, et al. Detection of first relapse in cutaneous melanoma patients: implications for the formulation of evidence-based follow-up guidelines. *Ann Surg Oncol* 2007;14(6):1924–1933. [PubMed: 17357855]
7. Ferreres JR, Marcoval J, Fodge K, et al. The utility of ancillary tests in monitoring cutaneous melanoma patients to detect visceral metastasis. *J Eur Acad Dermatol Venereol* 2015;29(12):2493–2495. [PubMed: 25059751]
8. Leiter U, Buettner PG, Eigentler TK, et al. Is detection of melanoma metastasis during surveillance in an early phase of development associated with a survival benefit? *Melanoma Res* 2010;20(3): 240–246. [PubMed: 20216239]
9. Garbe C, Paul A, Kohler-Spath H, et al. Prospective evaluation of a follow-up schedule in cutaneous melanoma patients: recommendations for an effective follow-up strategy. *J Clin Oncol* 2003;21(3): 520–529. [PubMed: 12560444]
10. Kaste SC, Pappo AS, Jenkins JJ, 3rd, et al. Malignant melanoma in children: imaging spectrum. *Pediatr Radiol* 1996;26(11):800–805. [PubMed: 8929381]
11. Buzaid AC, Sandler AB, Mani S, et al. Role of computed tomography in the staging of primary melanoma. *J Clin Oncol* 1993;11(4):638–643. [PubMed: 8478659]
12. Gold JS, Jaques DP, Busam KJ, et al. Yield and predictors of radiologic studies for identifying distant metastases in melanoma patients with a positive sentinel lymph node biopsy. *Ann Surg Oncol* 2007;14(7):2133–2140. [PubMed: 17453294]
13. Aaron C. LE Tan, Lo Serigne, Victor Liu, Guminski Alexander David, Long Georgina V., Menzies Alexander M.. Utility of 1-year FDG-PET (PET) to determine outcomes from anti-PD-1 (PD1) based therapy in patients (pts) with metastatic melanoma (MM). 2018; Chicago, IL, USA.

14. Corey Rearick FD, Lin Yan, Rose Amy, Cindy Sander, Davis Michael, Benos Panayiotis V, Tawbi Hussein Abdul-Hassan, Tarhini Ahmad A., Kirkwood John M., Davar Diwakar. Surveillance for melanoma (MEL): Results of a database study of stage I-III MEL.; 2018; Chicago, IL, USA.
15. Xing Y, Bronstein Y, Ross MI, et al. Contemporary diagnostic imaging modalities for the staging and surveillance of melanoma patients: a meta-analysis. *J Natl Cancer Inst* 2011;103(2):129–142. [PubMed: 21081714]
16. Rodriguez Rivera AM, Alabbas H, Ramjaun A, et al. Value of positron emission tomography scan in stage III cutaneous melanoma: a systematic review and meta-analysis. *Surg Oncol* 2014;23(1): 11–16. [PubMed: 24556310]
17. Hafner J, Schmid MH, Kempf W, et al. Baseline staging in cutaneous malignant melanoma. *Br J Dermatol* 2004;150(4):677–686. [PubMed: 15099363]
18. Meyers MO, Yeh JJ, Frank J, et al. Method of detection of initial recurrence of stage II/III cutaneous melanoma: analysis of the utility of follow-up staging. *Ann Surg Oncol* 2009;16(4): 941–947. [PubMed: 19101766]
19. Francken AB, Bastiaannet E, Hoekstra HJ. Follow-up in patients with localised primary cutaneous melanoma. *Lancet Oncol* 2005;6(8):608–621. [PubMed: 16054572]
20. Saenz NC, Saenz-Badillos J, Busam K, et al. Childhood melanoma survival. *Cancer* 1999;85(3): 750–754. [PubMed: 10091749]
21. Romano E, Scordo M, Dusza SW, et al. Site and timing of first relapse in stage III melanoma patients: implications for follow-up guidelines. *J Clin Oncol* 2010;28(18):3042–3047. [PubMed: 20479405]
22. Paradelo S, Fonseca E, Pita-Fernandez S, et al. Spitzoid and non-spitzoid melanoma in children: a prognostic comparative study. *J Eur Acad Dermatol Venereol* 2013;27(10):1214–1221. [PubMed: 22928628]
23. Pol-Rodriguez M, Lee S, Silvers DN, et al. Influence of age on survival in childhood spitzoid melanomas. *Cancer* 2007;109(8):1579–1583. [PubMed: 17326059]
24. Zedek DC, McCalmont TH. Spitz nevi, atypical spitzoid neoplasms, and spitzoid melanoma. *Clin Lab Med* 2011;31(2):311–320. [PubMed: 21549244]
25. Moore-Olufemi S, Herzog C, Warneke C, et al. Outcomes in pediatric melanoma: comparing prepubertal to adolescent pediatric patients. *Ann Surg* 2011;253(6):1211–1215. [PubMed: 21451389]
26. Balch CM, Gershenwald JE, Soong SJ, et al. Final version of 2009 AJCC melanoma staging and classification. *J Clin Oncol* 2009;27(36):6199–6206.
27. Manola J, Atkins M, Ibrahim J, et al. Prognostic factors in metastatic melanoma: a pooled analysis of Eastern Cooperative Oncology Group trials. *J Clin Oncol* 2000;18(22):3782–3793. [PubMed: 11078491]
28. Furue M, Ito T, Wada N, et al. Melanoma and Immune Checkpoint Inhibitors. *Curr Oncol Rep* 2018;20(3):29. [PubMed: 29569208]
29. Dummer R, Ascierto PA, Gogas HJ, et al. Encorafenib plus binimetinib versus vemurafenib or encorafenib in patients with BRAF-mutant melanoma (COLUMBUS): a multicentre, open-label, randomised phase 3 trial. *Lancet Oncol* 2018.
30. Marconcini R, Spagnolo F, Stucci LS, et al. Current status and perspectives in immunotherapy for metastatic melanoma. *Oncotarget* 2018;9(15):12452–12470. [PubMed: 29552325]
31. Fazel R, Krumholz HM, Wang Y, et al. Exposure to low-dose ionizing radiation from medical imaging procedures. *N Engl J Med* 2009;361(9):849–857. [PubMed: 19710483]
32. Mathews JD, Forsythe AV, Brady Z, et al. Cancer risk in 680,000 people exposed to computed tomography scans in childhood or adolescence: data linkage study of 11 million Australians. *BMJ* 2013;346:f2360. [PubMed: 23694687]
33. Pearce MS, Salotti JA, Little MP, et al. Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study. *Lancet* 2012;380(9840):499–505. [PubMed: 22681860]
34. Linet MS, Kim KP, Rajaraman P. Children's exposure to diagnostic medical radiation and cancer risk: epidemiologic and dosimetric considerations. *Pediatr Radiol* 2009;39 Suppl 1:S4–26. [PubMed: 19083224]

35. Hendee WR, O'Connor MK. Radiation risks of medical imaging: separating fact from fantasy. *Radiology* 2012;264(2):312–321. [PubMed: 22821690]
36. Martin CJ. Effective dose: how should it be applied to medical exposures? *Br J Radiol* 2007;80(956):639–647. [PubMed: 17646189]
37. Harreld JH, Helton KJ, Kaddoum RN, et al. The effects of propofol on cerebral perfusion MRI in children. *Neuroradiology* 2013;55(8):1049–1056. [PubMed: 23673874]
38. Jacola LMAD, Hall L, White L, Russel K, Schreiber JE, Rossi M, Moore A, Gajjar A. The Relationship between Procedural Sedation during Treatment and Neurocognitive Outcomes in Survivors of Pediatric Medulloblastoma 2017; New Orleans, LA, USA p I–366.
39. Dunnick NR, Applegate KE, Arenson RL. The inappropriate use of imaging studies: a report of the 2004 Intersociety Conference. *J Am Coll Radiol* 2005;2(5):401–406. [PubMed: 17411843]
40. Mooney MM, Mettlin C, Michalek AM, et al. Life-long screening of patients with intermediate-thickness cutaneous melanoma for asymptomatic pulmonary recurrences: a cost-effectiveness analysis. *Cancer* 1997;80(6):1052–1064. [PubMed: 9305705]

Figure 1.
Schema of treatment, imaging, and strata based upon AJCC stage during and after therapy.

Figure 2.

5-year-old patient with diagnosis of spitzoid melanoma, primary site right leg above the knee with positive sentinel node right groin at diagnosis. Three years from diagnosis (A) coronal maximum intensity pixel (MIP), (B) fused and axial (C) fused PET-CT images demonstrate a metabolically active focus in the proximal right femur. Axial CT images (D) in bone windows shows a typical non-ossifying fibroma.

Figure 3.

17-year-old patient with incompletely excised conventional melanoma, primary of the back, underwent resection of primary site of disease as well as sentinel-node positive right axilla. PET-CT obtained 9 months after diagnosis revealed metabolically active right cervical lymph node as shown on coronal fused (A), coronal maximum intensity pixel (MIP, B) and axial fused (C) images.

TABLE 1

Patient Characteristics

Variable	Number
Age in years median (range)	14 (3.2–22.1)
Gender	
Male	10
Female	11
Histologic Type	
Spitzoid	11
Conventional melanoma	10
Race	
White	15
Black	2
Other	4
Primary site	
Head and neck	6
Trunk	7
Extremities	8
Stratum	
A	16
B1	2
B2	3
Status	
Alive	17
Dead of disease	4

TABLE 2

Characteristics of the suspicious scans and outcomes by melanoma histologic subtype

Variable		Spitzoid (No. of patients=11)	Conventional melanoma (No. of patients =10)
Images	Total	236	162
	PET/CT	86	61
	CT Chest/Abdomen/Pelvis	81	57
	CT Chest	11	8
	CT Brain	10	7
	MRI Brain	48	29
	Median cost/patient in USA dollars *	32,718	23,420
Suspicious scans number (%)		13 (5.8%)	20 (14%)
Follow-up of images			
	Stable	4	7
	Regressed	7	4
	Progressed	2	9
Biopsy	Relapse	1	4
	Benign	1	2
	No biopsy	11	14
Detection of relapse			
	Clinical	0	1
	Imaging	1	3
Status	NED	10	7
	DOD	1	3

* Excluding cost of anesthesia

Abbreviations: NED, no evidence of disease; DOD, dead of disease