



NUCLEAR MEDICINE FOR PRECISIONDIAGNOSIS OF MALIGNANT MELANOMA: A LITERATURE REVIEW

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ABSTRACT

Malignant melanoma (MM) is a rare skin cancer that is increasing constantly. It accounts for the most cause of death of all skin cancer. High accuracy in MM staging is crucial to give exact information about the prognosis and facilitate the use of the most effective therapy available. The gold standard for skin cancer diagnosis is tissue biopsy, therefore precisely detecting the primary tumor site is crucial. It has high risk of dissemination to regional lymph nodes and visceral organs. Lymph node involvement and distant metastasis are the key prognostic value of MM. Nuclear medicine has been used to detect various primary and metastatic cancer including skin cancer. The aim of this literature review is to discuss about the role of nuclear medicine specifically positron emission tomography (PET), single-photon emission tomography (SPECT), and planar gamma imaging for the diagnosis of MM. We gather literature searches and books related using combined keywords such as “gamma camera”, “SPECT”, “PET”, “malignant melanoma”, “histopathology”. The data we use are limited to 10 years of this review article. Nuclear medicine technique, such as lymphoscintigraphy using gamma camera or SPECT/CT is recommended for early stage of MM, while PET/CT is recommended and have high sensitivity for advance stage of MM and evaluating disease recurrence. Utilising nuclear medicine to aid in accurate diagnostic of MM will give opportunity of a better outcome.

Keywords: diagnostic; malignant melanoma; nuclear medicine, skin cancer

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INTRODUCTION

Malignant melanoma (MM) is a rare skin cancer present as brown/ black, or nonuniform macule or nodule. MM easily spread to vital organs such as the lungs, the liver, and the brain (Sundararajan *et al.*, 2024). Among fair skin population like North America, North Europe, Australia, New Zealand, the incident of MM rises 4-6% each year (Davis *et al.*, 2019). In Southeast Asia, estimation of MM incident is 2,354 person per year (Matthews *et al.*, 2017). In 2020, incident of MM in Indonesia is 1,609 person (*International Agency for Research on Cancer*, 2024). Mortality of MM varies, in early stage, the 5-year survival rate is 95-97% for stage IA and 90-92% for stage IB, but drastically lowered to 10-30% for stage IV, with survival of only 6 to 8 months (Bailey *et al.*, 2012; Delgado & Delgado, 2017; Tan & Dewi, 2015).

Malignant melanoma is divided into four clinical types (Figure 1). Superficial spreading melanoma (SSM) is the most common type especially at the age of 4 to 5 decades. Predilection in male is on the trunk, but in female is on the extremities. Another location is the head and neck. Clinically, this lesion is slightly protruding, brownish black, or reddish with irregular margin, skin line on the surface of the lesion is disappearing. The structure of the lesion can change due to part growth and regression, causing annular or nodules if

invasive. Another type is nodular melanoma (NM), this type seen mostly in 5 to 6 decades, male, on the head; neck; and trunk. Clinically appear as a protruding tumor, a dome-like brown or black tumor. It can grow as an invasive tumor from the beginning, causing ulcers and bleeding. Histopathologically, it appears as an atypical tumor invading the dermis. These tumor cells are uniform, big, and rounded spread in epidermis with variable thickness. These melanocytes can be found in cell nests that signify an invasive nature. Macrophage and dense lymphocyte can also be found in the dermis (Bailey *et al.*, 2012; Cipto & Suriadiredja, 2016).

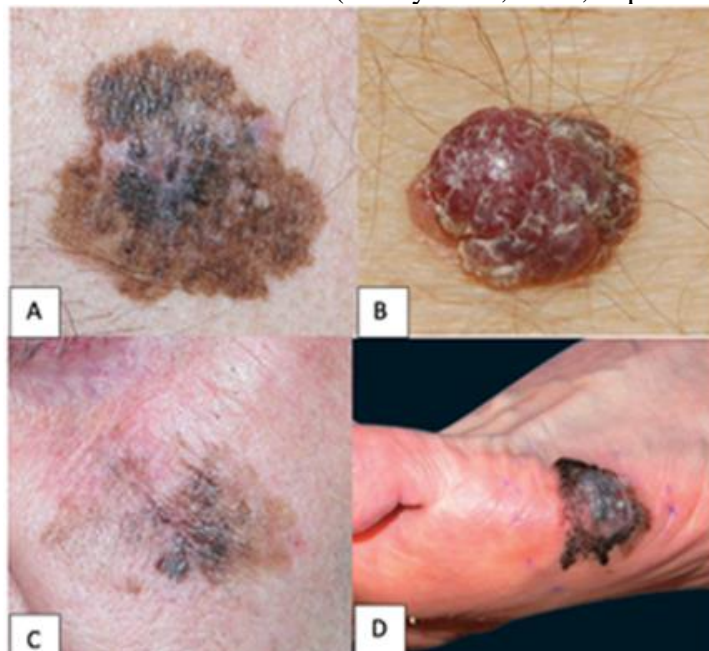


Figure 1. Malignant Melanoma Classification. **A.** Superficial spreading melanoma (SSM). **B.** Nodular melanoma (NM). **C.** Lentigo melanoma maligna (LMM). **D.** Acral lentiginous melanoma (ALM) (Bailey *et al.*, 2012).

The third MM type is lentigo malignant melanoma (LMM). It is mostly found in 6 to 7 decades, on the face, arms, and extremities. This melanoma mostly spreads to the lateral part of the body. The fourth type is acral lentiginous melanoma (ALM) which is predilected in foot sole and palm. Clinically appear as black maculae with protruding parts or nodes. Histopathologically appear as atypic tumor cell, usually solitary along dermo-epidermal acantholytic epidermis, and irregular (Bailey *et al.*, 2012; Cipto & Suriadiredja, 2016). Diagnosis of early MM based on acronym ABCD, stands for asymmetry of the lesion, irregular border, color of black, blueish, brown, reddish, and gray, diameter of 6 mm or more, may include elevation on the surface of the lesion (Bailey *et al.*, 2012; Cipto & Suriadiredja, 2016). The acronym also applied to seven diagnostic criteria of MM divided into major and minor criteria. Suspicion of MM should be considered if there is 1 major or 3 minor criteria. The major criteria are change in lesion size, irregular shape, and change in lesion color. The minor criteria are diameter of lesion more than 7mm, presence of inflammatory process, crusted or bleeding, change in sensation like itching (Isaac *et al.*, 2020; Tan & Dewi, 2015).

In terms of metastasis MM, the incidence of intermediate metastasis or metastasis that involve the non-regional lymphatic station ranges from 3.1% to 7.8% (Simonetti *et al.*, 2022). The conventional imaging such as CXR, as well as CT or MRI has low true-positive value and low specificity to detect distant metastases of MM ranging from 0% to 0.5% and 8% to 15% respectively (Bailey *et al.*, 2012). Imaging studies such as computed tomography (CT) scan and magnetic resonance imaging (MRI) clearly depicted spatial resolution and soft tissue contrast (Isaac *et al.*, 2020). Lymph node assessment with ultrasound also have low sensitivity of 24% (Simonetti *et al.*, 2022). Through conventional imaging, the ability to detect small

metastatic is very limited considering continuous size measurement of the tumor is decisive for tumor therapy evaluation (Candil *et al.*, 2012; Isaac *et al.*, 2020). Moreover, distant metastases can develop in 30% of patients with localized MM, therefore a routine and precise evaluation is needed (Scott *et al.*, 2022). Nuclear medicine, PET have a sensitivity ranged from 78% to 100% to detect metastatic lesions of MM up to 6 months earlier than conventional imaging (Candil *et al.*, 2012). The detection of sentinel lymph node by SPECT/CT is 89.6% and 50.4% by planar lymphoscintigraphy (Doepker *et al.*, 2017).

The use of nuclear in medicine today, especially in cancer, serves as diagnostic, therapy and evaluation, and prognostic value. With many radiotracers that can be utilized to detect MM aid in multiple targets of detecting MM using nuclear medicine (Wei *et al.*, 2018). On the other hand, a convenient gamma camera could aid in MM mapping in a real time manner (Judge *et al.*, 2023). Since the survival rate of MM decrease significantly as the stage is higher, it is important to acquire precise staging as a guide to best treatment method available. The aim of this literature review is to discuss about the role of nuclear medicine specifically positron emission tomography (PET), single-photon emission tomography (SPECT), and planar gamma imaging for the diagnosis of MM. This review consists of overview of nuclear medicine, a working principle of nuclear medicine, modalities of nuclear medicine, and potential accurate diagnostic approach for MM using nuclear medicine. The purpose of this review is to discuss the role of nuclear medicine specifically positron emission tomography (PET), single photon emission tomography (SPECT), and gamma planar imaging in diagnosing MM.

METHOD

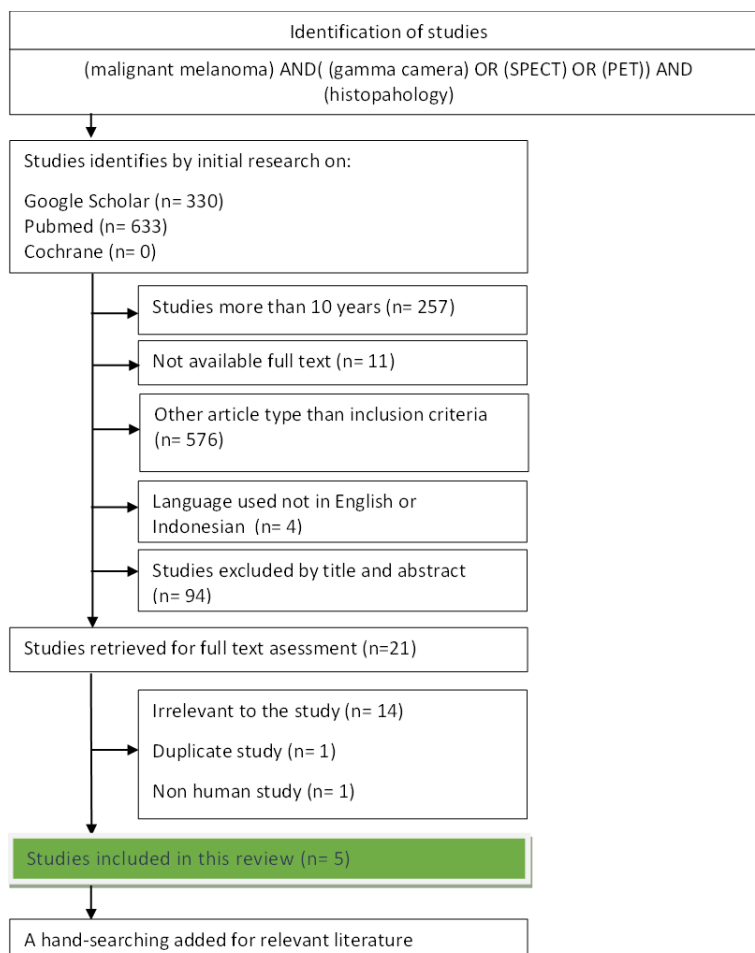


Figure 2. Flowchart of Literature Assessment

Data included in this paper are secondary data from previous researches and or text books that covered related topic. Resources used are limited to the past 10 years from 2014 to 2024. Resources are available in English and Indonesian language. List of keywords we use are according to PIO query. We use keywords such as: (1) Population: malignant melanoma; (2) Intervention: gamma camera, SPECT, PET; and (3) Outcome: histopathology. All keywords are separated with AND/OR. For journal database we use Google Scholar, Pubmed (pubmed.ncbi.nlm.nih.gov/) and Cochrane library (cochranelibrary.com). The inclusion criteria for this review were (1) studies that conduct nuclear medicine as diagnostic tool for MM, (2) studies that conducted within 10 years from 2014 to 2024, (3) article type including clinical trial, meta-analysis, randomized controlled trial, systematic review, (4) available full text. The exclusion criteria were (1) studies not in English or Indonesian, (2) abstracts, not available full text, (3) non-human study. The assessment we conducted are described in Figure 2. For the online article and books sources are included to explore more about the theoretical and epidemiological forms.

RESULT

Table 1.
Prognostic Value of Nuclear Medicine in Melanoma

Study	Study type	Type of melanoma	Nuclear medicine modality	Result
Forschner A, <i>et al.</i> (2017) N = 107	Prospective cohort	superficial melanoma, nodular melanoma, lentigo malignant melanoma, acral lentiginous melanoma, mucosal melanoma, other melanoma, stage I-IV	¹⁸ F-FDG-PET/CT	51% experiencing major change in treatment plan, 19% tumor free and 30% with previously unrecognized metastases
Collarino A, <i>et al.</i> (2023) N = 18	Retrospective	Valvular melanoma, Breslow thickness 1-4 mm, clinically negative node	Pre operative lymphatic mapping by planar imaging using ^{99m} Tc-nanocolloid	72.2% had negative SN with no groin recurrences and high survival rates. 27.8% had positive SN, some experiencing cancer-related deaths
Koskivuo I, <i>et al.</i> (2016) N= 110	Retrospective	Cutaneous melanoma stage IIB-IIC (Breslow thickness 2.2-15 mm) or IIIA-IIIB (Breslow thickness 0.5-13mm)	¹⁸ F-FDG-PET/CT each every 6 months for 5 consecutive years	41% recurrence detected at a median 19 months after negative PET/CT scan with 24% of it were detected at early stage of follow up, 45% was true negative, 14% was false positive
Rivera, <i>et al.</i> (2014) N = 623	Systematic review and meta analysis	Stage III melanoma	FGD-PET	89.42% sensitivity to detect systemic metastases and 88.78% specificity
Jeremiasse B, <i>et al.</i> (2023) N= 15	Clinical trial	Mixed of patient with melanoma, squamous cell carcinoma, and sarcoma	^{99m} -technetium nanocolloid (ICG-TC) and imaging with lymphoscintigraphy and SPECT-CT preoperatively. Fluorescence and gamma probe was used intraoperatively.	67% patient had transcutaneously visible lymph node, which 95% detected intraoperatively with fluorescent and 100% with radioactive. More lymph node were identified during operation using ICG-TC.

A total of 5 studies were included in this review. Collarino *et al.*, Forschner *et al.*, and Koskivuo *et al.* evaluate the value of nuclear medicine for melanoma survival (Collarino *et al.*, 2023; Forschner *et al.*, 2017; Koskivuo *et al.*, 2016). While Rivera *et al.* specifically study

about the utilization FDG-PET in MM (Rodriguez Rivera et al., 2014). Jeremiassé *et al.* discuss about the probe target used in nuclear medicine (Jeremiassé *et al.*, 2023). The management strategy of MM can greatly be different when using FDG-PET/CT over conventional CT. Changes including enlargement or reduction of the surgical field and changing to (1) systemic treatment or (2) systemic treatment and palliative surgery or (3) palliative surgery or (4) palliative radiotherapy or (5) isolated extremity perfusion. Survival of melanoma by utilizing nuclear medicine are described in Table 1.

DISCUSSION

Malignant Melanoma (MM)

Malignant melanoma is most common in whites especially those who highly exposed to sun, has blue or green eyes, blonde or red hair, has typical naevus for more than 100 in total, has atypical naevus, family history with MM, or mutation in p16. Age predilection varies based on MM type, with average diagnosed at age 52 years. Clinically in the early stage the lesion is flat, brownish, not shiny, and smooth. By the time, it became irregular, dark brown or black. In histopathology, the thinning epidermis shows proliferation of melanocyte like atypical spindle arranged half irregular, centralized in the middle. The dermis contains melanophage, lymphocyte, and actinic elastosis degeneration (Bailey *et al.*, 2012; Cipto & Suriadiredja, 2016). Amelanotic, desmoplastic, acral lentiginous, nodular, lentigo maligna, and superficial spreading are the subtypes of melanoma. The superficial spreading subtype is the most common in melanoma (70%) (Naik, 2021). Epidemiologically, there were 324,635 new cases of melanoma and 57,043 deaths from melanoma worldwide in 2020 (Dougherty et al., 2024).

Staging of MM helps clinicians to assess patient prognosis and best treatment regimen (Davis *et al.*, 2019). It is important to ensure accurate staging, moreover for advanced MM since higher stage of the disease possess higher risk of mortality (Cachin *et al.*, 2014). Furthermore, 30% of patient diagnosed as localized MM develop distant metastases (Scott *et al.*, 2022). Metastatic melanoma is difficult to treat, showing low cure and survival rates after surgical resection and radiation therapy. Cancer cells have unique molecular properties at the cellular level that allow them to evade apoptosis, as well as unlimited growth potential without the need for growth factors, angiogenesis, or metastasis (Naik, 2021). Nuclear imaging has high sensitivity in assessing deep soft tissue, lymph node, and visceral metastases (El-Shourbagy *et al.*, 2020; Paschali, 2015). A nuclear imaging technique, PET/CT is recommended to primarily assess patient at high risk of distant metastases, as well as detecting recurrent metastases (Paschali, 2015).

Nuclear medicine

Nuclear medicine is a technology of using intracellular contrast agent by injecting native form of radionuclides/radioactive agent as the tracer (1) to detect the process of specific disease as to picture the anatomic without disturbing vital biological processes, which can be captured as an image using special devices or modalities as a tool to aid in diagnosis, and/or (2) to label a corresponding radiopharmaceutical to aid in disease treatment (Khandani, 2020; Paschali, 2015). Other definition of nuclear medicine is a medical specialization that applied manmade radio nuclear for diagnostic, therapy, and biomedical research (Moerlein *et al.*, 2020).

The modality of nuclear medicine are positron emission tomography (PET), single-photon emission tomography (SPECT), and planar gamma imaging. PET and SPECT can detect various target such as small molecule-based probes targeting melanin, peptide-based targeting α -Melanocyte-stimulating hormone (α -MSH) and or targeting the integrin family, metabotropic glutamate 1 receptor, the very late antigen-4, indoleamine 2,3-dioxygenase,

immune checkpoints, human copper transporter 1, antibody-based, and CXCR4 (Wei *et al.*, 2018).

Radiotracer that is available for use in melanoma include ^{99m}Tc -sulfur colloid (particle size, 15-5000 nm), ^{99m}Tc -nanocolloid (5-100 nm), and ^{99m}Tc -antimony trisulfide, and ^{99m}Tc -tilmanocept being the most advantageous radiotracer. ^{99m}Tc -tilmanocept have rapid clearance, high SLN extraction and low distal node accumulation. Lymphatic mapping can also be done with hybrid tracer using fluorescent or blue dye using a near-infrared dye called indocyanine green (ICG) (Tardelli *et al.*, 2016). However blue dye has low detection rate with only 60% of SLN staining blue. ICG alone has shown a safe and accurate method for detection of SLN with sensitivity up to 97%. In pediatric, a ^{99m}Tc nanocolloid in combination with optional blue dye injection has been the standard of care. A study by Jeremiassé B, et al (2023) shows that ICG-TC is also helpful for visual guidance and no adverse event occurred in pediatric (Jeremiassé *et al.*, 2023). Utilizing fluorescent gives real time detection of SLN, however the fact that near-infrared dyes are invisible to human eye, a gamma camera is needed to aid in visualization. However, radioactive tracer is crucial in case of evaluating the head-neck region. In patients whom the number of the lymph node cannot be predicted correctly for example on the trunk, SLN excision using ^{99m}Tc radiocolloid followed by SPECT/CT remains the gold standard and could not be substituted by near-infrared dyes (Stoffels *et al.*, 2015).

Today, nuclear is mostly used for diagnostic, primarily guiding for cancer staging (Zanco *et al.*, 2019). PET evaluation has four main functions in oncology. First, for diagnosing cancer. Second, for staging, determine metastases. Third, to make certain the response for therapy, as well as recurrency. Four, specifically for sarcoma, is for detecting the most malignant part to guide a biopsy procedure, the help from imaging is needed in obscure tumor biopsy considering the gold standard of cancer diagnosis is tissue biopsy (Mannelli, 2019; Paschali, 2015).

One characteristic of cancer cells is unproportional glucose intake. Modification of aerobic metabolism and tendency to have low glucose-6-phosphate enzyme – for glucose phosphorylation to expel it from cell – makes the cell to have high ability to bind glucose. Cancer cells with the characteristic of excessive glucose utilizing is the foundation of using 2-[^{18}F]-fluoro-2-deoxy-D-glucose (FDG) as radiotracer in the positron emission tomography computed tomography (PET/CT) evaluation (Figure 3) (Moerlein *et al.*, 2020; Oriuchi *et al.*, 2020). Another radiotracer worth mention is benzamine and benzamine derivatives such as ^{123}I -BZA₂ with the ability to bind to melanin pigment which is even higher than ^{18}F -FDG, however it is still on phase III clinical study (Cachin *et al.*, 2014).

The latest imaging modality in nuclear medicine, PET can detect radio nuclear that radiates positron, for example fluorine-18, gallium-68, nitrogen –13, and rubidium-82. To detect cancer cells, mostly using fluorine-18. The use of only PET has its flaw of overestimation especially for structures that have low attenuation like the lungs. Therefore, created a new technology of hybrid PET and CT scan (PET/CT), where CT will minimize the overestimation of metabolic activity (Figure 4). Utilization of CT is done without contrast, usually done in seconds, while PET needs several minutes for each position. Whole body PET/CT imaging usually needs 20-25 minutes. Fusion PET/CT can give anatomic and metabolic information. The image of PET is colored on CT (“colored ghost”). In moving objects like thorax and abdomen, information of malignancy location can move, causing the interpretation of the area need to be more careful (Moerlein *et al.*, 2020).



Figure 3. PET-CT axial view of left lower extremity showing slightly hypodense lesion and proven as a metastatic lesion on biopsy (arrowhead) (Moerlein *et al.*, 2020).

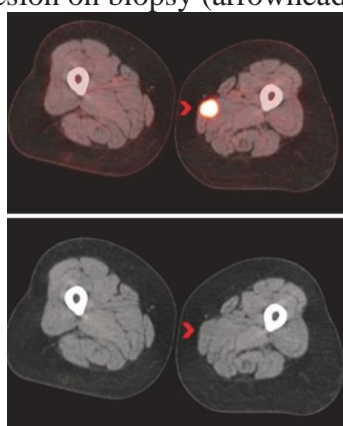


Figure 4. PET-CT axial view of left lower extremity showing slightly hypodense lesion and proven as a metastatic lesion on biopsy (arrowhead) (Moerlein *et al.*, 2020).

Application of Nuclear Medicine for the Diagnostic of Malignant Melanoma

Since MM is among the high FDG avidity lesions known, nuclear medicine have potential to help aid MM diagnosis (Perissinotti *et al.*, 2018). High accuracy in staging MM is very important in order to give exact information about the prognosis and facilitate the use of the most effective therapy available. Its frequent multifocality of metastases causes poor outcomes. Moreover, in the population of middle-aged and older men, low socioeconomic status and person with nodular type MM who are at high risk of advanced disease (Geller *et al.*, 2011). Melanoma can spread through lymphatic nodes, mainly regional and visceral organs (Davis *et al.*, 2019; Tan & Dewi, 2015). The thickest the MM, the higher the regional lymph node involvement (Delgado & Delgado, 2017). Evaluating tumor in sentinel lymph node is an important prognostic factor. Biopsy of the sentinel lymph node together with regional lymphadenectomy result in better melanoma-specific survival in patient with medium thickness melanoma dan sentinel node lymph tumor (Moerlein *et al.*, 2020; Perissinotti *et al.*, 2018).

Sentinel lymph node biopsy is the standard of care of nodal staging in the early stage. The MM skin lesion with thickness of 1-4 mm and more than 4mm pose risk of 8-30% and 40% lymph node metastases respectively. In MM with <0.75mm thickness, the risk of metastases is only 1%, and sentinel lymph node biopsy is not regularly performed. It is otherwise considerable if there is significant uncertainty about the adequacy of microstaging, such as ulceration, high mitotic rate, and lymphovascular invasion. False negative percentage of sentinel node biopsy is around 0-38% and the mean false negative percentage is 12.5%, varies

from 0% in the extremities and 34% in the complex region like the head and neck. Nuclear medicine is needed to present cancer cell mapping of the patient body. Study conducted by Collarino A, *et al.*, showed SPECT/CT result in higher detection of SN than planar imaging, however it is not statistically significant ($p= 0.317$) (Collarino *et al.*, 2023). In cases where sentinel lymph node biopsy is less likely and evacuation of sentinel node is failed, routine evaluation with lymphoscintigraphy is indicated because it provides more precise location of the lymph node biopsy better than FDG-PET/CT (Paschali, 2015; Perissinotti *et al.*, 2018).

Lymphatic mapping can also be done with radioactive tracer with gamma camera using ^{99m}Tc -colloids or ^{99m}Tc -tilmanocept (Perissinotti *et al.*, 2018). The use of near-infrared fluorescent agent dye has several shortages, such as the need of deemed environment for visualization, limited tissue penetration and easily diluted (El-Shourbagy *et al.*, 2020; Khandani, 2020; Wei *et al.*, 2018). Gamma cameras are available as handheld gamma camera or portable gamma camera (van den Berg *et al.*, 2016). Identification of sentinel lymph node in the complex anatomical area (pelvis, head/neck) is better done with hybrid evaluation using radioactive/fluorescent. Hybrid imaging detects nuclear activity and fluorescent (combination of ICG- ^{99m}Tc -Nanocoll), radioactive tracer helps clearer visualization due to the limited penetration of fluorescent (Perissinotti *et al.*, 2018).

If the sentinel node is located near the tracer injection site or deeper, then SPECT/CT can be utilized. This imaging has better sensitivity than gamma camera (Perissinotti *et al.*, 2018). Furthermore, preoperative and intraoperative SPECT/CT have higher detection rates of the sentinel node(s) (Tardelli *et al.*, 2016). The latest radio nuclear technique using PET has higher sensitivity than SPECT due to unrestricted by lead (Stoffels *et al.*, 2015). The indication to use PET is to detect the regional or distal metastases in the initial diagnostic, for surveillance purpose of the high risk of metastases patient, determine target lesion in patient with risk of relapse, and evaluate the therapy response (Zanco *et al.*, 2019). Hybrid PET/CT (Figure 4) is better in represent a three dimensional mapping for resection of patient with oligometastases as well as evaluate therapy response (Perissinotti *et al.*, 2018). Utilizing FDG PET to detect lymph node metastases is dependent on lymph node size. A volume of 78 mm^3 or more ensures a high specificity which can reach up to 97%. Even so, the sensitivity is low in the early stage of MM and hence it is not recommended in asymptomatic patients with stage I and II melanoma (Candil *et al.*, 2012). Study conducted by Rivera A, *et al* showed that FDG-PET overall sensitivity of 89.42% and specificity 88.78% (Rodriguez Rivera *et al.*, 2014). In addition to sentinel lymph node mapping by ^{99m}Tc -nanocolloid, ICG-TC can be considered as a modality for pediatric patients (Jeremiassé *et al.*, 2023).

Nuclear medicine work principle is using radionuclide as a tracer that can be read as an image using specific tool/techniques, such as gamma camera, SPECT/CT, or PET/CT. It can be utilized to detect cancer cells and its metastases. Malignant melanoma is a rare skin disease but increasing in its prevalence throughout each year (Davis *et al.*, 2019). It is important to perform accurate staging due to significant increase in mortality in advanced stage of MM (Scott *et al.*, 2022). It is important to perform a precise sentinel node biopsy because it determines the prognostic of MM. A sentinel node biopsy followed by regional lymphadenectomy result in better melanoma-specific survival (Moerlein *et al.*, 2020; Perissinotti *et al.*, 2018). A nuclear medicine technique such as lymphoscintigraphy using gamma camera or SPECT/CT is recommended for early stage (stage I-II) (Paschali, 2015; Perissinotti *et al.*, 2018). The use of SPECT/CT over gamma camera provide better sensitivity when the sentinel node is located near the tracer injection site or deeper (Perissinotti *et al.*, 2018). Since ^{18}F -FDG PET/CT cannot detect micro metastasis, it is not recommended for the early stage of the disease. However, in MM stage I-II with intermediate/high-risk lesions

(thickness of more than equal to 1 mm) or high-risk (thickness of >4mm), 18F-FDG PET/CT have a potential role to aid the assessment of MM. A 18F-FDG PET/CT is more accurate and have high sensitivity for staging advanced MM (stage III-IV) (Zanco *et al.*, 2019). The application of 18F-FDG PET/CT is based on one characteristic of cancer cells, that is excessive glucose utilization, which MM is one of the cancers with high avidity to FDG.

Nuclear medicine can shift management plan of MM patient (Forschner *et al.*, 2017; Trinh *et al.*, 2018). This changes may result from additional or more complete finding of the sentinel node. However, potential changes in disease diagnostic approach due to detailed image of MM visualized by nuclear medicine are at an increased risk of cancellation of sentinel node biopsy, which could have a negative impact on lapse-survival (Trinh *et al.*, 2018). The development of novel radiolabeled tracers to detect malignancy, guide therapy, and identify the cellular microenvironment is ongoing. Many tracers are being studied in various stages of preclinical and clinical development. One of them is melanin imaging, which is highly specific for melanoma patients. 18F labeling of benzamide derivatives such as 5-FPN (18F-5-fluoro-N-[2-(diethylamino)ethyl]picolinamide) and MEL050 (18F-6-fluoro-N-[2-(diethylamino)ethyl]pyridine-3-carboxamide) has shown superior *in vivo* imaging performance to 18F-FDG (Dougherty *et al.*, 2024).

CONCLUSION

Malignant melanoma is a rare but deadly skin cancer in advanced stage. Early and precise diagnosis are important in managing MM leading to higher survival rate. Nuclear medicine takes a role in accurately mapping MM metastases for assuring the most accurate diagnosis. Lymphoscintigraphy using gamma camera or SPECT/CT is recommended for early stage of MM, while PET/CT is recommended and have high sensitivity for advance stage of MM and evaluating disease recurrence. Sentinel lymphatic node biopsy followed by resection of regional lymphatic node results in better prognosis.

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